

Clinical Significance of *Bacillus* Species Isolated From Blood Cultures

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ABSTRACT: To determine the clinical significance of blood isolates of *Bacillus*, we reviewed all blood cultures obtained at North Carolina Memorial Hospital between 1981 and 1985. Over the five-year study period the number of patients (incidence per 10,000 hospital admissions) from whom *Bacillus* was isolated increased from 4.97 in 1981 to 12.5 in 1985. The incidence per 1,000 blood cultures also increased from 1.12 in 1981 to 2.33 in 1985. Review of the medical records of 78 of the 95 patients (82%) with positive cultures allowed retrospective classification of five isolates (6.4%) as clinically significant, 33 isolates (42.3%) as possibly significant, and 40 isolates (51.3%) as nonsignificant. Underlying diseases in patients with clinically significant *Bacillus* bacteremia included burn trauma in two, leukemia in one, carcinoma in one, and gastrointestinal hemorrhage in one. All isolates judged to be clinically significant and the majority of possibly significant isolates were *B. cereus*. We conclude that the isolation of *Bacillus* species from blood cultures is clinically significant in 5% to 10% of cases, that the incidence of *Bacillus* bacteremia is increasing, and that burn trauma should be added to the list of conditions known to predispose to clinically significant *Bacillus* bacteremia.

THE GENUS *Bacillus* comprises a heterogeneous group of motile, aerobic, spore-forming, gram-positive microorganisms.¹ *Bacillus* species are ubiquitous in nature and are frequently discounted as contaminants when isolated in cultures of clinical material. However, *Bacillus* spp are capable of causing a range of human infection such as superficial wound or skin infections²⁻⁶ closed space infections such as endophthalmitis,⁷ septic arthritis,⁶ or fasciitis and myositis^{4,5,8}; and severe systemic diseases such as pneumonia,^{2,4,5,9,10} meningitis,^{5,11,12} and endocarditis.^{4,8,11,13} Bacteremia rarely accompanies superficial wound infections, occasionally accompanies closed space infections, and frequently accompanies severe systemic diseases.¹⁴ *Bacillus* spp are increasingly recognized as serious pathogens in immunocompromised patients.^{4,9,13,15,16}

To determine the significance of blood isolates of this organism at a university hospital we attempted to study the clinical isolates and medical records of all patients seen at North Carolina Memorial Hospital from 1981 through 1985 identified by the microbiology laboratory as having

Bacillus spp detected in blood cultures. The medical records of 78 of the 95 patients (82%) with positive cultures were available for retrospective review of patient characteristics, clinical course, possible source of bacteremia, and physician's interpretation of the laboratory findings. Using strict criteria, isolates were retrospectively classified as significant (S), possibly significant (PS), or nonsignificant (NS). We present here our results of speciating these 78 isolates and interpreting their clinical significance.

MATERIALS AND METHODS

The study was conducted at North Carolina Memorial Hospital, a 580-bed acute-care teaching hospital for the University of North Carolina School of Medicine. Records of all blood cultures processed by the microbiology laboratory during the years 1981 through 1985 were reviewed using a computerized retrieval system for the identification of *Bacillus* spp. Of the 95 strains identified, 89 were available for speciation and susceptibility testing. Charts of 78 patients were available for review. A retrospective determination of the clinical significance of the blood culture was made by one of us (S.M.S.) using criteria adapted from Broome.¹⁷ Patients were considered to have significant bacteremia if they met one of the following criteria: (1) two or more positive blood cultures for the organism, (2) one positive blood culture

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TABLE 1. Distribution of Clinical and Laboratory Features in 78 Patients Determined to Have Significant (S), Possibly Significant (PS), or Nonsignificant (NS) Isolates of *Bacillus* spp

	Significance of Blood Culture		
	S	PS	NS
Number of patients	5 (6%)	33 (42%)	40 (51%)
Male	3 (60%)	17 (52%)	23 (58%)
Female	2 (40%)	16 (48%)	17 (42%)
White	4 (80%)	15 (45%)	28 (70%)
Nonwhite	1 (20%)	18 (55%)	12 (30%)
Mean age, years (range)	59 (12-92)	46 (1-91)	40 (0-77)
Location			
Ward	3	17	24
ICU	2	10	7
Emergency room	-	6	9
Service			
Medicine	2	9	22
Pediatrics	-	2	5
Surgery	2	13	3
Obstetrics/Gynecology	1	3	1
Emergency room	-	6	9
≥2 blood cultures obtained	4	24	23
Blood culture with >1 organism isolated	1	13	4
Physician's assessment			
Significant	4	10	1
Nonsignificant	-	12	16
Not mentioned	1	11	23
Fever (> 38.3 C)	4	24	9
Hypotension	1	3	2
Tachycardia	4	17	17
Tachypnea	3	20	19
Oliguria	1	1	-
Peripheral intravenous line	3	14	15
Central intravenous line	1	7	3
Hickman catheter	1	4	-
Arterial catheter	2	7	4
Respiratory therapy	1	10	6
Oxygen therapy	2	8	7
Endotracheal tube	2	6	5
Nasogastric tube	1	4	4
Indwelling bladder catheter	2	6	7
Antibiotics	1	8	14
Antacids or H ₂ blockers	1	5	4
Steroids	0	1	3
Cytotoxic agents	1	3	1
Increased WBC	2	18	14
Elevated serum creatinine	-	4	-
<i>Bacillus</i> spp			
<i>B. cereus</i>	5	23	18
<i>B. megaterium</i>	-	4	4
<i>B. subtilis</i>	-	2	2
<i>B. pumilus</i>	-	1	4
<i>B. polymyxa</i>	-	1	2
Other	-	2	6

and an isolate of the organism from another site, or (3) one positive blood culture plus three clinical or laboratory criteria suggestive of sepsis (oliguria, hypotension, tachycardia, tachypnea, fever, an elevated peripheral leukocyte count, or a recently elevated serum creatinine value). Cultures judged to be possibly significant included those from patients whose clinical condition was complicated by other illnesses or by the isolation of other organisms from the bloodstream.

The details of the blood culture methods used at North Carolina Memorial Hospital have been previously described.¹⁸ Organisms were identified as *Bacillus* spp, non-*B. anthracis*, in the microbiology laboratory if they were motile, catalase positive, aerobic spore-forming gram-positive rods. All

isolates obtained from blood cultures were stored at -70 C in 10% skim milk (Difco, Detroit, Mich). Isolates were speciated in the hospital epidemiology laboratory according to colonial morphology after 24 to 48 hours' incubation at 35 C on sheep blood agar, Gram's stain morphology, and results from API 50CH and API 20E biochemical profiles using a schemata provided by API (Analytab Products, Plainview, NY).¹⁹ This system correctly identified seven different American Type Culture Collection (ATCC) strains of *Bacillus*: *B. cereus* 14579, *B. polymyxa* 842, *B. sphaericus* 14577, *B. macerans* 8244, *B. circulans* 34513, *B. megaterium* 14581, and *B. mycoides* 6462.

RESULTS

Bacillus spp were isolated from 98 blood cultures from 95 patients at North Carolina Memorial Hospital between 1981 and 1985. The number of patients from whom *Bacillus* was isolated (incidence per 10,000 hospital admissions) was as follows: 1981—11 patients (4.97), 1982—13 patients (5.88), 1983—15 patients (6.58), 1984—27 patients (11.5), and 1985—29 patients (12.5). The incidence of *Bacillus* per 1,000 blood cultures also increased in this time period: 1981—1.12, 1982—1.42, 1983—1.43, 1984—2.33, and 1985—2.33. The increased incidence of isolation may be explained in part by the limited institution of the isolator technique for blood cultures in October 1984.

Review of the medical records of 78 of the 95 patients with positive cultures enabled retrospective classification of five isolates (6.4%) as significant, 33 isolates (42.3%) as possibly significant, and 40 isolates (51.3%) as nonsignificant (Table 1). None of the patients with missing charts had more than one culture positive for *Bacillus* spp. Only two patients had more than one blood culture positive for *Bacillus* spp within a 24-hour period, and two others had *Bacillus* spp cultured from a second site. Patients judged to have significant bacteremia were somewhat older than other patients, but the three groups were similar with respect to gender, race, hospital location, and hospital service. Five patients had cultures retrospectively determined to be significant; the physicians assessed four cultures to be significant at the time of isolation, but made no mention of the laboratory finding for the majority of patients whose cultures were assessed as nonsignificant. Patients whose cultures were in the significant category tended to have had a greater number of vascular and respiratory procedures, but they had no difference in antibiotic, antacid, steroid, or cytotoxic therapy.

TABLE 2. Characteristics of Patients With Significant *Bacillus* Infections

Patient	Age, Sex	Service	Primary Diagnosis	Blood Cultures No. Positive/Total	Other Cultures	Comments
1	53, M	Medicine	Leukemia, intracranial hemorrhage	3/many	Hickman site (<i>Bacillus</i> sp)	Multiple brain abscesses attributed to <i>Bacillus</i> , white blood cell count 500/cu mm
2	92, F	Medicine	Gastrointestinal hemorrhage	2/3	Urine (<i>P aeruginosa</i> , <i>E coli</i>)	Cellulitis at sight of peripheral intravascular line
3	77, M	Burn Unit	Burn, 65% total body surface	1/2	Wound biopsy: <i>Bacillus</i> sp	Multiple intravascular lines
4	12, M	Burn Unit	Burn, 92% total body surface	1/1	Respiratory tract (<i>Bacillus</i> sp) Blood (<i>S aureus</i>)	Multiple intravascular lines, three days after skin graft
5	51, F	Gynecology	Metastatic uterine carcinoma	1/2	None	Recent chemotherapy

All isolates judged to be significant were identified as *B cereus*. Isolates from possibly significant and nonsignificant groups were predominantly *B cereus*, but also included seven other species.

The characteristics of the five patients deemed to have significant cultures are outlined in Table 2. Underlying diseases included burn trauma (two patients), pelvic carcinoma (one patient), acute myelogenous leukemia (one), and gastrointestinal hemorrhage (one).

Isolates were determined to be possibly significant in 33 patients. Whereas 17 met clinical or laboratory criteria for significant bacteremia, 12 had coexisting conditions that could have accounted for the clinical findings and 13 had polymicrobial blood cultures without documentation of *Bacillus* spp from a second site. The most common underlying conditions were abdominal disease (ten), burn wounds (eight), and diarrhea (three).

DISCUSSION

The incidence of isolation of *Bacillus* species as a function of the number of blood cultures and the incidence of *Bacillus* bacteremia as a function of number of hospital admissions gradually increased between 1981 and 1985 at our hospital. *Bacillus* remains an infrequent cause of bacteremia, however, even in a tertiary care institution. Our isolation rate of *Bacillus* from blood cultures of 0.1% to 0.2% is similar to the 0.1% to 0.4% reported in the literature.^{3,9,20}

Risk factors for *Bacillus* bacteremia identified in previous reports have included intravenous drug abuse,^{8,11,15} immunosuppressive medication and/or neutropenia,^{4,13,15,16} and indwelling intravenous catheters.^{4,13,15,16} Of our five patients with significant *Bacillus* bacteremia, only one had a previously described risk factor; Patient 1 had

neutropenia due to chemotherapy. The remaining four patients clearly had impaired host defenses by virtue of age (Patient 2), extensive burns (Patients 3 and 4), or metastatic carcinoma (Patient 5).

Burn trauma was a potential predisposing factor in two patients in the group with significant isolates and eight in the group with possibly significant isolates. Serious *Bacillus* infection of burn wounds has been previously noted.^{3,21} *B cereus* is known to produce hemolysins and phospholipases, which potentially play a role in its pathogenic action in burn wounds. In light of the number of patients with burn injuries determined to have significant or possibly significant bacteremia, we believe that blood cultures positive for *Bacillus* spp after burn injuries should not automatically be dismissed as contaminants, and burn wounds should be added to the list of conditions predisposing to *Bacillus* bacteremia.

Cotton et al¹³ reported that five of 17 immunosuppressed patients with *Bacillus* bacteremia had recurrent bacteremia, and in four of these a Hickman-Broviac catheter in place at the time of the original cultures had not been removed. More recently, Banerjee et al¹⁶ reported that 12 of 24 episodes of *Bacillus* bacteremia in patients with cancer were clinically significant, and that four of these 12 episodes were associated with a Hickman catheter. Four patients in our review were neutropenic and had catheters of this variety. All received appropriate antibiotics, and the organism was not recultured from three patients judged to have possibly significant bacteremia. Patient 1, however, had persistently positive blood cultures that did not revert to negative until after the catheter had been removed. We support the recommendations that chronic indwelling catheters be removed from high-risk patients who have two or more

cultures positive for *Bacillus*, and that further cultures be drawn when there has been only a single culture.^{13,16} Catheter removal alone was reported by Sliman et al⁴ to be sufficient therapy for two immunocompromised but nonneutropenic patients.

Bacillus species infrequently cause central nervous system infection, but meningitis, shunt infections, and brain abscess due to these organisms have been reported.^{5,8,11,12,14} Most patients with central nervous system infection had potential predisposing factors such as neurosurgery, often with the use of a temporary ventriculostomy, age less than 30 days, leukemia or other tumors, spinal anesthesia, intravenous drug abuse or endocarditis, and otitis or mastoiditis. Although the exact microbiologic cause of the brain abscesses in Patient 1 was not proven, it was likely *B cereus*.

Using the API 50CH and API 20E systems we were able to speciate most of the 78 strains of *Bacillus* reported in this paper. *Bergey's Manual of Systematic Bacteriology*¹ lists 34 well characterized species, but only a few are commonly pathogenic for man. Although local and systemic infections are most commonly caused by *B cereus*, followed by *B subtilis*, a variety of *Bacillus* species have been reported to cause human infection, including *B sphaericus*, *B licheniformis*, *B pumilus*, *B alvei*, *B macerans*, *B brevis*, *B circulans*, *B laterosporus*, *B coagulans*, and *B thuringiensis*.¹ In our series only *B cereus* was isolated from patients with significant bacteremia. This is in contrast with a recent report in which six of 12 isolates associated with bacteremia were non-*B cereus*.¹³ It seems likely that a variety of *Bacillus* spp may in fact be pathogenic for man at least occasionally, and especially in immunocompromised patients.

Microdilution susceptibility testing of all 89 of our clinically derived isolates revealed all *B cereus* strains to be susceptible to vancomycin, imipenem, chloramphenicol, clindamycin, gentamicin, and ciprofloxacin. Non-*B cereus* strains were most susceptible to vancomycin, imipenem, and ciprofloxacin. Disk susceptibility testing revealed that *B cereus* was rarely susceptible to penicillins, semisynthetic penicillins, or cephalosporins. In contrast, many non-*B cereus* strains were susceptible to penicillins, semisynthetic penicillins, and cephalosporins, but marked variability was noted among species. Conversely, *B cereus* was usually susceptible to clindamycin, but many non-*B cereus* isolates were resistant.¹⁸ Our results were similar to susceptibilities reported in the literature.^{2,4,5,7,8,16,22}

Since *Bacillus* spp are capable of causing serious

life-threatening infections, especially in immunocompromised patients, it is important to emphasize that most *B cereus* isolates and many non-*B cereus* isolates are resistant to penicillins, semisynthetic penicillins, and cephalosporins, including third-generation cephalosporins. For this reason, most recent publications advise the use of vancomycin^{4,13,14,16} or imipenem^{14,16} for empiric coverage in immunocompromised patients who have had either a gram-positive aerobic *Bacillus* isolated from blood, or therapy for an established *Bacillus* infection until the results of in vitro susceptibility tests are available. Case series and reviews also support the use of clindamycin for treatment of susceptible *Bacillus* infections.^{4,7,8,15} The combination of clindamycin and gentamicin has been reported to be more effective than either agent alone in curing experimental *B cereus* panophthalmitis in rabbits.⁷

Based on our series and reports in the literature, it appears that *Bacillus* spp should be considered as potential pathogens when isolated from the blood, especially in immunocompromised patients, intravenous drug abusers, and burn patients. Our retrospective review classified five of 78 (6.4%) blood isolates of *Bacillus* as clinically significant. This is similar to the range of 5% to 10% reported in the literature.¹³ Drugs that are active against *Bacillus* species should be included in the empiric coverage of patients who are immunocompromised and who have a gram-positive aerobic *Bacillus* isolated from their blood, at least until full identification has been made.

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