though the biphasic nature of the onset of illness is unusual for this infection.

Our patient was successfully treated for Rocky Mountain "spotless" fever, though the diagnosis was not proved until the results of serologic studies became available six weeks after stay in hospital. The eight-day course of tetracycline was administered because of the history of tick exposure and the sudden onset of high fever, headache, myalgia, mild liver function abnormalities and the possibility of a hemolytic episode. In a patient in whom the sudden onset of a severe febrile illness develops within two weeks of possible tick exposure, empiric use of tetracycline may be indicated. Although the presence of the typical rash of Rocky Mountain spotted fever can be helpful in the differential diagnosis of tick-borne fever, the absence of cutaneous findings may be consistent with multiple causes of tick-borne fever, including *R rickettsii.*

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Bordetella bronchiseptica Bacteremia

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Bordetella bronchiseptica, a Gram-negative nonfermentative bacillus, has been extensively studied as a veterinary pathogen and in animal models of bacterial superinfection following viral respiratory tract disease.[1] There are few reports of disease in humans caused by this organism. We describe the case of a patient in whom *B bronchiseptica* bacteremia developed in hospital and persisted for ten days, despite treatment with antimicrobial agents to which the organism was susceptible in vitro. The clinical course and autopsy findings in this patient are described and previously reported cases of *B bronchiseptica* infection in humans are summarized.

Report of a Case

The patient, a 70-year-old black man, was admitted to the Veterans Administration Medical Center because of weight loss, anorexia and intermittent abdominal pain for two months. There was no history of respiratory tract infection, contact with animals or previous illness. On physical examination he was noted to have icterus and an enlarged liver; stool specimens were guaiac positive. A chest roentgenogram showed a subtle density in the right midlung field. Liver function tests showed an aspartate aminotransferase (AST, formerly SGOT) level of 200 IU and an alkaline phosphatase value of 980 IU per liter. The total bilirubin level was 7.7 mg per dl, of which 4.3 mg per dl was direct reacting. The peripheral leukocyte count was 4,500 per μl, the hemoglobin 13.3 grams per dl and the hematocrit 37.9%.

Metastatic cancer was suspected, and the following special studies were done: barium enema, liver-spleen radioisotope scan, abdominal ultrasound, endoscopic retrograde cholangiopancreatography, whole lung tomography and bronchoscopy. None of the above showed abnormalities. Serologic tests for hepatitis A and B viruses, α-fetoprotein, antimitochondrial antibody, cytomegalovirus, Epstein-Barr virus, toxoplasma and Q fever were negative. Results of serum immunoglobulins and a serum protein electrophoresis were normal. Contrast studies of the gastrointestinal tract showed a small duodenal ulcer, and treatment with cimetidine was begun on the 12th hospital day.

An elevated temperature was noted on the 18th hospital day, and one of two blood cultures done grew a Gram-negative bacillus from the aerobic bottle after 24 hours. Three additional blood cultures were taken and, again, one of three aerobic bottles was positive. Therapy that had been initiated with a "third-generation" cephalosporin (cefoperazone sodium) was changed to gentamicin sulfate, 1.5 mg per kg of body weight every eight hours, when antibiotic susceptibility studies showed that the organism was resistant to

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cefoperazone. The Gram-negative bacilli from both positive blood cultures were identified as *Bordetella bronchiseptica* by selective biochemical and negative fermentation reactions. Continued fever prompted the addition of ampicillin and clindamycin to the antibiotic regimen; however, blood cultures continued to grow only *B bronchiseptica* (Figure 1). An increasing serum bilirubin concentration and a falling hematocrit were noted on the 24th hospital day and, despite multiple transfusions, the patient suffered a cardiopulmonary arrest. The hematocrit was 15% and, despite continued transfusion, intubation and mechanical ventilation, the patient died on the 29th hospital day. Blood cultures done before death continued to grow *B bronchiseptica.*

Autopsy Findings

At autopsy a ruptured spleen was found, to which was attached a well-circumscribed hematoma, equivalent to 600 ml of blood. The intestines and the heart and lungs were free of significant gross lesions. A thickened pleural scar overlying the right lung accounted for the density appearing on an x-ray film of the chest. The liver weighed 1,500 grams and had a smooth surface. The intrahepatic and extrahepatic ducts were normal in caliber. The biliary system was free of calculi, and the bile itself was unremarkable.

Microscopic examination of the spleen showed massive numbers of sickled erythrocytes in association with infarcted splenic tissue. A fragment of splenic capsule and attached pericapsular fat showed extensive infiltration by polymorphonuclear leukocytes. An adjacent minor splenic artery exhibited occlusion of the lumen with dissection of the muscular wall and polymorphonuclear leukocytic invasion peripherally. Liver sections showed fibrosis of portal areas with mild reduplication of bile ductules and prominent mononuclear cell infiltration. Examination of sinusoidal spaces showed numerous sickled erythrocytes. Kupffer's cells were prominent, and erythrophagocytosis was visible. Postmortem culture of liver, spleen and blood specimens grew *Bordetella bronchiseptica.*

Microbiology

The Gram-negative coccobacillus initially isolated from blood cultures was identified as *B bronchiseptica* by the API-20E system (API Analytab Products, Ayerst Laboratories, Plainville, NY). Characteristic observations included positive citrate and rapid conversion of urea. The organism was motile and showed one to two polar flagella by Bacto flagella staining (Difco Laboratories, Detroit, Mich) and was noted to be peritrichous by a shadowing technique on unstained organisms using electron microscopy. Identification of the organism was confirmed by the Centers for Disease Control in Atlanta by means of differential biochemistry, growth characteristics on media and serologically.

Susceptibility testing showed resistance of the organism to ampicillin, cephalothin, chloramphenicol, carbenicillin and amikacin. Growth of the organism was inhibited in vitro by achievable concentrations of gentamicin, tetracycline and trimethoprim/sulfamethoxazole (Table 1). One hour after the patient was

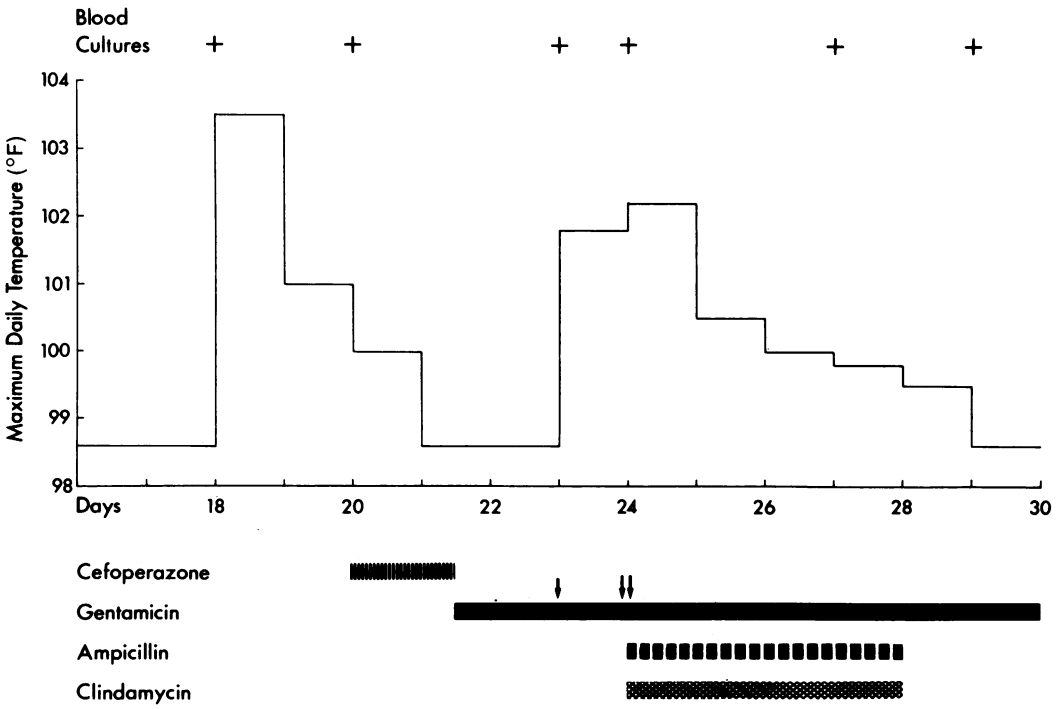

Figure 1.—Maximum daily temperature and time of positive blood cultures and antibiotic therapy from the 18th through the 29th day in hospital. ↓=gentamicin sulfate concentration: premedication level 1.0 μg per ml, postmedication level 4.8 μg per ml; ↓↓=serum bactericidal activity measured: premedication 1:16, postmedication 1:64.

TABLE 1.—*Minimal Inhibitory Concentration (MIC) Testing of* Bordetella bronchiseptica

Antibiotic	*MIC*	*Antibiotic*	*MIC*
Ampicillin	> 16 μg/ml	Amikacin	24 μg/ml
Cephalothin	> 64 μg/ml	Cefamandole nafate	> 64 μg/ml
Gentamicin sulfate	2 μg/ml	Cefoxitin sodium	> 64 μg/ml
Tetracycline	8 μg/ml	Colistin sulfate	4 μg/ml
Carbenicillin	>512 μg/ml	Nitrofurantoin	> 64 μg/ml
Chloramphenicol	> 32 μg/ml	Trimethoprim/sulfamethoxazole	2/38 μg/ml
Tobramycin	4 μg/ml	Clindamycin	> 64 μg/ml

given a dose of gentamicin, his serum was bactericidal for the *B bronchiseptica* at a dilution of or greater than 1:8 when an inoculum of 10^5 organisms per milliliter was used.

Comments

B bronchiseptica is infrequently isolated from human clinical specimens and is even less often a cause of disease. Two recent surveys of nonfermentative Gram-negative organisms address the issue of pathogenicity. Pedersen and co-workers speciated 565 nonfermenting Gram-negative bacilli isolated in a two-year period:[2] 12 were *B bronchiseptica,* all were isolated from sputum samples and none were associated with disease. In a more recent study, Gardner and associates identified 18 of 184 nonfermenters isolated from specimens in Boston as *B bronchiseptica.*[3] In all, 16 were found in sputum specimens, one in urine and the other, in one case discussed later, in blood. Thus, it is unusual to identify *B bronchiseptica* in clinical specimens and neither has prolonged bacteremia been reported previously.

In all, we found seven cases of human infection reported in the literature. The organism was first characterized by McGowan[4] who described a laboratory epidemic of tracheobronchitis and pneumonia in dogs, rabbits and guinea pigs. *B bronchiseptica* was isolated in pure culture from the nasopharynx of a laboratory worker with a history of chronic catarrh. In 1926 Brown[5] reported a case of typical whooping cough in a child with a sick pet rabbit and *B bronchiseptica* was grown in specimens from the nasopharynx of both the child and the rabbit. Kristensen and Lantrop[6] in Denmark and Krepler and Flamm[7] in Germany have each reported the case of a respiratory tract infection caused by *B bronchiseptica.* Chang and colleagues[8] described the case of a child in whom posttraumatic meningitis with *B bronchiseptica* developed. Finally, two cases of bacteremia and lethal infection have been described. Gardner and co-workers[3] discuss the case of an elderly immunosuppressed man in whom a terminal bacteremia developed with both *B bronchiseptica* and *Streptococcus pneumoniae* while he was receiving corticosteroids and azathioprine. Recently Ghosh and Tranter[9] reported isolating *B bronchiseptica* from specimens of blood and tracheal aspirate from a malnourished alcoholic patient with a fatal aspiration pneumonia.

In our patient, nosocomial infection resulted in a prolonged bacteremia without an antecedent pulmonary infection, contact with an animal or an apparent port of entry. Although he was not obviously immunosuppressed, he may have been particularly susceptible to this unusual infection for two reasons. First, he entered the hospital with cholestatic liver disease that eluded classification despite intensive clinical and postmortem study. Second, the patient probably had a sickling hemoglobinopathy, most likely hemoglobin AS (sickle cell trait). Unfortunately, this was not suspected during life, and a hemoglobin electrophoresis was not done. However, the pathologic findings were consistent with sickle cell trait. Intravascular sickling leading to splenic infarction has been described in up to 20% of patients with sickle cell trait subject to the stress of serious illness.[10] Sickled hemoglobin probably caused the multiple splenic infarctions that led to rupture of the spleen. Virtual destruction of the spleen may have further diminished his ability to remove bacteria from the blood and provided a nidus for continued bacteremia.

This case shows that *Bordetella bronchiseptica* is a human pathogen that may cause prolonged lethal bacteremia. Cultures of blood specimens taken before and during appropriate antibiotic therapy were positive, albeit usually only one of two or three sets grew *B bronchiseptica.* This is consistent with continuous, low-level bacteremia as in an intravascular infection or undrained abscess. Multiple splenic infarctions and splenic arteritis may have provided a site for microabscesses with access to the bloodstream. Liver disease and a sickle cell hemoglobinopathy in this patient may have resulted in further inability to clear bacteremia.

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