

A Multistate Outbreak of *Serratia marcescens* Bloodstream Infection Associated with Contaminated Intravenous Magnesium Sulfate from a Compounding Pharmacy

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Background. In contrast to pharmaceutical manufacturers, compounding pharmacies adhere to different quality-control standards, which may increase the likelihood of undetected outbreaks. In 2005, the Centers for Disease Control and Prevention received reports of cases of *Serratia marcescens* bloodstream infection occurring in patients who underwent cardiac surgical procedures in Los Angeles, California, and in New Jersey. An investigation was initiated to determine whether there was a common underlying cause.

Methods. A matched case-control study was conducted in Los Angeles. Case record review and environmental testing were conducted in New Jersey. The Centers for Disease Control and Prevention performed a multistate case-finding investigation; isolates were compared using pulsed-field gel electrophoresis analysis.

Results. Nationally distributed magnesium sulfate solution (MgSO₄) from compounding pharmacy X was the only significant risk factor for *S. marcescens* bloodstream infection (odds ratio, 6.4; 95% confidence interval, 1.1–38.3) among 6 Los Angeles case patients and 18 control subjects. Five New Jersey case patients received MgSO₄ from a single lot produced by compounding pharmacy X; culture of samples from open and unopened 50-mL bags in this lot yielded *S. marcescens*. Seven additional case patients from 3 different states were identified. Isolates from all 18 case patients and from samples of MgSO₄ demonstrated indistinguishable pulsed-field gel electrophoresis patterns. Compounding pharmacy X voluntarily recalled the product. Neither the pharmacy nor the US Food and Drug Administration could identify a source of contamination in their investigations of compounding pharmacy X.

Conclusions. A multistate outbreak of *S. marcescens* bloodstream infection was linked to contaminated MgSO₄ distributed nationally by a compounding pharmacy. Health care personnel should take into account the different quality standards and regulation of compounded parenteral medications distributed in large quantities during investigations of outbreaks of bloodstream infection.

Compounding pharmacies were originated to provide “customized medication for an individual patient in response to a licensed practitioner’s prescription” [1] and continue to serve an important role in patient care.

However, in contrast to pharmaceutical manufacturers, compounding pharmacies adhere to different quality-control standards and regulations, specifically with regard to sterility testing of the final product. This may increase the likelihood of undetected outbreaks resulting from the distribution of large amounts of contaminated product to multiple states. Since 1990, the US Food and Drug Administration (FDA) and the Centers for Disease Control and Prevention (CDC) have eval-

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uated reports of >55 quality problems associated with compounded preparations, including failed sterility and potency testing, many of which have resulted in recalls, patient injury, and death [2]. Multiple outbreaks of infection caused by contaminated medications from compounding pharmacies have been reported [3–7]; however, prior to this outbreak, none have involved the multistate distribution of compounded intravenous medication.

Serratia marcescens is an aerobic gram-negative bacillus that is a recognized cause of health care–associated bloodstream infection (BSI). The bacteria thrive in moist environments and have been cultured from a variety of sources throughout health care settings, including multidose medication vials [8], disinfectants [9–12], hand soaps [13], and the hands and fingernails of health care workers [14, 15]. In 2005, the CDC Division of Healthcare Quality Promotion (DHQP) was notified of 2 *S. marcescens* bloodstream infection clusters, the first of which occurred in a hospital in Los Angeles County, California, in January 2005, and the second of which occurred among patients in a cardiac and pulmonary specialty hospital in New Jersey (NJ) in March 2005. We report how the identification of these clusters led to the discovery of a multistate outbreak of health care–acquired BSI caused by compounded intravenous magnesium sulfate (MgSO₄) solution and the relevant issues surrounding the regulation of compounding pharmacies in the United States.

LOS ANGELES INVESTIGATION

In January 2005, infection-control personnel at a Los Angeles County hospital (LA Hospital) identified an increase in the number of *S. marcescens* BSIs after cardiac procedures. When no obvious source could be identified, the CDC DHQP was asked to investigate.

Methods. To confirm whether the *S. marcescens* BSI cluster represented an outbreak, we reviewed microbiology records at the LA Hospital for cultures yielding *S. marcescens* from January 2004 through January 2005 and compared the *S. marcescens* BSI rate from the year before the outbreak with the rate during the outbreak. All recent *S. marcescens* isolates from the LA Hospital had been analyzed using PFGE by the Los Angeles County Public Health Laboratory staff prior to our arrival. Because all case patients had been hospitalized in the cardiac surgery unit (CSU) prior to infection, a case was defined by the following criteria: a culture-confirmed *S. marcescens* BSI [16] in a patient treated in the CSU in January 2005, with the isolate demonstrating a PFGE pattern indistinguishable from the outbreak strain. To determine risk factors for illness, we conducted a matched case-control study. Control subjects were defined as patients who did not have a documented *S. marcescens* BSI and who were present in the CSU within 4 h of the matched case patient having a blood culture positive for *S.*

marcescens. Each case patient was matched to 3 randomly selected control subjects. Data from the 24-h period prior to the case patient having a culture positive for *S. marcescens* were collected for both case patients and matched control subjects. Factors assessed included demographic and clinical characteristics of the patients and exposure to devices, procedures, medications, and personnel in the operating room and CSU.

We also reviewed CSU and operating room infection-control practices and policies and interviewed personnel in groups. On the basis of information from observation and interviews, environmental samples were obtained for culture. Cultured sites included sinks, counters and other surfaces, cleaning solutions, soap, water, ice, and multidose medication vials (open and unopened) from the operating room and CSU. Of note, medications used during the outbreak were no longer available for testing, with the exception of insulin. Environmental specimens from the LA Hospital were screened for *S. marcescens* at the CDC DHQP laboratory (Atlanta, GA).

All data were collected on standardized forms and analyzed using SAS software (SAS Institute). Cochran-Mantel-Haenszel ORs and 95% CIs were calculated to compare categorical variables, and the Wilcoxon 2-sample test using *t* approximation was used to compare continuous variables.

Results. From 5 January through 16 January 2005, 6 case patients in the LA Hospital were identified as having *S. marcescens* BSI, all of whom had indistinguishable PFGE banding patterns. All patients were in the CSU when they received the diagnosis of *S. marcescens* BSI. The percentage of all *S. marcescens* culture results from blood samples increased significantly, from 11% (7 of 63 cultures) in 2004 to 60% (6 of 10) in January 2005 ($P < .001$).

The 6 case patients and 18 control subjects were similar with regard to age and sex (table 1). All 6 case patients (100%) had received intravenous MgSO₄ from compounding pharmacy X during the 24 h prior to diagnosis of infection, compared with 7 (39%) of 18 control subjects (matched OR, 6.4; 95% CI, 1.1–38.3; $P < .01$). All intravenous MgSO₄ used in the CSU was supplied by compounding pharmacy X and was not used elsewhere in the hospital. No other risk factors were significantly associated with *S. marcescens* BSI. No major infection-control issues were identified, and environmental cultures did not yield *S. marcescens*.

Although the epidemiologic data supported MgSO₄ as the source of the outbreak, none of the MgSO₄ that was used in the CSU during the outbreak period was available for testing. Furthermore, no additional cases were identified at the LA Hospital. While deciding how to proceed with the investigation, CDC DHQP received notification of a second outbreak of *S. marcescens* BSI among patients in a NJ cardiac and pulmonary specialty hospital (NJ Hospital) in March 2005.

Table 1. Characteristics of and risk factors for *Serratia marcescens* bloodstream infection in patients in a Los Angeles hospital, January 2005.

Characteristic or risk factor	Case patients	Control subjects	OR (95% CI) ^a	P ^a
Male sex	4 (67)	10 (56)64
Age, median years (range)	60 (44–88)	70 (53–81)39
Diabetes mellitus	2 (33)	7 (39)	0.7 (0.1–8.4)	
Temperature, ≥38.3°C	4 (67)	4 (22)	3.7 (0.7–19.1)	
Drug received				
Magnesium sulfate	6 (100)	7 (39)	6.4 (1.1–38.3)	
Ranitidine	5 (83)	6 (33)	10.0 (0.9–116.6)	
Midazolam	3 (50)	1 (6)	9.0 (0.9–86.5)	
Furosemide	4 (67)	3 (17)	10.0 (0.9–108.5)	
Serum protein albumin	3 (50)	2 (11)	7.4 (0.8–72.6)	

NOTE. Data are no. (%) of patients, unless otherwise indicated. Data in boldface font indicate a statistically significant difference between case patients and control subjects.

^a P values and 95% CIs are based on χ^2 analysis for categorical variables and the Wilcoxon 2-sample test using *t* approximation for continuous variables.

NJ INVESTIGATION, MARCH 2005

Methods. We defined a case as *S. marcescens* BSI occurring in a patient hospitalized in a NJ Hospital from January through March 2005. Cases were identified by review of infection-control, microbiologic, and medical records. To determine common exposures, we reviewed the medical records of case patients for clinical and demographic characteristics and exposure to devices, procedures, and medications. We also reviewed pharmacy procedures, infection-control policies, and practices in the operating room and CSU. All results of environmental cultures performed by infection-control practitioners, including results of culture of medical equipment and samples from opened and unopened bags of intravenous solution, were similarly reviewed.

NJ Hospital clinical and environmental specimens were sent to the NJ Hospital microbiology laboratory for culture using standard methods. A representative sample of *S. marcescens* isolates from LA Hospital case patients and all isolates from the NJ Hospital (clinical and environmental) were sent to the CDC DHQP laboratory for species confirmation and PFGE analysis [17–19].

Results. Five case patients, who received a diagnosis of *S. marcescens* BSI during 2–10 March 2005, were identified in the NJ Hospital. All were admitted electively to undergo cardiovascular surgical procedures and received intravenous MgSO₄ from compounding pharmacy X within 48 h prior to the onset of BSI signs. Review of infection-control procedures identified no major breaches. Culture of samples of intravenous infusion administered to 1 patient at the time of BSI symptom onset and from the remaining MgSO₄ for that patient yielded *S. marcescens*. Culture of a sample from an unopened bag of intravenous MgSO₄ in the same lot also yielded *S. marcescens*.

S. marcescens isolates from all patients at the NJ Hospital and from the open and unopened bags of MgSO₄ had indistinguishable PFGE banding patterns from those of isolates from the 6 case patients at LA Hospital. The epidemiologic and molecular links of the 2 outbreaks prompted a multistate investigation.

MULTISTATE CASE-FINDING AND COMPOUNDING PHARMACY X INVESTIGATIONS

Methods

For the multistate investigation, we defined a suspect case as *S. marcescens* BSI occurring within 72 h after receipt of intravenous MgSO₄ supplied by compounding pharmacy X from January 2004 through March 2005. We defined a confirmed case as a suspect case with a clinical isolate demonstrating a PFGE banding pattern related to the outbreak strain [17, 18]. A possible case was defined as a suspect case with a clinical isolate that was not available for PFGE analysis.

Case-finding was conducted using multiple methods: (1) contact of hospitals that received the known contaminated MgSO₄ lot according to sales records, (2) nationwide alert of public health officials using the CDC's Epidemic Information Exchange and health alert notifications, and (3) review of clinical isolates of *S. marcescens* from microbiology laboratories at institutions that received contaminated product. Persons reporting suspect cases completed a standard case-report form, which included demographic and clinical characteristics of case patients and the timing, doses, and source of intravenous MgSO₄ received.

CDC staff interviewed representatives of compounding pharmacy X to determine the distribution of the contaminated lots

and to learn about the infection-control practices employed during MgSO₄ compounding. The FDA and the State Board of Pharmacy conducted inspections of compounding pharmacy X's facility in March 2005.

Microbiologic and laboratory methods. A representative sample of *S. marcescens* isolates from LA Hospital case patients, all isolates from NJ Hospital, and the available isolates from suspect case patients were sent to the CDC DHQP laboratory for species confirmation and PFGE analysis [17–19]. Sterility testing and culture of samples from unopened MgSO₄ bags was performed by the FDA Northeast Regional Laboratory (Jamaica, NY). All FDA isolates were sent to the CDC DHQP laboratory for PFGE analysis and comparison with the outbreak strain.

Statistical analysis. All data were collected on standardized forms and analyzed using SAS software (SAS Institute) or EpiInfo, version 3.3.2 (CDC). Statistical tests are described in the Part 1 Methods section.

Results

Interviews with representatives from compounding pharmacy X revealed that the initial contaminated lot discovered in NJ (lot A) contained 240 units that were shipped to 5 hospitals in 5 states, including NJ. Two of the remaining 4 hospitals identified case patients with *S. marcescens* BSI upon notification. Because LA Hospital did not receive MgSO₄ from lot A, we determined that >1 lot was contaminated. Case-finding was subsequently broadened to include cases of *S. marcescens* BSI occurring after infusion with MgSO₄ from any lot prepared and distributed by compounding pharmacy X from January 2004 to the present time.

A total of 50 suspect cases in 11 states (figures 1 and 2) were identified. Eighteen cases met the definition for confirmed *S. marcescens* BSI. Seven of 50 case patients did not have isolates available for testing and were considered to have possible cases. The remaining 25 isolates were genetically unrelated by PFGE and thus excluded. Confirmed cases were diagnosed from 5 January through 26 March 2005 (figure 1) and involved 5 states: California (6 cases), NJ (5 cases), North Carolina (3 cases), New York (2 cases), and Massachusetts (2 cases). The clinical characteristics of the 18 confirmed case patients are described in table 2.

S. marcescens isolates from the 18 case patients and unopened bags of MgSO₄ demonstrated genetically related PFGE banding patterns (within 3 bands difference), supporting our hypothesis that the MgSO₄ was the source of the outbreak (figure 2) [18]. The FDA performed sterility testing on 20 units from lot A, 3 (15%) of which yielded growth of *S. marcescens*, which was confirmed by PFGE to be indistinguishable from the outbreak strain. Sterility testing of samples from unopened bags of MgSO₄ from other lots revealed that 2 (10%) of 20 units from

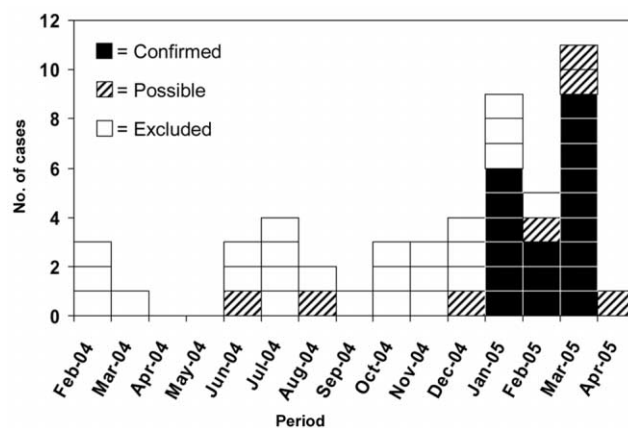


Figure 1. Cases of *Serratia marcescens* bloodstream infection following infusion with magnesium sulfate solution (MgSO₄) from compounding pharmacy X in 50 patients in multiple states during January 2004–May 2005. A confirmed case was defined as *S. marcescens* bloodstream infection occurring within 72 h after receipt of intravenous MgSO₄ supplied by compounding pharmacy X from January 2004 through March 2005 in which the isolate matched the outbreak strain. A possible case was defined as *S. marcescens* bloodstream infection occurring within 72 h after receipt of intravenous MgSO₄ supplied by compounding pharmacy X from January 2004 through March 2005 in which no isolate was available for testing. An excluded case was defined as an *S. marcescens* bloodstream infection occurring within 72 h after receipt of intravenous MgSO₄ supplied by compounding pharmacy X from January 2004 through March 2005 in which the isolate did not match the outbreak strain.

an additional lot (lot B) yielded growth of multiple gram-negative bacteria, including *Pseudomonas aeruginosa*, *Alcaligenes xylosoxidans*, *Acinetobacter lwoffii*, and *Chromobacterium violaceum*. Case-finding for cases of infection with the latter 3 organisms among purchasers of MgSO₄ from compounding pharmacy X identified no related cases of BSI. Specific lot numbers of MgSO₄ administered to patients were only available for NJ case patients.

Compounding pharmacy X is operated as an outsourcing pharmacy (i.e., a pharmacy that provides medications to other pharmacies) and prepared compounded products for hospitals in every state, except Ohio. The pharmacy compounded MgSO₄ in multiple doses and purchased sterile components from pharmaceutical manufacturers. Each lot of 50-mL admixtures of MgSO₄ consisted of 240 units, and 1 lot was typically sent to multiple facilities. No recent changes in the compounding process were reported by the company. The State Board of Pharmacy, the FDA, and compounding pharmacy X representatives each investigated the facility where the product was prepared to determine the source of contamination. The pharmacy did not test and retain samples of each lot for sterility, and no definitive source could be identified.

On the basis of the results of the Los Angeles and NJ investigations, compounding pharmacy X voluntarily recalled lot

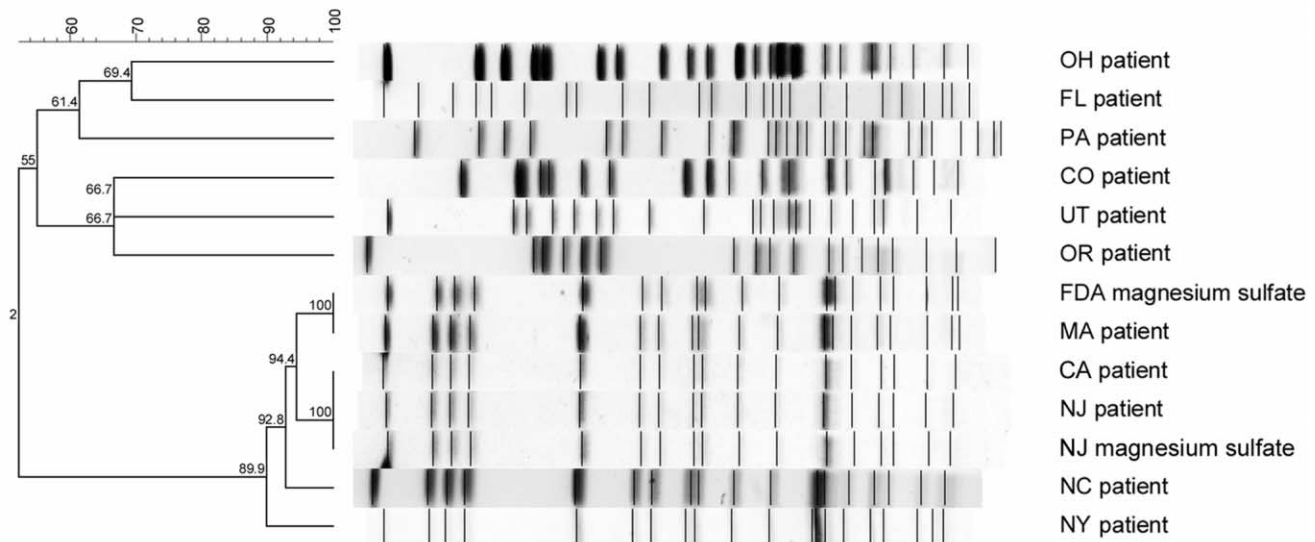


Figure 2. Dendrogram of *Serratia marcescens* isolates from a multistate outbreak of bloodstream infection caused by contaminated magnesium sulfate solution in the United States during January 2004–May 2005. FDA, US Food and Drug Administration.

A on 18 March 2005. On 8 April 2005, after learning of the contamination of lot B, compounding pharmacy X issued a second recall of all lots of 50-mL admixtures of $MgSO_4$ because of “a potential lack of sterility assurance for these products” [20]. The firm voluntarily ceased production and distribution of the product. No additional cases of *S. marcescens* BSI associated with compounding pharmacy X $MgSO_4$ were identified after the second product recall.

DISCUSSION

We describe a national health care–associated outbreak of *S. marcescens* BSI caused by contaminated intravenous medication produced by a compounding pharmacy. Initially, it appeared that compounding pharmacy X was a pharmaceutical manufacturer; however, the investigation revealed that the company adhered to the limited regulations of a compounding pharmacy. This presented challenges associated with oversight, outbreak detection, and authority to intervene during an outbreak that do not occur with pharmaceutical manufacturers. The multi-state distribution of large quantities of sterile compounded medications, coupled with critical differences between pharmaceutical compounding and manufacturing, have important patient safety implications for clinicians, pharmacists, public health officials, and the general public.

Because of the concern that some pharmacies were manufacturing medications without prescriptions under the limited regulation of compounding [21, 22], the FDA released guidance

to assist the investigation of compounding pharmacies [21]. These guidelines, however, are not enforceable by law. Rather, compounding pharmacies are regulated by state laws governing the practices of pharmacies. Two of 9 activities considered to be inappropriate for compounding pharmacies that are outlined in the FDA document are relevant to this investigation.

The first act deemed to be inappropriate by the FDA is the compounding of drugs in anticipation of receiving prescriptions, except in very limited quantities in relation to the amount of drugs compounded after receiving valid prescriptions. Compounding pharmacy X stated during the investigation that they did not receive prescriptions for individual patients on which to base anticipatory batches, nor had they ever received them. After inspection of compounding pharmacy X, the State Board of Pharmacy issued a warning notice indicating that compounding pharmacy X was not operating as a pharmacy because of preparation of anticipatory batches of compounded medication without prescriptions. This represents a failure to operate in conformance with applicable state laws regulating pharmacy practice—the second activity deemed inappropriate by the FDA.

Several factors delayed the detection of this outbreak. Most intravenous solutions are purchased from wholesale distributors who purchase these products from pharmaceutical manufacturers that adhere to FDA requirements. The $MgSO_4$ from compounding pharmacy X appeared to be similar to manufactured products, which may have delayed suspicion of the

Table 2. Demographic and clinical characteristics of confirmed cases of *Serratia marcescens* bloodstream infection caused by contaminated magnesium sulfate solution in 5 states, January–March 2005.

Characteristic	Case patients (n = 18)
Age, median years (range)	65 (17–88)
Male sex	13 (72)
Underwent cardiothoracic surgery in the 14 days prior to infection	8 (44)
Hospitalized in an intensive care unit at time of illness	7 (39)
Signs and symptoms	
Temperature $\geq 38.3^{\circ}\text{C}$	18 (100)
Hypotension ^a	4 (22)
Clinical outcome	
Required blood pressure support during illness	6 (33)
Death due to <i>S. marcescens</i> infection	0 (0)
Death unrelated to <i>S. marcescens</i> infection	1 (6)
Recovered	17 (94)

NOTE. Data are no. (%) of patients, unless otherwise indicated. A confirmed case was defined as *S. marcescens* bloodstream infection occurring within 72 h after receipt of intravenous magnesium sulfate solution supplied by compounding pharmacy X from January 2004 through March 2005 that matches the outbreak strain.

^a Mean blood pressure, <70 mmHg.

solution as a source of infection at the LA Hospital. Neither hospital pharmacy was aware that the product was compounded; there was no specific indication on the package labeling, and the company's Web site did not specify that the product was compounded. Of note, a similar product in the same dose is available from a pharmaceutical manufacturer [23] that differs from the compounding pharmacy X product only in total volume (100 mL vs. 50 mL). Prior to this outbreak, many involved clinicians, pharmacy staff, and public health officials were unaware of the differences between compounded and manufactured sterile products.

One important quality-control issue that separates pharmaceutical manufacturing from compounding is the requirement for manufacturers to test and retain samples of each lot of intravenous medication for sterility. The US Pharmacopeial Convention, an FDA-recognized compendium that sets standards for pharmacies involved in the compounding of sterile products [2, 24], states that compounders are responsible for ensuring that compounded sterile products are "correctly sterilized" [2, p. 1930]. However, there is no requirement for sterility testing of the final compounded product or for retention of product for future sterility testing. Because no MgSO_4 was retained or tested for sterility after production by compounding pharmacy X, the FDA and the CDC had to locate remaining unopened product from hospitals to perform testing, which may have further delayed identification of the outbreak.

Another important distinction between compounding pharmacies and manufacturers is manipulation of previously sterilized components by compounders, leading to an increased likelihood of the final product being contaminated. MgSO_4

production by compounding pharmacy X required individual handling of each bag by a pharmacist, which is standard practice for a compounding pharmacy. Manufacturers produce large quantities of pharmaceuticals with automated machines, decreasing human handling, and most admixing and dilution steps occur prior to final sterilization. When contamination occurs during manufacture, it is more likely to be detected by sterility testing at the end of the process. The individual handling of the product during compounding increases the likelihood of intermittent contamination, because each unit may not be subject to the same breach in infection control. An outbreak resulting from intermittent contamination is less likely to cause an obvious cluster of disease, making an outbreak difficult to detect. The widespread distribution of contaminated product to multiple states further decreases the likelihood of outbreak detection, because several state health departments need to be simultaneously alerted.

A possible source of contamination in this outbreak was the hands of the compounding pharmacist(s). Several facts support this mechanism. First, only 50-mL bags of the product were involved, despite the fact that several other larger dose bags of MgSO_4 are made by the company using the same process and components. Because of its small size, a 50-mL bag of solution is difficult to manipulate without touching the entry port where medication is injected. Secondly, the discovery of polymicrobial contamination of lot B with multiple gram-negative species, several of which are typically environmental organisms, supports product handling as the most likely mode of transmission.

Several limitations to this investigation exist. Neither the FDA nor compounding pharmacy X identified the source of

contamination of the MgSO₄ during the compounding process; however, some evidence suggests contamination from product handling. Secondly, *P. aeruginosa*, one of the organisms identified in lot B, is too commonly isolated to perform adequate case-finding nationally. Therefore, it is likely that the number of BSI cases caused by the contamination of this product presented in our article is an under-representation of the actual number.

Despite having generally lower quality-control standards than pharmaceutical manufacturers, compounding pharmacies are increasingly used by hospitals as a source of parenteral medications—often because of their lower cost. Hospital pharmacists and administrations should be aware of the risks associated with compounded sterile medications and should consider them before purchasing the products. Investigators should also take these risks into account when investigating an outbreak of BSI.

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References

- Galson S. Statement before the senate committee on health, education, labor and pensions hearing on “Federal and State Role in Pharmacy Compounding and Reconstitution: Exploring the Right Mix to Protect Patients.” Washington, DC: 2003. Available at: <http://www.fda.gov/ola/2003/pharmacycompound1023.html>. Accessed 30 May 2006.
- Kastango ES, Bradshaw BD. USP chapter 797: establishing a practice standard for compounding sterile preparations in pharmacy. *Am J Health Syst Pharm* 2004; 61:1928–38.
- Centers for Disease Control and Prevention. Exophiala infection from contaminated injectable steroids prepared by a compounding pharmacy—United States. *MMWR Morb Mortal Wkly Rep* 2002; 51: 1109–12.
- Civen RH, Alexander RC, Brunner W, et al. An outbreak of *Serratia marcescens* infections following epidural and intra-articular steroid injections associated with betamethasone compounded at a community pharmacy. In: Program and abstracts of the 39th Annual Meeting of the Infectious Diseases Society of America (San Francisco). Alexandria, VA: Infectious Diseases Society of America, 2001:201.
- Perz JF, Craig AS, Stratton CW, Bodner SJ, Phillips WE Jr, Schaffner W. *Pseudomonas putida* septicemia in a special care nursery due to contaminated flush solutions prepared in a hospital pharmacy. *J Clin Microbiol* 2005; 43:5316–8.
- Jones TF, Feler CA, Simmons BP, et al. Neurologic complications including paralysis after a medication error involving implanted intrathecal catheters. *Am J Med* 2002; 112:31–6.
- Held MR, Begier EM, Beardsley DS, et al. Life-threatening sepsis due to *Burkholderia cepacia* from contaminated intravenous flush solutions prepared by a compounding pharmacy in another state. *Pediatrics* 2006; 118:e212–5.
- Grohskopf LA, Roth VR, Feikin DR, et al. *Serratia liquefaciens* bloodstream infections from contamination of epoetin alfa at a hemodialysis center. *N Engl J Med* 2001; 344:1491–7.
- Ehrenkranz NJ, Cleary T. *Serratia marcescens* contaminated disinfectants. *Lancet* 1981; 1:1154–5.
- Nakashima AK, Highsmith AK, Martone WJ. Survival of *Serratia marcescens* in benzalkonium chloride and in multiple-dose medication vials: relationship to epidemic septic arthritis. *J Clin Microbiol* 1987; 25: 1019–21.
- Nakashima AK, McCarthy MA, Martone WJ, Anderson RL. Epidemic septic arthritis caused by *Serratia marcescens* and associated with a benzalkonium chloride antiseptic. *J Clin Microbiol* 1987; 25:1014–8.
- Vigeant P, Loo VG, Bertrand C, et al. An outbreak of *Serratia marcescens* infections related to contaminated chlorhexidine. *Infect Control Hosp Epidemiol* 1998; 19:791–4.
- Sartor C, Jacomo V, Duvivier C, Tissot-Dupont H, Sambuc R, Drancourt M. Nosocomial *Serratia marcescens* infections associated with extrinsic contamination of a liquid nonmedicated soap. *Infect Control Hosp Epidemiol* 2000; 21:196–9.
- Hejazi A, Aucken HM, Falkiner FR. Epidemiology and susceptibility of *Serratia marcescens* in a large general hospital over an 8-year period. *J Hosp Infect* 2000; 45:42–6.
- Passaro DJ, Waring L, Armstrong R, et al. Postoperative *Serratia marcescens* wound infections traced to an out-of-hospital source. *J Infect Dis* 1997; 175:992–5.
- CDC definitions for nosocomial infections, 1988. *Am Rev Respir Dis* 1989; 139:1058–9.
- Wrestler JC, Lipes BD, Birren BW, Lai E. Pulsed-field gel electrophoresis. *Methods Enzymol* 1996; 270:255–72.
- 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; 33:2233–9.
- NCCLS. Performance standards for antimicrobial susceptibility tests. Wayne, PA: NCCLS, 2004; 24:M100–S14.
- PharMEDium. PharMEDium services initiates nationwide magnesium solution recall of all 50 ml admixtures of MgSO₄ in 5% dextrose because of a potential lack of sterility assurance. Available at: http://www.fda.gov/oc/po/firmrecalls/pharmedium04_05html. Accessed 21 February 2006.
- Guidance for FDA staff and industry compliance policy guides manual section 460.200 pharmacy compounding. Available at: http://www.fda.gov/OHRMS/DOCKETS/98fr/02D-0242_gdl0001.pdf. Accessed 6 February 2006.
- Allen LV Jr. Contemporary pharmaceutical compounding. *Ann Pharmacother* 2003; 37:1526–8.
- Food and Drug Administration. Prescription and over-the-counter drug product list. 17th ed. Washington, D.C. Cumulative supplement number 6, 1997. Available at: <http://www.pharmwatch.org/comp/cpg.shtml>. Accessed 30 May 2006.
- Pharmaceutical compounding—sterile preparations. In: The United States pharmacopeia, 27th rev., and the national formulary. 22nd ed. Rockville, MD: United States Pharmacopeial Convention, 2004: 2350–70.