Burkholderia incident in Belgian hospitals

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*Picture*: Daniel Stevens, University hospital, Brussels.
The incident

2/2/2014: Hospital-C, Walloon Brabant
- 2 patients infected with *B. cepacia* (endo-tracheal aspirate),
- hospitalized in IC-ward,
- 1 strain available for analysis by NRC

6/12/2013: Hospital-B, Hainaut
- 2 patients infected with *B. cepacia* (urine, bronchial aspirate),
- hospitalized in IC-ward,
- 1 strain available for analysis by NRC

Soap not sampled

End of November 2013: Hospital-A, Liège
- 30/09/2013 - 2/12/2013
- **14 patients** infected/colonized with *Burkholderia cepacia*
- hospitalized in several intensive care wards
- **43 B. cepacia positive samples:**
  - 26 respiratory (9 patients),
  - 8 blood cultures (3 patients),
  - 9 urinary (4 patients)
- 7 strains available for analysis by the National Reference Center (NRC)

Microbiology lab. & Hospital Hygiene team: outbreak investigation: case listing, review of the literature, environmental sampling...

*B. cepacia* confirmed in the same liquid soap
The liquid soap
Dermalex® hospital derma lotion (batch no. 713-0909)

- surface-active components, no disinfectants
- for hand hygiene of healthcare workers and for corporal hygiene of patients

Since August 27, 2013, the contaminated batch was delivered in 37 hospital sites (10,945 beds) in Belgium.

- **Flanders region:** 13 hospitals (3,485 beds)
- **Brussels region:** 13 hospitals (3,378 beds) including 2 expertise units for cystic fibrosis (CF)
- **Walloon region:** 11 hospitals (4,082 beds)

- The company was informed about the incident (3/12/2013)
- An independent laboratory analyzed the batch and confirmed the presence of *Burkholderia cepacia* (5/12/2013)
- The company recalled the soap (6/12/2013)
**Burkholderia**

**Family**  *Burkholderiaceae*

**Genus**  *Burkholderia*: Gram-negative, aerobic, non-fermenting, motile bacillus, colonize a large variety of ecological niches (water, soil, fruits, vegetables)

**Species**  many different *Burkholderia* species,

  - some species are able to break down toxic compounds, pesticides, herbicides and polychlorinated biphenyls (PCBs),...
  - some are **pathogenic** for:

    **Plants:**  *B. cepacia* = onions (onion rot), garlic, tobacco,

    **Animals:**  *B. mallei* = glanders in horses, donkeys,

    **Humans:**  *B. pseudomallei* = melioidosis or Whitmore’s disease (endemic in Southeast Asia & Northern Australia)

  *B. mallei* & *B. pseudomallei*: **potential biological warfare agents** (level-3)

  - *Burkholderia cepacia complex (Bcc)* = group of 18 species:  *B. cepacia*, *B. cenocepacia*, *B. lata*, *B. multivorans*, *B. pseudomultivorans*, *B. contaminans*, *B. diffusa*, *B. dolosa*, ...
**Burkholderia cepacia**

- Formerly: *Pseudomonas cepacia*
- Cause rarely infections in the healthy host

- **Opportunistic pathogen:** hospitalized patients, weakened immune system, chronic pulmonary diseases (respiratory & urinary infections, bacteremia, arthritis, peritonitis,...)

- Major **nosocomial pathogen:** *life-threatening* among patients with cystic fibrosis, chronic granulomatous disease, sickle cell anaemia. Contamination among CF-patients can lead to severe *‘Cepacia syndrome’* = fatal necrotizing pneumonia and septicemia among CF-patients.

  Belgian CF-Register, 2011: annual prevalence of Bcc among CF-patients = 3.6%

- High **intrinsic multi-resistance**, infections difficult to treat, formation of biofilms

- **Identification on species level** difficult in the routine microbiology laboratory

- *Burkholderia* can *survive (long time) and multiply in aqueous hospital environments*, transmission from contaminated liquids and surfaces, colonized staff (hands) and person-to-person spread.
Epidemiological & microbiological investigation
(16/12/2013)

**Aims:**
1- register all *Burkholderia spp* isolated in acute care hospitals > 27/8/2013
2- estimate the incidence of *Burkholderia* among hospitalized, non-CF patients in exposed and in non-exposed hospitals.

**Case definition:**

**Confirmed case:**
- hospitalized patient colonized/infected with *B. cepacia, MLST-type ST848* (confirmed by the NRC) isolated from clinical/screening sample > 27/8/2013

**Probable/possible case:**
- hospitalized patient colonized/infected with *Burkholderia spp.* from clinical/screening samples > 27/8/2013

**Conditions:** no (known) antecedents of previous *Burkholderia* carriage/infection strain not available for identification/confirmation by NRC current or previous hospitalization in an exposed hospital.
Methods:

- Hospital questionnaire: calculation of Bcc incidence in exposed/non-exposed hospitals

- Patient questionnaire: for each patient with *Burkholderia* positive clinical or screening sample > 27/8

- Hospitals with cases (> 27/8) sent the available strains to the NRC for analysis:
  - culture on agar plate, MALDI-TOF mass spectrometry,
  - randomly amplified polymorphic DNA typing (RAPD-typing) of Bcc strains,
  - multilocus sequence typing analysis (MLST-typing)
Results

General hospitals in Belgium (n=106):
- Hospital sites: 195
- Hospital beds: 52,599

Participation:
- 136 hospital sites (n=38,220 beds)
=70% of all Belgian hospital sites

No participation:
- 59 hospital sites (n=14,379 beds)
- 59 non-exposed sites

Incidence of Burkholderia*:
- 0.19 cases/10,000 HD

Exposed hospital sites:
- 37 sites (n=10,945 beds)

Burkholderia spp isolated
- 14/37 hospital sites (38%)
- 31 patients
  (11 strains available, clin. samples)

Not-related:
Other species, MLST-type:
- 3 patients:
  B. cepacia, ST840
  B. cenocepacia IIIb, ST854
  B. cenocepacia IIIb, ST864

Burkholderia cepacia with confirmed link
(MLST-type ST848):
- 8 patients
  - Hospital A, B, C
  - All ICU-patients,
  - 3 patients died

Non-exposed hospital sites:
- 99 sites (n=27,275 beds)

Burkholderia spp isolated
- 35/99 hospital sites (35%)
- 29 patients
  (11 strains available, clin. samples)

Not related:
Other species, MLST-type: 11 patients:
- B. cenocepacia IIa, ST32 (n=1)
- B. cenocepacia IIa, ST217 (n=2)
- B. contaminans, ST482 (n=1)
- B. multivorans (n=6) ST25, ST615, ST742, ST749, ST751, ST819
- B. gladioli (n=1)

* Incidence: CF patients excluded
Epidemic curve for non-cystic fibrosis patients with clinical *Burkholderia* samples in exposed hospitals (> 27/08/2013)

- **Soap delivered**
- **Soap recalled**
- **Investigation**
- **Horizontal transmission**
- **Unexplained case**

**Colors and strains:**
- **Yellow:** *B. cepacia*, ST848
- **Green:** *Burkholderia*, other species and MLST-type
- **Blue:** *Burkholderia* strain not available for analysis

**Timeline:**
- September 2013
- October
- November
- December
- January 2014
- February

**Cases:**
- W-35
- W-36
- W-37
- W-38
- W-39
- W-40
- W-41
- W-42
- W-43
- W-44
- W-45
- W-46
- W-47
- W-48
- W-49
- W-50
- W-51
- W-52
- W-1
- W-2
- W-3
- W-4
- W-5
- W-6
- W-7
Discussion

- *B. cepacia* is a **frequent colonizer** of aqueous solutions, antiseptics, disinfectants and devices used in the hospital.

- Liquids can be contaminated ‘intrinsically’ or ‘extrinsically’.

- ‘**Outbreaks**’ and ‘**pseudo-outbreaks**’ are reported in ICU-units, oncology units, hemodialysis.

*Examples*

- mouthwash,
- nasal spray,
- sublingual probes,
- paracetamol,
- benzalkonium chloride antiseptic wipes,
- antiseptics (povidone-iodine, chlorhexidine),
- diapers,
- soap and lotions,
- solutions for inhalation, irrigation, intravenous use (anaesthetic Fentanyl, 1977)
- ... more recently, a deodorant (the Netherlands: Sept. 2014),
- local anaesthetic eye drops (Nov. 2014)
**Discussion**

**batch no. 713-0909:**
- ‘Intrinsic contamination’ in the conservation tank preceding conditioning.
- Applied methods for identification of *Burkholderia* were inappropriate (ISO 21149, cosmetics)
  - Cosmetics should not contain pathogens, some products need additional tests.
- The first conditioned products of the batch showed no contamination, the majority of the remaining batch was contaminated (prolonged time allowing bacterial growth).

*Sutton, S. and Jimenez, L.* (http://www.americanpharmaceuticalreview.com/Featured-Articles/)

*B. cepacia* alone is cited in **34%** of the non-sterile recalls from the years 2004-2011.

*A Review of Reported Recalls Involving Microbiological Control 2004-2011 with Emphasis on FDA Considerations of “Objectionable Organisms”*

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[Image]
Conclusions

- 70% of all Belgian hospital sites participated (including all exposed hospitals).
- A comparable % of exposed and non-exposed hospital sites had *Burholderia* cases during the critical period (> August 27),
- The incidence of *Burkholderia* cases was higher in exposed hospitals compared to non-exposed hospitals: 0.19 cases/10,000 HD versus 0.08 cases/10,000 HD.
- Because of the long delay (15 weeks) between delivery and recall of the contaminated soap, only few *Burkholderia* strains were available for analysis by the NRC:
  - 11 strains from exposed hospitals: among them 8 with the same *Burkholderia* species and MLST-type as the contaminated soap = *Burkholderia cepacia*, ST848,
  - 11 strains from non-exposed hospitals: all with a different *Burkholderia spp.* and MLST-type than the contaminated soap.
Conclusions

- At least 3 exposed hospitals had to deal with *Burkholderia cepacia* attributable to the use of the contaminated soap.

- This is probably an underestimation (lack of strains available for NRC confirmation).

- In exposed hospitals, among 29 non-CF patients with *Burkholderia* isolated > August 27:
  - 8 cases were confirmed cases: same species and MLST-type as contaminated soap,
  - 18 cases were possibly related (but sample no longer available),
  - 3 cases were not related (other species, MLST-type).

- No data available on storage and use of the contaminated soap in the exposed hospitals.
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