HHS Public Access

Author manuscript

*Transpl Infect Dis*. Author manuscript; available in PMC 2024 February 01.

Published in final edited form as:

*Transpl Infect Dis*. 2020 April ; 22(2): e13256. doi:10.1111/tid.13256.

# Donor-derived transmission through lung transplantation of carbapenem-resistant *Acinetobacter baumannii* producing the OXA-23 carbapenemase during an ongoing healthcare facility outbreak

**Ana C. Bardossy**[1,2], **Emily A. Snavely**[3], **Elizabeth Nazarian**[3], **Pallavi Annambhotla**[2], **Sridhar V. Basavaraju**[2], **Dana Pepe**[4,5], **Meghan Maloney**[5], **Kimberlee A. Musser**[3], **Wolfgang Haas**[3], **Nicolas Barros**[6], **Virginia M. Pierce**[7,8], **Maroya Walters**[2], **Lauren Epstein**[2]

[1]Epidemic Intelligence Service, Centers for Disease Control and Prevention, Atlanta, GA, USA

[2]Division of Healthcare Quality Promotion, National Center for Emerging and Zoonotic Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, GA, USA

[3]Wadsworth Center, New York State Department of Health, Albany, NY, USA

[4]Yale School of Medicine, New Haven, CT, USA

[5]Connecticut Department of Public Health, Healthcare-Associated Infections Antimicrobial Resistance Program, Hartford, CT, USA

[6]Transplant Infectious Diseases and Compromised Host Program, Massachusetts General Hospital, Boston, MA, USA

[7]Microbiology Laboratory, Pathology Service, Massachusetts General Hospital, Boston, MA, USA

[8]Department of Pathology, Harvard Medical School, Boston, MA, USA

## Abstract

We describe a rare instance of donor-derived OXA-23-producing carbapenem-resistant *Acinetobacter baumannii* transmission during lung transplantation and the subsequent public health response. This investigation highlights how transplantation can introduce rare multidrug-resistant organisms into different healthcare facilities and regions.

### Keywords

carbapenem-resistant *Acinetobacter baumannii*; donor-derived transmission; lung transplantation

**Correspondence**: Ana C. Bardossy, Epidemic Intelligence, Service Officer, Division of Healthcare, Quality Promotion, Centers for Disease, Control and Prevention, 1600 Clifton Road, NE, Mailstop H16-3, Atlanta, GA 30329-4027, USA. okl1@cdc.gov.

AUTHOR CONTRIBUTION

AB, ES, EN, PA, DP, MM, KM, WH, NB, VP, and LE contributed with data collection. AB and LE reviewed the literature. AB, ES, SB, MW, and LE drafted the manuscript. All authors revised the manuscript critically and approved the final manuscript.

## 1 | INTRODUCTION

*Acinetobacter baumannii* is an environmental pathogen and a recognized cause of healthcare-associated infections.[1] Outbreaks of infections caused by *A baumannii* are often due to persistent environmental contamination and person-to-person spread mediated by healthcare workers.[2] Carbapenem-resistant *A baumannii* (CRAB) is a serious public health threat and accounts for nearly half of all *A baumannii* isolated from healthcare-associated infections in the United States.[3] OXA-23 is an acquired beta-lactamase with carbapenemase activity that has been found in nearly 50% of US CRAB isolates.[4] We describe a rare instance of OXA-23-producing CRAB transmission through organ transplantation and the public health response.

## 2 | CASE REPORT

On August 20, 2018, the Connecticut Department of Public Health (CDPH) notified the Centers for Disease Control and Prevention (CDC) of an OXA-23-producing CRAB isolate recovered from the sputum of a hospitalized patient who subsequently died and became a solid organ donor. The donor, a 55-year-old male without any recent healthcare exposure, was the 7th person identified as part of an ongoing CRAB outbreak at the healthcare facility. CRAB is a reportable laboratory finding in Connecticut[5], and CDPH had been working closely with the healthcare facility for several weeks prior to the identification of the donor to track and stop the outbreak.

The donor initially presented with an extensive subarachnoid hemorrhage after falling down a flight of stairs. His neurologic status deteriorated during the hospitalization, and he was intubated 5 days after admission. On hospital day 9, the patient developed a fever and copious secretions; a sputum culture was collected as part of the clinical evaluation for pneumonia, and he was started empirically on cefepime and vancomycin. The patient died 14 days after admission, and both lungs (1 recipient), kidneys (2 recipients), and liver (1 recipient) were transplanted at three healthcare facilities in Connecticut and Massachusetts, all of which were different than the donor hospital. CRAB isolated from donor sputum was identified as OXA-23-producing by the CDC Antibiotic Resistance Laboratory Network (AR Laboratory Network) Northeast Regional Laboratory, the Wadsworth Center (WC), after all organs had been transplanted. The recipient transplant centers were notified of the results.

Blood, urine, and respiratory cultures were obtained from the four organ recipients as part of the post-transplant clinical evaluation. Cultures of the donor's lungs were performed immediately prior to transplantation at the recipient healthcare facility. The peri-operative antibiotic regimen included cefepime, vancomycin, micafungin, inhaled tobramycin, and inhaled amphotericin B. Post-operatively, the lung recipient was placed into special isolation precautions, which included a private, positive pressure room with healthcare personnel using contact precautions (ie, gown and gloves) and a surgical mask upon entry to the room. CRAB was identified on post-operative day 2.

From post-operative day 1 through post-operative day 11, the lung recipient had no clinical manifestations of infection. On post-operative day 12, the patient developed leukocytosis; chest computed tomography did not show evidence of pneumonia, but bronchoscopy revealed adherent mucus with nearly complete occlusion of the anastomoses, with a bronchoalveolar lavage culture identifying CRAB. Given concerns regarding the integrity of the bronchial anastomosis, the patient was started on intravenous tigecycline (one initial dose of 100 mg, followed by 50 mg every 12 hours) for 19 days and nebulized colistin for 45 days for treatment of CRAB. He was discharged from the hospital on post-operative day 18. Nearly 6 months following transplantation, the patient remained colonized with CRAB based on surveillance cultures of the lungs. A review of institutional clinical microbiology data during the 9 months following the transplant was conducted in order to identify secondary transmission in the facility; no patients with CRAB isolates that had similar antimicrobial susceptibility profiles as the lung recipien's CRAB isolate were determined to be epidemiologically linked to the lung recipient. CRAB was not identified from the other three organ recipients.

## 3 | MICROBIOLOGICAL INVESTIGATION

One CRAB isolate from the donor and two isolates (R-1, R-2) from the lung recipient obtained from a bronchoalveolar lavage on post-operative day 28 were tested at the WC to confirm species by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry, obtain antimicrobial susceptibilities by broth microdilution, and determine the carbapenem resistance mechanism by real-time polymerase chain reaction. Whole genome sequencing (WGS) was used for further isolate characterization, and pulsed-field gel electrophoresis (PFGE) was performed to assess isolate relatedness. All three isolates were confirmed to be *A baumannii* sequence type 2, harbored $bla_{\text{OXA-23}}$, and were resistant to at least five classes of antimicrobials; one of the recipient isolates (R-2) was also resistant to colistin (Table 1). Identical AR gene profiles were identified across the three isolates, with $bla_{\text{OXA-23}}$ located on transposon Tn2006. Using WGS, the isolates from the lung recipient and organ donor differed by 2-4 single-nucleotide polymorphisms (SNPs); the PFGE patterns from the recipient and donor isolates varied by 4-5 bands (Figure 1).

## 4 | DISCUSSION

We describe a case of donor-derived CRAB transmission during lung transplantation with important public health implications. While most reported CRAB outbreaks have occurred among patients in a single healthcare facility, this case illustrates the potential for multidrug-resistant organisms (MDROs) to move between facilities though transplantation, facilitating the spread of MDROs across regions. This case also highlights the importance of regional collaborations between healthcare facilities and public health authorities to respond to emerging resistance and prevent the spread of MDROs.

Public health laboratories play a critical role in identifying emerging antibiotic resistance, as demonstrated in this investigation. Most clinical laboratories are unable to detect carbapenemase production among CRAB as there is no reliable phenotypic test to detect carbapenemase production in *Acinetobacter* spp.[6], and few clinical laboratories have the

capacity for molecular detection of carbapenemases.[7] In 2016, CDC established the AR Laboratory Network to support nationwide capacity to rapidly detect antibiotic resistance mechanisms using advanced diagnostics.[8] The AR Laboratory Network provides testing supplies and financial support for specimen collection and shipment.

This case illustrates the resources available through the AR Laboratory Network to detect emerging resistance and facilitate a public health response. Prior to the confirmation of OXA-23-producing CRAB from the donor, the regional AR Laboratory was working closely with the healthcare facility and CDPH to routinely test clinical isolates for OXA-23 during the CRAB outbreak investigation in order to inform response and infection prevention strategies. As a result of this collaboration, effective communication had been established between the healthcare facility, CDPH, and the AR Laboratory Network, which provided an important framework for sharing information. Once the patient was identified as part of the outbreak, the healthcare facility quickly notified CDPH regarding his status as an organ donor. CDPH promptly notified CDC for assistance and CDC coordinated with the Massachusetts Department of Public Health and the Organ Procurement and Transplantation Network (OPTN) to identify recipient facilities and to retrieve isolates from the recipients for further testing. All isolates from the donor and lung recipient were tested at the same AR Laboratory Network regional laboratory.

WGS was essential to confirm transmission of OXA-23-producing CRAB. Despite a close epidemiologic link, PFGE patterns from the recipien's isolates differed from the donor isolate by 4-5 bands, suggesting that the donor and recipient isolates were less likely to be genetically related.[9] In contrast, WGS analysis indicated that the donor and recipien's isolates were closely related, varying by <5 SNPs, which supported the epidemiologic hypothesis of donor-derived CRAB. Previous analyses have shown that the band-based techniques used in PFGE to assess relatedness of *A baumannii* isolates may be less sensitive than WGS.[10,11]

Donor-derived infections caused by MDROs transmitted during transplantation have been reported[12] and may become more common. The risk of MDRO transmission is increased if there is an infection or colonization of the transplanted organ.[12] The OPTN policy requires Organ Procurement Organizations and transplant hospitals to report suspected donor-derived transmissions to either the OPTN Patient Safety Portal or the transplant hospital's Patient Safety Contact.[13] However, even when an infection is not suspected to be donor-derived, it must be reported if that pathogen is listed on the OPTN list of Pathogens of Special Interest.[14] The addition of carbapenemase-producing organisms to this list is under consideration. Establishing a standard method to share information regarding emerging and high-concern multidrug resistance among facilities would inform appropriate infection prevention measures to prevent the spread of MDROs within the recipien's healthcare facility and optimize testing and treatment for recipients.

This investigation highlights how transplantation can introduce MDROs into different healthcare facilities and regions. Donor culture results should be promptly shared with recipient healthcare centers in order to enable implementation of infection control measures

to prevent spread within the recipients' healthcare facilities and to inform treatment of clinical infections.

## 5 | DISCLAIMER

The findings and conclusions in the manuscript are those of the authors and do not necessarily represent the official views of the US Centers for Disease Control and Prevention or the Department of Health and Human Services.

## ACKNOWLEDGEMENTS

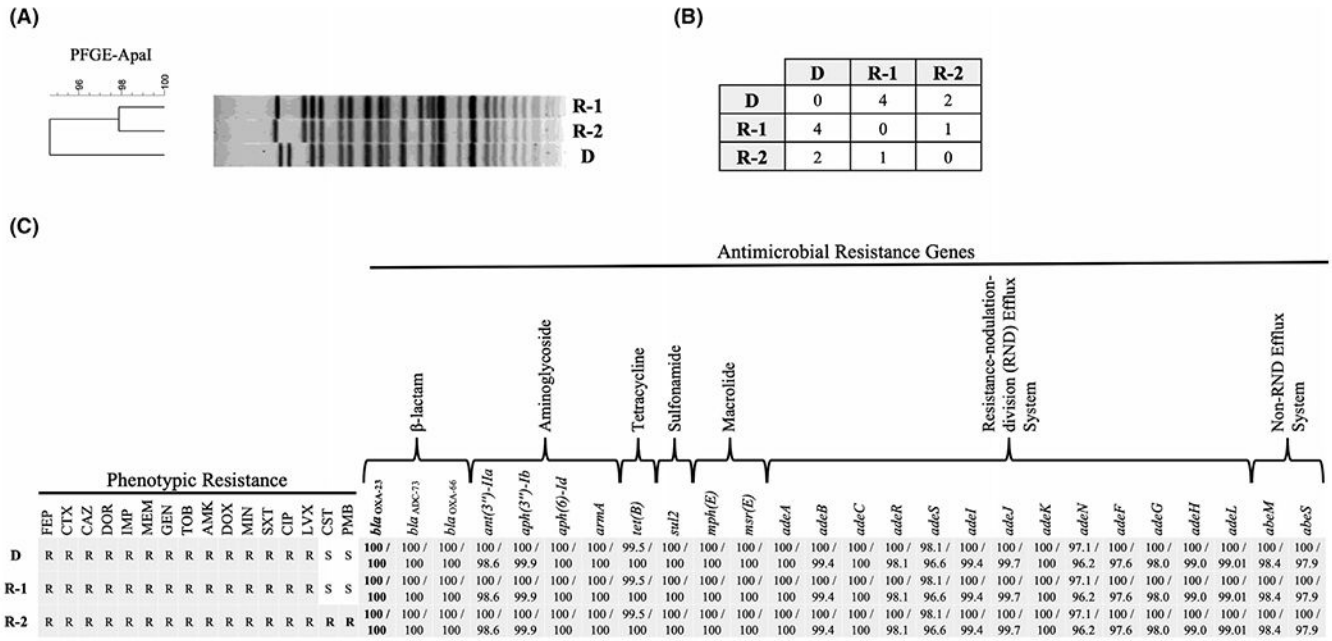
We thank our colleagues James Bowman, MD, and Marilyn Levi, MD, from Health Resources and Services Administration, Division of Transplantation, for reviewing the manuscript and providing important insight and expertise. As an Instructor of Medicine at Yale School of Medicine, Dr Pepe was supported by the Center for Disease Control Sponsored Leaders in Epidemiology, Antimicrobial Stewardship, and Public Health (LEAP) Fellowship which allowed her to serve as clinical liaison to the Connecticut Department of Public Health during this work.

## REFERENCES

1. Peleg AY, Seifert H, Paterson DL. *Acinetobacter baumannii*: emergence of a successful pathogen. Clin Microbiol Rev. 2008;21:538–582. [PubMed: 18625687]
2. Thom KA, Rock C, Jackson SS, et al. Factors leading to transmission risk of *Acinetobacter baumannii*. Crit Care Med. 2017;45(7):e633–e639. [PubMed: 28398924]
3. Centers for Disease Control and Prevention. CDC's antibiotic resistance patient safety atlas. Accessed July 5, 2019. https://gis.cdc.gov/grasp/PSA/MapView.html
4. Daniels J, Albrecht V, Vlachos N, Stevens V, Rasheed J, Karlsson M, Halpin A. Molecular Characterization of Carbapenem-Resistant Acinetobacter baumannii in the United States, 2013-2015. Abstract #200. International Conference On Emerging Infectious Diseases, Atlanta, United States, August 26-29, 2018.
5. Connecticut Epidemiologist. Accessed June 14, 2019. https://portal.ct.gov/-/media/Departments-and-Agencies/DPH/dph/infectious_diseases/pdf_forms_/ReportableDiseases.pdf?la=en
6. Simner PJ, Johnson JK, Brasso WB, et al. Multicenter evaluation of the modified carbapenem inactivation method and the carba NP for detection of carbapenemase-producing *Pseudomonas aeruginosa and Acinetobacter baumannii*. J Clin Microbiol. 2017;56(l):e01369–e1417. [PubMed: 29118172]
7. Shugart A, Walters MS, Weiner LM, Lonsway D, Kallen AJ. Hospital microbiology laboratory practices for Enterobacteriaceae: centers for disease control and prevention national healthcare safety network (NHSN) annual survey, 2015 and 2016. Infect Control Hosp Epidemiol. 2018;39(9):1115–1117. [PubMed: 30039775]
8. Lab Capacity: Antibiotic Resistance Laboratory Network (AR Lab Network). Accessed July 24, 2019. https://www.cdc.gov/drugresistance/solutions-initiative/ar-lab-network.html#anchor_1522340404
9. Tenover FC, Arbeit RD, Goering RV, et al. Interpreting chromosomal DNA restriction patterns produced by pulsed-field gel electrophoresis: criteria for bacterial strain typing. J Clin Microbiol. 1995;33(9):2233–3223. [PubMed: 7494007]
10. Turton JF, Baddal B, Perry C. Use of the accessory genome for characterization and typing of *Acinetobacter baumannii*. J Clin Micro. 2011;49(4):1260–1266.
11. Lewis T High-throughput whole-genome sequencing to dissect the epidemiology of *Acinetobacter baumannii* isolates from a hospital outbreak. J Hosp Infect. 2010;75(1):37–41. [PubMed: 20299126]
12. Mularoni A, Bertani A, Vizzini G, et al. Outcome of transplantation using organs from donors infected or colonized with carbapenem-resistant gram-negative bacteria. Am J Transplant. 2015;15(10):2674–2682. [PubMed: 25981339]

13. Organ Procurement and Transplantation Network. Frequently asked questions about PDDTE policy changes. Accessed November 5, 2019. https://optn.transplant.hrsa.gov/resources/patient-safety/frequently-asked-questions-about-pddte-policy-changes/

14. Organ Procurement and Transplantation Network. List of special pathogens. Accessed June 14, 2019. https://optn.transplant.hrsa.gov/media/1911/special_pathogens_list.pdf




| | D | R-1 | R-2 |
|---|---|---|---|
| D | 0 | 4 | 2 |
| R-1 | 4 | 0 | 1 |
| R-2 | 2 | 1 | 0 |

| | FEP | CTX | CAZ | DOR | IMP | MEM | GEN | TOB | AMK | DOX | MIN | SXT | CIP | LVX | CST | PMB | *bla* OXA-23 | *bla* ADC-73 | *bla* OXA-66 | *aml(3'')-IIa* | *aph(3'')-Ib* | *aph(6)-Id* | *armA* | *tet(B)* | *sul2* | *mph(E)* | *msr(E)* | *adeA* | *adeB* | *adeC* | *adeR* | *adeS* | *adeI* | *adeJ* | *adeK* | *adeN* | *adeF* | *adeG* | *adeH* | *adeL* | *abeM* | *abeS* |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| D | R | R | R | R | R | R | R | R | R | R | R | R | R | R | S | S | 100 / 100 | 100 / 100 | 100 / 100 | 100 / 98.6 | 100 / 99.9 | 100 / 100 | 100 / 100 | 99.5 / 100 | 100 / 100 | 100 / 100 | 100 / 100 | 100 / 100 | 100 / 99.4 | 100 / 100 | 100 / 98.1 | 98.1 / 96.6 | 100 / 99.4 | 100 / 99.7 | 100 / 100 | 97.1 / 96.2 | 100 / 97.6 | 100 / 98.0 | 100 / 99.0 | 100 / 99.01 | 100 / 98.4 | 100 / 97.9 |
| R-1 | R | R | R | R | R | R | R | R | R | R | R | R | R | R | S | S | 100 / 100 | 100 / 100 | 100 / 100 | 100 / 98.6 | 100 / 99.9 | 100 / 100 | 100 / 100 | 99.5 / 100 | 100 / 100 | 100 / 100 | 100 / 100 | 100 / 100 | 100 / 99.4 | 100 / 100 | 100 / 98.1 | 98.1 / 96.6 | 100 / 99.4 | 100 / 99.7 | 100 / 100 | 97.1 / 96.2 | 100 / 97.6 | 100 / 98.0 | 100 / 99.0 | 100 / 99.01 | 100 / 98.4 | 100 / 97.9 |
| R-2 | R | R | R | R | R | R | R | R | R | R | R | R | R | R | R | R | 100 / 100 | 100 / 100 | 100 / 100 | 100 / 98.6 | 100 / 99.9 | 100 / 100 | 100 / 100 | 99.5 / 100 | 100 / 100 | 100 / 100 | 100 / 100 | 100 / 100 | 100 / 99.4 | 100 / 100 | 100 / 98.1 | 98.1 / 96.6 | 100 / 99.4 | 100 / 99.7 | 100 / 100 | 97.1 / 96.2 | 100 / 97.6 | 100 / 98.0 | 100 / 99.0 | 100 / 99.01 | 100 / 98.4 | 100 / 97.9 |

**FIGURE 1.**

Phenotypic and genetic characterization of *Acinetobacter baumannii* isolates using PFGE and WGS. A. Pulsed-field gel electrophoresis (PFGE) of donor (D) and recipient (R-1 and R-2) isolates. The recipient isolates PFGE patterns differ from the PFGE pattern seen in the donor isolate by 5 and 4 bands B. SNP matrix. Isolates are 1-4 SNPs different from each other. C. Antimicrobial resistance (AR) phenotypes and resistance genes identified. Unlike the D and R-1 isolates, R-2 was resistant to all antimicrobials tested, including colistin and polymyxin B. AR gene profiles were identical between all three isolates (% coverage/ % identity). FEP, cefepime; CTX, cefotaxime; CAZ, ceftazidime; DOR, doripenem; IMP, imipenem; MEM, meropenem; GEN, gentamicin; TOB, tobramycin; AMK, amikacin; DOX, doxycycline; MIN, minocycline; SXT, trimethoprim-sulfamethoxazole; CIP, ciprofloxacin; LVX, levofloxacin; CST, colistin; PMB, polymyxin B

**TABLE 1**

Phenotypic antibiotic susceptibility profiles of the donor and recipient *Acinetobacter baumannii* isolates

| | | Donor | | R-1 | | R-2 | |
|---|---|---|---|---|---|---|---|
| **Antibiotic Class** | **Agent** | **MIC (μg/mL)** | **Interpretation*** | **MIC (μg/mL)** | **Interpretation*** | **MIC (μg/mL)** | **Interpretation*** |
| Beta-lactam | Cefepime | >16 | R | >16 | R | >16 | R |
| | Cefotaxime | >32 | R | >32 | R | >32 | R |
| | Ceftazidime | >16 | R | >16 | R | >16 | R |
| | Doripenem | >2 | R | >2 | R | >2 | R |
| | Imipenem | >8 | R | >8 | R | >8 | R |
| | Meropenem | >8 | R | >8 | R | >8 | R |
| Polymyxins | Colistin | ≤0.25 | S | 1 | S | >4 | R |
| | Polymyxin B | ≤0.25 | S | 0.5 | S | >4 | R |
| Aminoglycoside | Gentamicin | >8 | R | >8 | R | >8 | R |
| | Tobramycin | >8 | R | >8 | R | >8 | R |
| | Amikacin | >32 | R | >32 | R | >32 | R |
| Tetracycline | Doxycycline | >16 | R | >16 | R | >16 | R |
| | Minocycline | 16 | R | 16 | R | 16 | R |
| Glycylcycline | Tigecycline** | 1 | -- | 2 | -- | 1 | -- |
| Fluoroquinolone | Ciprofloxacin | >2 | R | >2 | R | >2 | R |
| | Levofloxacin | >8 | R | >8 | R | >8 | R |
| Folate Pathway Antagonist | Trimethoprim/sulfamethoxazole | >4 | R | >4 | R | >4 | R |

Abbreviations: R, Resistant; S, Susceptible.

* Interpretation according to CLSI M100 ed 28.

** There are no established CLSI or FDA breakpoints for Tigecycline and *Acinetobacter baumannii*.