

## Bacteremia Caused by a Novel *Bordetella* Species, “*B. hinzii*”

B. T. COOKSON,<sup>1\*</sup> P. VANDAMME,<sup>2</sup> L. C. CARLSON,<sup>1</sup> A. M. LARSON,<sup>1</sup> J. V. L. SHEFFIELD,<sup>3</sup>  
K. KERSTERS,<sup>2</sup> AND D. H. SPACH<sup>3,4</sup>

Departments of Laboratory Medicine<sup>1</sup> and Medicine<sup>3</sup> and the Division of Infectious Diseases,<sup>4</sup> University of Washington, Seattle, Washington 98195, and Laboratorium voor Microbiologie, University of Ghent, Ghent, Belgium<sup>2</sup>

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***Bordetella* spp. cause respiratory tract diseases in warm-blooded animals. Only *Bordetella bronchiseptica* has been reported to cause bacteremia in humans, and this rare infection usually occurs with pneumonia in immunocompromised patients. We describe “*Bordetella hinzii*” bacteremia in an AIDS patient without a respiratory illness. Combining biochemical phenotyping with fatty acid analysis permitted preliminary identification of this previously undescribed pathogen; identity was confirmed by DNA-DNA hybridization. This report extends the spectrum of human infections caused by the bordetellae.**

Members of the genus *Bordetella* are well known to cause respiratory tract diseases in a variety of hosts. *Bordetella pertussis* and *Bordetella parapertussis* are etiologic agents of the human illness called whooping cough (15). *Bordetella bronchiseptica* is primarily a veterinary pathogen that causes snuffles in rabbits, atrophic rhinitis in swine, and kennel cough in dogs; rare human infections can result in pneumonia with or without bacteremia (20). Disease caused by *Bordetella avium* has been described only for poultry (rhinotracheitis) (7, 9, 17). Here, we report bacteremia caused by “*Bordetella hinzii*” in an immunocompromised patient without evidence of respiratory infection. “*B. hinzii*,” a recent addition to the genus *Bordetella* (18), can cause secondary or opportunistic respiratory infections in poultry. Although it is similar to *B. avium*, we distinguished this isolate by combining biochemical phenotyping with whole-cell fatty acid analysis and confirmed its identity by using additional genotypic methods. This report both introduces “*B. hinzii*” as a potential human pathogen and extends the spectrum of infections caused by the bordetellae.

**Case report.** A 42-year-old homosexual man with AIDS and an indwelling left subclavian Groshong catheter was admitted to Harborview Medical Center because of fever and left-upper-extremity swelling. Ten months prior to admission, the patient was admitted with *Pneumocystis carinii* pneumonia and dermatomal herpes zoster viral infection. Six months prior to admission, the patient developed fever, photophobia, aphasia, and right hemiplegia. Magnetic resonance imaging showed an area of focal linear enhancement in the left frontal-parietal cortex; a thrombosed intracranial artery with normal surrounding brain tissue was found at craniotomy. Pathologic examination of the thrombosed vessel revealed necrotizing arteritis and gram-negative cocci within macrophages. No organisms were seen in the surrounding cerebral cortex, and all cultures from biopsy material were sterile. A transthoracic echocardiogram showed no valvular vegetation. A left subclavian Groshong catheter was inserted. Vancomycin (1 g every 12 h) and ceftriaxone (2 g every 24 h) were administered intravenously for 4 weeks. At the completion of antimicrobial treatment, the catheter was not removed because venous access was difficult and blood tests were frequent. Azithromycin (250 mg daily)

was subsequently administered for 5 months, and during this period, the aphasia and hemiplegia resolved and follow-up computerized tomography demonstrated resolution of the abnormality.

Three months prior to admission, the patient's CD4 count was 31 cells per mm<sup>3</sup>. Three days prior to admission, pain and swelling developed in his left shoulder and arm. He denied coryza, dyspnea, or cough. The patient was an unemployed interior decorator who lived alone without pets. In recent months, he had neither traveled nor eaten unusual foods. Medications on admission, all oral and taken once daily, included 250 mg of azithromycin, 100 mg of dapsone, 150 mg of trazodone, and 500 mg of naproxen. The physical examination at admission showed a temperature of 39.3°C and left-upper-extremity erythema and edema. Initial laboratory studies showed a hematocrit of 30%, a leukocyte count of  $5.2 \times 10^9$ /liter, and a platelet count of  $170 \times 10^9$ /liter. A chest radiograph was without evidence of pneumonia; the patient did not produce sputum for culture. A venous duplex examination showed an occlusive noncompressible thrombosis of the left internal jugular and subclavian veins. The Groshong catheter was removed, and the tip was sent for culture. Intravenous heparin and intravenous vancomycin (1 g twice daily) were administered. Seventeen hours after admission, the leukocyte count had risen to  $11.9 \times 10^9$ /liter. On the second hospital day, gram-negative rods grew from four of four blood cultures drawn at the time of admission. Coagulase-negative staphylococci also grew from three of four of these blood cultures, but only from cultures drawn through the Groshong catheter; the catheter tip was culture negative. The patient received 2 g of ceftriaxone intravenously. Subsequently, his leukocyte count decreased to  $4.7 \times 10^9$ /liter, his temperature returned to normal, and he remained afebrile for the duration of hospitalization. Peripheral intravenous access was lost on hospital day 3, and the patient refused central venous catheterization. Intramuscular ceftriaxone (1 g daily) and oral rifampin (600 mg twice daily) were started, and vancomycin was discontinued. On hospital day 6, the patient agreed to central venous catheterization, and his antimicrobial regimen was changed to intravenous ticarcillin-clavulanate (3.1 g every 6 h) and intravenous gentamicin (100 mg every 8 h). On hospital day 7, the gram-negative organism was identified as a *Bordetella* species resembling *Alcaligenes* spp. The patient's antimicrobial agents were changed to intravenous ampicillin-sulbactam (3 g every 6 h), but this was discontinued on hospital day 15, when an erythematous maculopapular eruption devel-

\* Corresponding author. Mailing address: Department of Laboratory Medicine, SB-10, University of Washington, 1959 N.E. Pacific St., Seattle, WA 98195. Fax: (206) 548-6189. Electronic mail address: cookson@zippy.labmed.washington.edu.

TABLE 1. Cellular fatty acid composition of selected *Bordetella* and *Alcaligenes* species<sup>a</sup>

Bacteria (no. of strains tested) <sup>b</sup>	% Fatty acid <sup>c</sup>																
	C <sub>10:0</sub>	C <sub>12:0</sub>	2-OH C <sub>12:0</sub>	C <sub>14:0</sub>	C <sub>15:0</sub>	2-OH C <sub>14:0</sub>	SUM in feature 3 <sup>d</sup>	C <sub>16:1</sub> ω <sub>7c</sub>	C <sub>16:0</sub>	C <sub>17:0</sub> cyc	C <sub>17:0</sub>	2-OH C <sub>16:0</sub>	3-OH C <sub>16:0</sub>	C <sub>18:1</sub> ω <sub>9c</sub>	C <sub>18:1</sub> ω <sub>7c</sub>	C <sub>18:0</sub>	C <sub>19:0</sub> cyc
" <i>B. hinzii</i> " isolate		0.53	2.03	0.65		3.14	6.57	20.58	36.95	19.13	0.73	0.57	T <sup>e</sup>	0.65	2.42	5.95	
<i>B. avium</i> (6)		0.70	2.42	1.17	T	2.98	6.81	3.82	37.65	36.15	0.67	1.07			1.06	5.17	0.98
<i>B. bronchiseptica</i> (2)		0.68	2.35	5.19			6.10	18.80	42.95	18.27	0.36			0.89	1.98	2.52	
<i>A. faecalis</i> (3)	1.12	2.22	2.10	1.18	0.56		8.38	16.35	38.65	21.10	0.62		T	0.80	6.04	1.11	T
<i>A. denitrificans</i> (3)		1.02	2.04	4.91	T		6.45	22.19	40.40	12.90	1.02		T	0.82	4.48	2.47	0.67
<i>A. xylosoxidans</i> (3)		0.70	2.48	1.05		2.97	6.86	23.41	39.33	14.00	0.61	0.57	T	0.85	4.30	3.27	

<sup>a</sup> Short chain fatty acid analysis by gas-liquid chromatography was performed according to the manufacturer's instructions (Microbial ID, Inc., Newark, Del.). Bacteria were incubated at 35°C in 5% CO<sub>2</sub> and harvested after 24 h of growth on Trypticase soy agar containing 5% sheep blood.

<sup>b</sup> Strains included *B. avium* ATCC 35086<sup>T</sup> and LMG 1851, 1854, 3524, 3549, and 3557; *B. bronchiseptica* ATCC 19395<sup>T</sup> and 10580; *A. faecalis* ATCC 8750<sup>T</sup> and LMG 1230 and 1868; *Alcaligenes denitrificans* subsp. *denitrificans* ATCC 15173<sup>T</sup> and LMG 186 and 3342; and *A. xylosoxidans* subsp. *xylosoxidans* ATCC 27061<sup>T</sup> and LMG 1866 and 1864.

<sup>c</sup> Mean area percentage of total fatty acids. Since only significant fatty acids are included, each row may not add up to 100%.

<sup>d</sup> "SUM in feature 3" includes C<sub>16:1</sub> iso 1 and/or 3-OH C<sub>14:0</sub> because they cannot be differentiated by this system.

<sup>e</sup> T, trace amount (<0.5%).

oped on the upper chest. Intravenous vancomycin (1 g every 12 h) and intravenous ceftazidime (1 g every 8 h) were substituted for the ampicillin-sulbactam. The patient completed another 2 weeks (4 weeks total) of intravenous antimicrobial therapy and was discharged to home. Multiple follow-up blood cultures were negative.

**Microbiological investigation.** Gram-negative rods grew in BACTEC 26 medium (Becton Dickinson Diagnostic Instrument Systems, Towson, Md.) inoculated with blood obtained from the patient by peripheral venipuncture and from his central indwelling catheter. These motile organisms were oxidase positive and assimilated adipate, L-malate, citrate, and phenylacetate (API-NFT; Biomerieux Vitek, Inc., Hazelwood, Mo.). They were nitrate and urease negative, with a biochemical phenotype (NFT profile 0000067) suggesting *B. avium*. Bacteria closely related to *B. avium*, i.e., the genus *Alcaligenes* (9) and *Bordetella* species other than *B. avium*, have previously been isolated from humans. In an attempt to verify the biochemical identification, we used whole-cell fatty acid analysis (Table 1). The taxonomy of the *Bordetella* and *Alcaligenes* genera is complex (5, 9, 11), and their fatty acid profiles are similar (8, 12). Table 1 shows they contain mostly C<sub>16:1</sub> ω<sub>7c</sub>, C<sub>16:0</sub>, C<sub>17:0</sub> cyc, C<sub>18:0</sub>, and "SUM in feature 3" (C<sub>16:1</sub> iso 1 and/or 3-OH C<sub>14:0</sub>). *Alcaligenes xylosoxidans*, *B. avium*, and the patient's isolate contain two hydroxy fatty acid derivatives (2-OH C<sub>14:0</sub> and 2-OH C<sub>16:0</sub>); the other bacteria do not. The fatty acid profile of our isolate most closely resembles that of *A. xylosoxidans* (Table 1), but biochemically these organisms are very different (NFT profile 1040477 for *A. xylosoxidans* includes the reactivities of our isolate [described above] plus nitrate reduction, glucose fermentation, and assimilation of D-gluconate and caprate). Finally, quantitative differences among the predominant fatty acid constituents distinguish our isolate from *B. avium*. Their C<sub>16:0</sub>, C<sub>18:0</sub>, and "SUM in feature 3" contents are similar, but their C<sub>16:1</sub> ω<sub>7c</sub> (isolate, 20.58% ± 0.60%; *B. avium* 3.82% ± 0.52% [mean ± standard error]) and C<sub>17:0</sub> cyc (isolate, 19.13% ± 1.5%; *B. avium*, 36.15% ± 0.95%) contents are different. Among other possibilities, these data suggested that the isolate may represent another species of the genus *Bordetella* that is biochemically similar to *B. avium*. We confirmed this hypothesis and identified the bacteria as "*B. hinzii*" by a detailed comparison with the "*B. hinzii*" type strain LMG 13501<sup>T</sup> (taxonomic and phylogenetic descriptions of "*B. hinzii*" will be published elsewhere [18]). Their protein electrophoretic profiles are virtually identical (data not shown), the DNA-DNA homology of the two strains determined by rena-

tation kinetics is 89%, and the molar guanosine plus cytosine (G+C) contents of their DNA determined by thermal denaturation are very similar (67% for the isolate and 66% for LMG13501<sup>T</sup> compared with 61.6 to 62.6% for *B. avium* [9]). These data confirm identification of the etiologic agent of bacteremia in this case as "*B. hinzii*."

It is interesting that "*B. hinzii*" bacteremia occurred in a patient without historical or clinical evidence of respiratory disease. *Bordetella* spp. are most commonly transmitted by respiratory droplets (19), and in cases of human bacteremia caused by *B. bronchiseptica* (2, 3, 20), primary respiratory tract infection most likely provides access to secondary hematogenous growth. When humans acquire *B. bronchiseptica*, it is usually through animal contact (4, 16, 20). In this case, a patient without animal exposure contracted bacteremia from an organism associated with, but not necessarily pathogenic for, chickens and turkeys. It should be noted that the only other known human isolate of "*B. hinzii*" was obtained from sputum in 1957 (incorrectly designated *Alcaligenes faecalis* [10]). Unfortunately, clinical details could not be recovered (18). Perhaps "*B. hinzii*" gained hematogenous access to our patient via the respiratory route without establishing a respiratory tract infection or via his Groshong catheter. It seems reasonable to speculate that the unusual features of this case result from the underlying immune deficiency of the patient. Indeed, numerous reports involving immunocompromised patients infected with *B. bronchiseptica* (1, 2, 4, 13, 16, 20) or *B. pertussis* (6, 14) have recently appeared. Although human infection by *B. avium* has not been reported, "*B. hinzii*" could be mistaken for this organism when biochemical data are used alone (as described above and in reference 18). The fatty acid profile of our isolate was suggestive of *A. xylosoxidans* (Table 1), and these seemingly conflicting data were resolved after identifying the isolate as "*B. hinzii*." In doing so, we have demonstrated the utility of combining biochemical phenotyping with fatty acid analysis for the characterization of a previously undescribed pathogen.

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