

Editorial

Nosocomial *Burkholderia cepacia* Outbreaks and Pseudo-Outbreaks

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Burkholderia cepacia is an aerobic, gram-negative, nonfermentative bacillus widely distributed in the environment, including in water, soil, fruits, and vegetables. *B. cepacia* often is found in liquid reservoirs or moist environments, reflecting the organism's innate ability to survive and grow in water sources with minimal nutritional sources. Since discovered as a phytopathogen, its microbiologic characterization has taken a circuitous path. First characterized microbiologically in the 1950s and 1960s, the organism was placed in the genus *Pseudomonas* in 1984.¹ However, subsequent characterization of the genus *Pseudomonas*, including rRNA-DNA hybridization, led to the proposal to establish a new genus *Burkholderia* with the type strain being *B. cepacia*.

The epidemiology of *B. cepacia* as a nosocomial pathogen has taken an equally interesting course. The first nosocomial outbreak reported was in 1966, when an outbreak of urinary tract infections in children was traced to contaminated water that was used as a bladder irrigant during cystoscopy.² Since that time, *B. cepacia* has been associated with many real and pseudo-outbreaks of bloodstream, urinary tract, respiratory tract, and other nosocomial infections.³ These outbreaks have been traced to a wide variety of sources including tap, distilled, or deionized water and intrinsically or extrinsically contaminated chlorhexidine, topical cocaine, benzalkonium chloride, povidone-iodine, savlon, quaternary ammonium solutions, or respiratory therapy equipment.

Much of the epidemiology of *B. cepacia* has been elucidated because of the propensity of this pathogen to cause colonization and infection in cystic fibrosis patients. In the mid-1980s, several authors showed that *B. cepacia* was increasing in prevalence in cystic fibrosis patients and that colonization and infection was associated with increased hospitalization, rapid pulmonary function decline, and death.⁴⁻⁶ In this population, the organism causes chronic respiratory colonization and intermittent exacerbations of bronchitis or pneumonia. Active surveillance in approximately 100 cystic fibrosis centers since 1986 has documented an annual incidence and prevalence of 1% and 3.5%, respectively. Studies have documented nosocomial transmission of *B. cepacia* in cystic fibrosis patients, associated with contaminated respiratory therapy equipment and via person-to-person transmission.⁷⁻⁹ In addition, *B. cepacia* has been documented to be transmitted in cystic fibrosis summer camps and in other social settings involving these patients.^{10,11} A strong association also has been found between *B. cepacia* colonization and prior aminoglycoside therapy, thus reemphasizing the need to review guidelines for antimicrobial usage and prophylaxis in patients with cystic fibrosis. These and other findings have led to the recommendation for cohorting of *B. cepacia*-colonized or *B. cepacia*-infected cystic fibrosis patients and for placement of these patients in contact isolation.¹¹ Implementation of these measures has led to decreased nosocomial transmission.¹²

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Considerable controversy has surrounded the issue of the source of *B cepacia* in cystic fibrosis patients. Since the organism is ubiquitous in the environment, it would be natural to think that this is the most likely source. However, Butler et al evaluated a number of environmental sources surrounding cystic fibrosis patients; *B cepacia* was recovered from 12 (21.8%) of 55 samples, but none of the strains had the same genotype as those associated with morbidity and mortality in the patients.¹³ Similarly, when Pegues et al studied *B cepacia* transmission in a cystic fibrosis summer camp, they found no correlation between environmental and patient *B cepacia* strains.¹¹ These and other studies of nosocomial transmission of *B cepacia* in cystic fibrosis patients suggest that contaminated respiratory therapy equipment and person-to-person transmission are more likely than the environment to be the source of colonization or infection.

The frequency of nosocomial *B cepacia* infections appears to be increasing.¹⁴ Although several factors may be contributing to this increase, the most important may be the microbiology laboratory's increased ability to isolate and identify this organism. In 1987, Tablan et al¹⁵ evaluated the proficiency of microbiology laboratories at cystic fibrosis centers and showed that, although 105 (95%) of 111 laboratories could identify *B cepacia* when given an isolate, only 36 (32%) of 115 could isolate and identify *B cepacia* from inoculated mock sputa. Subsequently, Carson et al¹⁶ showed that *B cepacia* selective media enhanced recovery rates; 73 (97%) of the 77 previously mentioned cystic fibrosis center microbiology laboratories were able to isolate and identify *B cepacia* from inoculated mock sputa when they used *B cepacia* selective media. Since that time, many institutions, particularly those where cystic fibrosis patients are seen, have incorporated the use of *B cepacia* selective media into their laboratory procedures.

An important tool in many epidemiologic investigations is determining the relatedness of strains identified from different patients or from patients and epidemiologically identified potential sources of colonization or infection. Such typing systems have been critical in unraveling the complex epidemiology of *B cepacia*. A study by Rabkin et al¹⁷ documented that a number of typing systems could be applied to *B cepacia* and could differentiate related from nonrelated strains. *B cepacia* was one of the first strains to be ribotyped, and ribotyping and pulsed-field gel electrophoresis have become the gold standard typing methods for this organism.¹⁸

The paper by Reboli et al¹⁹ shows that *B cepacia* can colonize or infect the respiratory tract of

patients without cystic fibrosis if directly inoculated into the respiratory tract. Their investigation of a cluster of intensive-care-unit patients with *B cepacia* colonization or infection identified contaminated albuterol as the source. Unfortunately, an epidemiologic investigation was not conducted, and the reason for cultures of the albuterol was not stated. Was this just one item in an extensive culture survey they conducted? Question also remains about the exact source of the contamination. Was it really extrinsic, or could it have been intrinsic contamination? Obtaining cultures of only 20 vials of a product with low-level contamination would not exclude the possibility of intrinsic contamination. Further, if this outbreak was occurring at the same time as the outbreak associated with intrinsic contamination of albuterol, that may have been the source of this outbreak, also. If the source of the outbreak was extrinsic contamination of the albuterol, what was the source of the contamination? Was water or other liquid that could have led to contamination used in the nebulizer? Once contaminated, use of the vials as multidose medications would have facilitated further transmission.

Another interesting chapter in the epidemiologic life of *B cepacia* occurred in the early 1980s, at which time there was a cluster of patients in whom *B cepacia* was recovered from blood cultures.²⁰ This apparent nosocomial bloodstream outbreak was found to be a cluster of pseudobacteremias; despite positive blood cultures, the patients did not have signs or symptoms consistent with a bloodstream infection. The cluster was traced epidemiologically to a povidone-iodine solution that had been used both to disinfect the blood culture bottles and as an antiseptic for preparing the patient's blood culture site. Subsequent cultures of unopened bottles of this product documented intrinsic contamination of the antiseptic. This was the first instance of intrinsic contamination of povidone-iodine antiseptic, a solution previously thought not to be capable of supporting bacterial growth. Investigation of the povidone-iodine manufacturing plant documented *B cepacia* contamination of the water distribution system. It has been hypothesized that *B cepacia* from the water could produce a slime, colonize the pipes of the water distribution system, protect itself by this slime from high concentrations of free iodine, and gradually develop resistance to the antibacterial activity of the povidone-iodine. Since 1980, there have been several other episodes of intrinsic contamination of povidone-iodine solutions, leading to both infections and pseudoinfections.^{20,21}

In this issue of the Journal, Gravel-Tropper et al²² describe an unusual cluster of patients with positive blood cultures for *B cepacia* in a neonatal inten-

sive-care unit. Medical record review suggested pseudobacteremia. Unfortunately, neither a case-control nor a cohort study was conducted. However, a review of case-patient exposures revealed that all had blood-gas determinations, and subsequent cultures of the blood-gas analyzer were positive for the same genotype of *B cepacia*. Several questions remain unanswered. Why were the initial cultures of the blood-gas analyzer negative for *B cepacia*? Why were 12 of 13 *B cepacia*-positive blood cultures obtained by the evening or night shift nurses? Either a systematic observational study or a questionnaire of the nursing personnel on actual practices might have identified whether the evening-shift and night-shift nurses were more likely than day-shift nurses to inoculate blood cultures after inoculation of the blood-gas analyzer. The exact mechanism of contamination of the blood-gas analyzer is unclear. Was someone diluting the blood or other solutions with water? Although it is stated that an investigation was initiated after the first two case-patients, it is unclear why it took 2½ years to solve the outbreak. An initial epidemiologic study, rather than merely a case review and culture survey, may have led to the earlier identification of the source of the outbreak.

The two outbreaks reported in this issue of the Journal demonstrate the importance of investigating clusters of *B cepacia* infections. When small clusters of colonization or infection with this organism occur, it should alert infection control personnel to the possibility of an outbreak. Ideally, once a cluster is identified, an intensive epidemiologic investigation should be conducted, using either a case-control or cohort approach, together with a laboratory investigation that includes molecular typing of the organism. In general, cultures of inanimate and animate objects should be directed by the epidemiologic results. Such investigations usually lead to the identification of the source, implementation of control measures, and termination of the outbreak. The epidemiology of *B cepacia* is continuing to be unraveled. Intrinsic or extrinsic *B cepacia* contamination of solutions or devices remains a potential hazard to our patients. Appropriate aseptic technique and education of our colleagues about disinfection, sterilization, and other infection control techniques can decrease the risk of such outbreaks in the future.

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