Serratia Outbreak Investigation

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Objectives

• To discuss the clinical ramifications of drug diversion in the form of infection outbreaks

• To describe investigation of a Serratia outbreak
Disclosures

• None
Background

• *Serratia marcescens*

  • is a Gram-negative, facultative anaerobic bacillus

  • *Enterobacteriaceae* family

  • Survives in environments and reservoirs such as drinking water, pipes, and hospital disinfectants, medical instrumentation

• It was discovered in 1819 by Bartolomeo Bizio in Padua, Italy. Bizio named the genus *Serratia* in honor of Italian physicist named Serratia, and chose *marcescens* for the species name after the Latin word for decay
Background

• Able to colonize the human gastrointestinal tract and skin for extended periods
• Transmitted predominantly by person-to-person contact
• Pneumonia, bloodstream infections, meningitis, and ocular and urinary tract infections are major sites
Background

- Well known as an important pathogen in healthcare and has been responsible for outbreaks, particularly in critically ill neonates and patients in intensive care units.
Background

- Fondness for growing on bread, wafers “bleeding bread”
- Thought to be a non pathogen
- Extensive use in military and healthcare as tracer organism
- Operation “Sea Spray”
Background

- **UW-Madison link:**
  - Waisman and Stone (1958) described the “red diaper syndrome,” the appearance of *S. marcescens* in soiled diapers of a female baby born in 1954 at the University of Wisconsin.
  - The parents noticed that soiled diapers that had been rinsed with plain water before being placed in a receptacle provided by a commercial diaper laundry service turned red. This first occurred 3 days after the infant had been discharged from the newborn nursery, and after a week, about one-third of the diapers became red after being placed in the receptacle.
  - The stool of the infant was cultured and *S. marcescens* was recovered.
  - The source of this “red diaper syndrome” was initially a mystery. The other parents who had infants born at the same time and who also stayed in the same newborn nursery were contacted, and red diapers were not observed by any of them. It was learned, however, that a biomedical laboratory that was within 500 yards of the hospital had been using *S. marcescens* in aerosol experiments. Apparently, live organisms were used in the tests and allowed to escape into the air around the laboratory.
• Another laboratory in an adjoining building reported *S. marcescens* as an airborne contaminant.
• The *S. marcescens* isolate used by the biomedical lab in the aerosol experiments was compared to the patient's isolate and the contaminant from the other lab, and all three had the same antigenic type.
• Thus, it is likely that the baby's *S. marcescens* gastrointestinal colonizer came from the strain used in the aerosol experiments.

The Waisman Center, UW-Madison


WAISMAN, HARRY A. & W. H. STONE. 1958. The presence of Serratia marcescens as the predominating organism in the intestinal tract of the newborn. The occurrence of the “Red Diaper Syndrome.” *Pediatrics* 21: 8-12. 608
University of Wisconsin-Madison
Serratia Investigation

• Infection control was notified of an unusually high number of bloodstream infections from *Serratia marcescens*.
• Ascertainment that it was a cluster
• Case definition
• Case control study
• Culturing data
• Connecting the dots
• **Case definition**

• Cases were defined as patients admitted during the cluster timeframe with blood cultures positive for *Serratia marcescens* at any time during their hospital stay, whose isolates were considered related or identical by molecular fingerprinting.
Outbreak Investigation

- Controls were randomly selected from patients who:
  - did not have positive blood cultures
  - and were admitted at the same time
  - and to the same unit as the case patients
  - in a 4:1 ratio.

- We abstracted relevant demographic and clinical variables by retrospective review of medical records. We analyzed categorical variables by the Chi-square test or two-tailed Fisher’s exact test, and continuous variables by the Student’s t-test. Bivariate analyses were performed in STATA 14.1 SE for Windows.
• During the *Serratia marcescens* cluster timeframe, a separate hospital investigation was started to examine a narcotic diversion that was identified soon after the first *Serratia* bloodstream infection was reported.

• The hospital epidemiologist was informed of the latter investigation, and led the analysis of possible connections between the cluster of bloodstream infections and the narcotic diversion.
Outbreak Investigation

- **Patient 1**, a 58 yo man with underlying Amyotrophic Lateral Sclerosis, was admitted on March 2nd for evaluation of:
  - 2 days of fevers, a petechial rash, and right ankle swelling.
  - Admission blood cultures were positive for *Serratia marcescens*, although a full evaluation of his respiratory, gastro-intestinal and genital-urinary systems failed to identify a cause for his bacteremia.
  - The synovial fluid analysis of his right ankle was normal, and the synovial fluid culture was negative.
  - The etiology of his *Serratia marcescens* bacteremia remained cryptogenic, although he made a full recovery after antibiotic treatment, and was discharged uneventfully in the care of his daughter.
Outbreak Investigation

- **Patient 2**, a 53 yo man with underlying esophageal carcinoma
- treated with recent chemotherapy
- electively admitted on March 10th for esophageal biopsies and laparoscopic staging.
- Found to have a perforated gastric ulcer at the time of the surgery, which was repaired without complications.
- His immediate postoperative course during the night shift was remarkable for poor pain control, which improved by the next morning on a PCA pump.
- On his second hospital day he developed sudden rigors, fevers to 40°C, hypotension, and septic shock with subsequent profound acidosis and disseminated intravascular coagulation.
- An intra-abdominal source of sepsis secondary to bowel ischemia was suspected, although an emergent exploratory laparotomy did not identify any bowel abnormalities.
- Blood cultures from day 2 of hospitalization returned positive for *Serratia marcescens*.
- Despite aggressive critical care management and prompt initiation of broad-spectrum intravenous antibiotics, he succumbed by the 3 of his hospital stay. A postmortem examination confirmed sepsis secondary to *Serratia* as the likely cause of death.
Outbreak Investigation

• **Patient 3**
  • 80 yo man with underlying adenocarcinoma of the lung
  • Admitted for resection of the left upper lobe and mediastinal lymph node dissection, and had a non-eventful course in the post-anesthesia care unit.
  • On the second post-operative day, he developed sepsis with rigors, hypotension, fevers, altered mental status, and respiratory failure.
  • Vasopressors were started, and he was intubated for airway protection. Blood cultures drawn during this clinical decompensation returned positive for *Serratia marcescens*.
  • The source was presumed to be the lung, although confirmatory sputum cultures were not available, and radiology imaging, while positive for a significant pneumothorax, did not conclusively show pneumonia. The patient gradually improved, and was discharged after 13 days.
Outbreak Investigation

• *Patient 4*
  • 50 yo inmate with underlying multiple sclerosis, transferred from an outside ED with fevers, confusion, and bilateral lower extremity weakness above his baseline.
  • Found to have pyelonephritis, with admission urine and blood cultures positive for *Serratia marcescens*.
  • Workup for meningitis was negative, with MRI brain imaging unchanged from his baseline, and benign CSF analysis. He recovered to his baseline level of function a few days after antibiotic treatment was started, and was discharged uneventfully.
Outbreak Investigation

• **Patient 5**
  • a 51 yo woman with colorectal carcinoma who underwent a laparoscopic resection of a solitary metastatic liver lesion on admission.
  • The surgery proceeded without complications.
  • Her day 1 postoperative course noted **difficulty controlling her pain despite having the maximum allowed opioid dosing on her PCA pump.**
  • She started experiencing fevers on day 2 of her hospital stay, but remained overall hemodynamically stable.
  • Her blood cultures drawn returned positive for *Serratia marcescens*.
  • She recovered fully after IV antibiotics were started, and was discharged uneventfully after 4 days of hospital stay.
Outbreak Investigation

• **Patient 6**
  - 67 yo man with recurrent prostate cancer and recurrent colon cancer, both metastatic,
  - admitted 27 days prior to his *Serratia* bacteremia event for exploratory laparotomy with lysis of adhesions, appendectomy, sigmoid colectomy with retroperitoneal lymph node dissection, primary colorectal anastomosis, and left ureteral stent placement.
  - He had a central venous port that had been placed several months previously for chemotherapy treatment, and was last used postoperatively for blood draws and various infusions, including opioids for pain control.
  - He presented for his scheduled oncology outpatient follow-up, 3 weeks after hospital discharge, and reported subjective fevers and chills at home. He was febrile in the office, and blood cultures were drawn peripherally and, with great difficulty, from the port.
  - He was admitted to the hospital the same evening, after his port blood cultures turned positive for *Serratia marcescens* within 7 hours. His peripheral blood cultures subsequently became positive at 15 hours, while his urine cultures had no growth.
  - He improved after port removal and IV antibiotics.
## Outbreak Investigation

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Cases (N =5)</th>
<th>Controls (N = 20)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N (%)</td>
<td>N (%)</td>
<td></td>
</tr>
<tr>
<td>Age (mean)</td>
<td>61.6</td>
<td>65.1</td>
<td>0.67</td>
</tr>
<tr>
<td>Male gender</td>
<td>4 (80)</td>
<td>10 (50)</td>
<td>0.23</td>
</tr>
<tr>
<td>Surgery</td>
<td>4 (80)</td>
<td>10 (50)</td>
<td>0.23</td>
</tr>
<tr>
<td>Bronchoscopy</td>
<td>1 (20)</td>
<td>1 (5)</td>
<td>0.27</td>
</tr>
<tr>
<td>Endoscopy</td>
<td>1 (20)</td>
<td>1 (5)</td>
<td>0.27</td>
</tr>
<tr>
<td>Underlying malignancy</td>
<td>4 (80)</td>
<td>6 (30)</td>
<td>0.041</td>
</tr>
<tr>
<td>Receipt of any IV narcotics</td>
<td>4 (80)</td>
<td>11 (55)</td>
<td>0.3</td>
</tr>
<tr>
<td>Receipt of IV hydromorphone</td>
<td>4 (80)</td>
<td>9 (45)</td>
<td>0.16</td>
</tr>
<tr>
<td>Post-Anesthesia Care Unit stay</td>
<td>4 (80)</td>
<td>4 (20)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Table 1. Demographic and clinical characteristics of cases and controls, bivariate analyses.
Figure 2. Pulsed-Field Gel Electrophoresis (PFGE) of Bacterial Isolates. Serratia bloodstream isolates from Patients 1-6 are represented as follows: Patient 1, 2, 3, 5, and 6 are in lines 2, 3, 4, 5, and 8, respectively; Patient 4’s isolate is in Lane 7.

<table>
<thead>
<tr>
<th>Category</th>
<th>No. of genetic differences compared with outbreak strain</th>
<th>Typical no. of fragment differences compared with outbreak pattern</th>
<th>Epidemiologic interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indistinguishable</td>
<td>0</td>
<td>0</td>
<td>Isolate is part of the outbreak</td>
</tr>
<tr>
<td>Closely related</td>
<td>1</td>
<td>2–3</td>
<td>Isolate is probably part of the outbreak</td>
</tr>
<tr>
<td>Possibly related</td>
<td>2</td>
<td>4–6</td>
<td>Isolate is possibly part of the outbreak</td>
</tr>
<tr>
<td>Different</td>
<td>≥3</td>
<td>≥7</td>
<td>Isolate is not part of the outbreak</td>
</tr>
</tbody>
</table>
Figure 3. Dendogram comparing banding patterns from PFGE and applying Tenover criteria to all isolates. Five of six isolates obtained during the outbreak determined to be indistinguishable confirming a common source. Unique isolate patterns for Serratia isolates discovered in May and June (patients 7 and 8) showing resolution of the outbreak.
Controlled Substance Diversion Investigation

• During the Serratia outbreak investigation, a parallel drug diversion investigation was ongoing.
• A nurse discovered 4 hydromorphone and 6 morphine patient-controlled analgesia (PCA) syringes with the tamper-evident caps no longer intact in the locked automated medication dispensing cabinet on a hospital nursing unit.
• The syringes were submitted to the hospital’s toxicology lab for testing, and 7 out of 10 syringes were found to have less than detectable levels of drug present.
• These results triggered the start of a Controlled Substance Diversion Investigation (CSDI), with teams from the Nursing, Pharmacy, Compliance, and Internal Audit departments.
• A surveillance camera was installed for subsequent review of all medication dispensing activity on the medical floor where the tampered syringes were found.
Controlled Substance Diversion Investigation

• Almost a month later, 3 more hydromorphone PCA syringes were found with tamper-evidence caps no longer intact in the automated dispensing cabinet of a different patient care unit.

• The analysis from an internal toxicology lab showed that less than detectable levels of medication were found in the syringes and this was later confirmed by independent lab.

• Ten additional samples of morphine and hydromorphone PCA syringes were then pulled from the NarcVault in Central Pharmacy and a few Accudose cabinets from different patient units throughout the hospital to help identify the potential source of diversion.

• One out of the 10 syringes did not contain the expected drug quantity (3mcg/mL instead of 200 mcg/mL of hydromorphone).
Controlled Substance Diversion Investigation

- the CSDI team met to discuss the implications of a potential hospital-wide narcotic diversion and formulate an action plan going forward. New morphine and hydromorphone PCA syringes were compounded in the presence of 2 staff members at all times, one of whom had a managerial role.

- All previously stocked morphine and hydromorphone PCA syringes were removed from all storage locations and the new syringes were restocked by two staff members, one of whom had a managerial role.

- Additional tamper-evident packaging was implemented including shrink wrapping and tamper-evident tape to provide additional control measures.

- Close monitoring of PCA activity in all operational processes continued as the source of diversion had not yet been identified.

- In total, 42 syringes with evidence of narcotic drug diversion were identified over the course of the investigation, and osmolality testing suggested that the syringes were filled with a saline or lactate ringers-like solution instead of active medication. A nurse was subsequently identified as the diverter and hospital employment was terminated.
Controlled Substance Diversion Investigation

• **Assessment of relationship between narcotic diversion and bloodstream infection**

  - The Pharmacy Manager notified the Hospital Epidemiologist of a potential link between the narcotic diversion and the *Serratia* cluster.

  - The results of the case-control study suggested that a short-term post-operative stay in the PACU was a common exposure immediately after admission for 4 of the 5 cluster patients (Patients 2, 3, 5, and 6).

  - At that time, it was recognized that although many of the control patients also had surgery shortly after their hospital admission, not all of them received immediate postoperative care in the PACU; instead, some were taken directly to the Intensive Care Unit after coming out of the operating room, where they received postoperative anesthesia care, bypassing the potential *Serratia* exposure.

  - Once the implicated employee responsible for the narcotic diversion was identified, review of her activity from automated medication dispensing cabinet established that she had indeed accessed the storage pockets of PCA syringes in the PACU Accudose cabinets within a short time period before PCA syringes were administered to Patients 2, 3, 5 and 6, respectively.

  - Although Patient 1 did not have surgery or stayed in the PACU during his hospitalization, the connection with the PACU nurse implicated in the narcotic diversion was ultimately established when it was recognized that Patient 1 was, in fact, her father, and had lived at her residential address before and after his hospitalization.
DRUG DIVERSION* SPREADS INFECTION FROM HEALTHCARE PROVIDERS TO PATIENTS

HEALTHCARE PROVIDER with Hepatitis C or other bloodborne infection tampers with injectable drug

CONTAMINATED INJECTION EQUIPMENT AND SUPPLIES present in the patient care environment

EXPOSURE OF PATIENT results from use of contaminated drug or equipment for patient injection or infusion

*Drug diversion occurs when prescription medicines are obtained or used illegally by healthcare providers.

FOR MORE INFORMATION, VISIT CDC.GOV/INJECTIONSAFETY/DRUGDIVERSION
Bacterial infections with drug diversion

- 1985: 3 cases of *Pseudomonas pickettii* bacteremia associated with a pharmacy technician at a Wisconsin hospital
- 1990: 16 cases of HCV infection associated with a certified-registered nurse anesthetist at a Texas hospital
- 1992: 45 cases of HCV infection associated with a surgical technician at a Texas ambulatory surgical center
- 1999: 26 cases of *Serratia marcescens* bacteremia associated with a respiratory therapist at a Pennsylvania hospital
- 2000: 9 cases of *Achromobacter xylosoxidans* bacteremia associated with a nurse at an Illinois hospital
- 2004: 15 cases of HCV infection associated with a certified-registered nurse anesthetist at a Texas hospital
- 2005: 5 cases of HCV infection associated with a radiology technician at a Florida hospital
- 2006: 9 cases of *Achromobacter xylosoxidans* bacteremia associated with a nurse at an Illinois hospital
- 2008: 5 cases of HCV infection associated with a radiology technician at a Florida hospital
- 2009: 18 cases of HCV infection associated with a surgical technician at a Colorado hospital
- 2011: 25 cases of gram-negative bacteremia associated with a nurse at a Minnesota hospital
- 2012: 45 cases of HCV infection associated with a radiology technician at hospitals in New Hampshire, Kansas, and Maryland
Serratia marcescens Bacteremia Traced to an Infused Narcotic


Abstract

BACKGROUND

From June 30, 1998, through March 31, 1999, several patients in the surgical intensive-care unit at the University of Maryland Medical System's Shock Trauma Center (Baltimore) developed Gram-negative bacteremia.

May 16, 2002

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Related Articles

PERSPECTIVE

Physicians and Addiction

A. Varghese
Summary

• In cases of an outbreak of an organism that is known to persist and thrive in the environment, in liquid, in infusate, consider drug diversion as a potential cause

• Molecular subtyping is essential to confirm a point source outbreak

• In instances of drug diversion investigation, essential to involve the hospital epidemiologist so surveillance for pathogens can be heightened