A large common point source nosocomial outbreak caused by ESBL-producing *Enterobacter cloacae* at one Belgian university hospital


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5 Cardiothoracic surgery Dept., CHU UCL Namur, 5530 Yvoir, Belgium CHU Dinant-Godinne UCL Namur, 5530 Yvoir, Belgium
• **University hospital**
  - 3 hospitalization sites (St Elisabeth Namur, Mont-Godinne, Dinant)
  - Bed Size: 946 beds (4300 Employees, 600 MDs)
  - Population of 450,000 inh. (Province of Namur)
  - 42,000 patients adm.; 500,000 polyclinic visits, 120,000 day care visits/year

• **Full medical coverage + specialized poles of activity**
  - onco-hematology, (autogenic/allogenic HSCT),
  - 400-500 cardiac surgery interventions /year
  - Cardiothoracic surgery: 30 lung transplant recipient/year
First episodes of clustered infections caused by ESBL-producing E. cloacae (I)

- **Alert triggered on Nov. 26th 2015**: post-operative infections by ESBL-producing *E. cloacae* in 4 cardiac surgery patients hospitalized in ICU at the time of microbiological sampling/result

- **Visit of ICUs** for observation of routine clinical practices

- **Reinforcement** of hand hygiene and infection control measures

- **Revision of care policies** (inhalation therapy, respiratory procedures, cleaning/disinfection practice of materials/equipment and environment)
Occurrence of the first clustered cases of ESBL-positive *E. cloacae* infections in ICU patients (Nov. 2015)

Patients 1 & 2 transferred from the same hospital; no screening specimens obtained upon admission

<table>
<thead>
<tr>
<th>Patient number</th>
<th>Age (yrs)</th>
<th>Date of Admission</th>
<th>Date of Intervention</th>
<th>Date of first isolation</th>
<th>Anatomical site</th>
<th>Infection</th>
<th>Clinical outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>P1</td>
<td>84</td>
<td>8/11/2015</td>
<td>9/11/2015</td>
<td>12/11/2015</td>
<td>Blood, ETA*</td>
<td>Sepsis, Pneumonia</td>
<td>Died (day 4)</td>
</tr>
<tr>
<td>P2</td>
<td>64</td>
<td>5/11/2015</td>
<td>10/11/2015</td>
<td>16/11/2015</td>
<td>Sternum, ETA</td>
<td>Sternitis, wound abscess</td>
<td>Chronic morbidity</td>
</tr>
</tbody>
</table>

*ETA= Endotracheal aspirates
Four patients in two different ICU units (ICU A and ICU B)
Monthly incidence of 3\textsuperscript{rd} Gen ceph-resistant \textit{Enterobacter cloacae} isolates detected in hospitalized patients (Mont-Godinne-2015)

### Nr isolates (1/patient)

<table>
<thead>
<tr>
<th>Month</th>
<th>E. cloacae (all)</th>
<th>E. cloacae C3G-R (AmpC)</th>
<th>E. cloacae C3G-R (ESBL+)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jan-15</td>
<td>20</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Feb-15</td>
<td>15</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Mar-15</td>
<td>15</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Apr-15</td>
<td>25</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>May-15</td>
<td>20</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Jun-15</td>
<td>30</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Jul-15</td>
<td>25</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Aug-15</td>
<td>20</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Sept-15</td>
<td>15</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Oct-15</td>
<td>20</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Nov-15</td>
<td>15</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Dec-15</td>
<td>20</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

**Jan-Oct-15:** 4/18 ESBL +
**Nov-Dec-15:** 20/24 ESBL +
First episode of clustered infections caused by ESBL-producing *E. cloacae* (II)

- **Progression of the outbreak** despite reinforced infection control measures (new carriers identified in several wards)
- **Intensification of surveillance cultures** (3x/week; collection of respiratory samples for all CS patients in ICU)
- **Cohorted nursing** with additional designed personnel
- **Repeated visits** to ICU and to OR (12/2015)
  - Observation of routine care practice
  - Microbiological sampling of the environment
  - Revision of selected procedures with altered standard practice (intubation/extubation, respiratory support care)
  - Reinforced cleaning disinfection of environment
- **Stop of lung transplantation programme** (10/12/2015)
- **Closure of CS hospitalization unit** to new admissions and **stop of all cardiac surgical activities** (during 2 weeks)

*Situation considered under control by Jan. 15, 2016*
Second epidemic wave of ESBL-producing *E. cloacae* (May-Sept. 2016)

Three infected CS patients
(sternitis (n=2), Pneumonia (n=1))

Rectal swab surveillance culture 3x/week
In CS unit and ICU until Wk 29
From Wk 30: Oropharyngeal swab surveillance culture before and after surgery / upon return in ICU

Rectal swab
Oro-pharyngeal asp
LRT aspirate
Surgical wound
Deep-seated infection

Wk18  Wk19  Wk20  Wk21  Wk22  Wk23  Wk24  Wk25  Wk26  Wk27  Wk28  Wk29  Wk30  Wk31  Wk32  Wk33  Wk34  Wk35  Wk36  Wk37  Wk38

5 cases of pneumonia
(3 in CS patients)

Attack rate: 50% (June-July 2016)
Microbiological investigations

- Typing of ESBL-producing *E. cloacae* isolates

**Single cluster** of *E. cloacae* (17/20 strains) associated with single Rep-PCR type (DL type 11)

**Similar antibioresistance type:**
(C3-G: I/R, Genta- Tobra-R, Cipro-I, SXT-R)
Carbapenem-S

**Genotyping of resistance:**

- $bla_{CTX-M-15}$ (+ $bla_{TEM-1}$)
- Aminoglycoside: $aacC2$
- Fluoroquinolones: $aac-6’-Ib-cr$, $qnrB$

-> **Clonal outbreak**
MLST type= **ST190** (not very prevalent/widespread clone)

Dendrogram of the isolates

Same isolate in both periods (phase I and II)
Case definition

- ESBL-producing *E. cloacae* in a respiratory sample of patients hospitalization in the ICU (period Nov-Dec. 2015)

- ESBL-producing *E. cloacae* (C3rdG, Genta-R, Cipro-I) in cardiac surgery patient (whatever the hospitalization unit) in any type of culture specimens (clinical specimens or surveillance culture) (period Jan.-Sept. 2016)

- Patients categorized as colonized or infected according to CDC definitions on the basis of retrospective review of medical records
Timing of colonisation by ESBL-producing *E. cloacae* from cardiac surgery intervention

- **According to patient status:**
  - Infected: mean: 1,4d; median: 2 d
  - Colonized: mean: 6,5d; median: 4 d

- **According to sampling site:**
  - Rectal swab: mean: 5,6 d; median 5 d  *(2 negative rectal swab results before becoming positive)* (low inoculum, oral -> bowel, antimicrobial prophylaxis)
  - Respiratory tract: mean: 1,4 d; median 1 d  *(several patient with positive RT and negative rectal swab culture results)*

Implementation of screening in the OR immediately after intervention *(at time of retransfer to ICU)*

New hypothesis in favor of early point source acquisition in the OR (rather than cross-transmission in ICU or in CS ward)
Case-control study assessing risk factors for carriage of ESBL-producing *E. cloacae*

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Case patients (n=26)</th>
<th>Control (n=49)</th>
<th>OR</th>
<th>CI95%</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, Mean years</td>
<td>63.8</td>
<td>64.4</td>
<td></td>
<td></td>
<td>.98</td>
</tr>
<tr>
<td>Male</td>
<td>20 (77)</td>
<td>38 (78)</td>
<td></td>
<td></td>
<td>.95</td>
</tr>
<tr>
<td>Previous history of stay to the ICU</td>
<td>25 (96)</td>
<td>44 (89)</td>
<td>2.8</td>
<td>0.3-23.6</td>
<td>.33</td>
</tr>
<tr>
<td>Duration of ICU stay &gt; 7 days</td>
<td>4 (15)</td>
<td>13 (27)</td>
<td>0.5</td>
<td>0.1-1.7</td>
<td>.27</td>
</tr>
<tr>
<td>Inhalation therapy/kinesitherapy</td>
<td>21 (81)</td>
<td>41 (84)</td>
<td>0.8</td>
<td>0.2-2.8</td>
<td>.75</td>
</tr>
<tr>
<td>Exposure to intubation</td>
<td>22 (85)</td>
<td>42 (86)</td>
<td>1.1</td>
<td>0.3-4.0</td>
<td>.89</td>
</tr>
<tr>
<td>Exposure to any type of surgery</td>
<td>25 (96)</td>
<td>39 (80)</td>
<td>6.4</td>
<td>1.0-42.3</td>
<td>.054</td>
</tr>
<tr>
<td>Exposure to cardiac surgery</td>
<td>24 (92)</td>
<td>7 (14)</td>
<td>72</td>
<td>19.9-259.9</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Exposure to TOE during surgery</td>
<td>24 (92)</td>
<td>6 (12)</td>
<td>89</td>
<td>23.5-314.4</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Rectal probe for temperature monitoring during surgery</td>
<td>22 (85)</td>
<td>14 (29)</td>
<td>14</td>
<td>4.5-41.8</td>
<td>&lt;.0001</td>
</tr>
</tbody>
</table>

Cardiac surgery: case patients had more complex and longer interventions
- valvular prosthesis surgery (n=14);
- Thoracic surgery (n=3; 2 bi-pulmonary transplantation),
- Coronar artery by-pass graft ing CABG (n=7)

Univariate conditional logistic regression analysis for the calculation of risk factors
tailed test of significance; P value <.05 considered statistically significant
Numerous breaks in procedures related TEE in the OR during cardiac surgery

Lack of appropriate maintenance/cleaning of the ultrasonographic instruments dedicated for cardiac surgery (blood stains/spots,...)

Inappropriate procedure of cleaning/disinfection of TEE probe (≠ high level disinfection)

Sterile lubrication gel K-Y monodose (5g) not always traced as single use

No use of protective sheath of the TEE probe during intervention, proximity contact of the probe with heater-cooler reservoir

Suboptimal storage conditions
Multiple sampling of environment and equipment/material in Cardiac surgery OR

7 days swab and enrichment culture on Letheen (lecithin/polysorbate) broth and on McConkey agar + ceftazidime (2 µg/ml)

>50 samples obtained: None were culture-positive for *Enterobacter cloacae*

All swab samples from TTE equipment: culture-negative

- Computers, keyboards, pads,....
- Artificial respirator circuit and intubation equipment set, heat exchanger CEC equipment
- Water, Solution, Liquids (cardioplegia solutions, antiseptic solutions, local anesthetics, sterile gel for TEE probe, ....)
- Tip/connector of thermal probes (rectal, esophageal, vesical)
- Transesophageal echocardiographic (TOE) equipment ((transducer tip, shaft, handle, socket,....)
# Report of Cardiac Surgery Nosocomial Outbreaks Associated with Transesophageal Echocardiography

<table>
<thead>
<tr>
<th>Author (year)</th>
<th>Country</th>
<th>Organism</th>
<th>Nr of affected patients</th>
<th>Duration of outbreak</th>
<th>Causal Link</th>
</tr>
</thead>
<tbody>
<tr>
<td>Levy (2003)</td>
<td>France</td>
<td><em>Legionella pneumophila</em></td>
<td>3</td>
<td>NR</td>
<td>Probable; contamination of TEE rinsing water</td>
</tr>
<tr>
<td>Kanemitsu (2004)</td>
<td>Japan</td>
<td><em>E. cloacae</em></td>
<td>17</td>
<td>2 months</td>
<td>Proven; TEE probe contamination</td>
</tr>
<tr>
<td>Bancroft (2006)</td>
<td>USA</td>
<td><em>E. coli</em></td>
<td>8</td>
<td>1 month</td>
<td>Unproven; TEE probe contamination</td>
</tr>
<tr>
<td>CDC MMWR (2011)</td>
<td>USA</td>
<td><em>P. aeruginosa</em></td>
<td>16</td>
<td>2 months</td>
<td>Proven; multidose ultrasound gel contamination</td>
</tr>
<tr>
<td>Vetter (2012)</td>
<td>Switzerland</td>
<td><em>S. marcescens</em></td>
<td>91</td>
<td>12 months</td>
<td>Proven; TEE probe contamination</td>
</tr>
<tr>
<td>Suleyman (2015)</td>
<td>USA</td>
<td><em>ESBL+ Salmonella enterica serov. Isangi</em></td>
<td>19</td>
<td>2 months</td>
<td>Probable; TEE probe contamination</td>
</tr>
</tbody>
</table>

OUTBREAK DATABASE ([https://www.outbreak-database.com](https://www.outbreak-database.com))
« Disconnect the socket » strategy

- **Repeated negative microbiological culture** of TEE probe specimens (12 swab samples/obtained at different time intervals)

- **Lack of visual (macroscopic) defects** of the TEE probe tip
  (Presence of microscopic surface scratches/defects of the probe tip possible/probable but not investigated...)

- **Decision to remove the 3D TEE probe** taken on Aug 8th, 2016 led to rapid termination of the outbreak
  (1 single asymptomatic intestinal carriage, 64 days after intervention)

*No single case since Sept 2nd, 2016*

....and the light bulb will go off
Major consequences of the outbreak

- Period May-Sept. 2016 (94 days)
  
  - **42 patients affected** (33 colonized, 9 infections)
  - **Attack rate: 50%** (40 of 81 pts with cardiac surgery and per-operative TEE) colonized/infected (respiratory tract/rectal swab) in the week after surgery
  - **9 infections** (pneumonia [n=7]; sternitis/mediastinitis [n=2])
  - **30-days crude mortality rate: 9.5%** (4 possible/probable link)
  - **Increase in the median LOS vs control patients**
    - Colonization : +1 day in ICU ; + 5 days in LOS
    - Infection : + 10 days in ICU; + 17 days in LOS

  **Decreased medical activity** (ward closure, stop of cardiac/lung transplantation surgery), major changes in organization at all levels
Conclusion

- Large point source outbreak caused by an ESBL-producing *E. cloacae* traced to contamination of TEE probe used intra-operatively in cardiac surgery patients

- Major medical and economical impact with decrease of activity and modifications of care organization

- Central role of the infection control team in the coordination of the outbreak management and implementation of appropriate containment strategies