



# Laboratory-acquired Human Glanders— Maryland, May 2000

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On May 5, 2000, the Baltimore City Health Department was notified by hospital infection-control staff of a serious systemic febrile illness in a microbiologist whose research at the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) involved several pathogenic bacteria, including *Burkholderia mallei*, the causative agent of glanders. This report summarizes the first human case of glanders in the United States since 1945, and emphasizes the importance of considering occupational exposures among laboratory workers with a febrile illness, the difficulty of characterizing unusual agents, including potential agents of biological terrorism such as glanders using routine laboratory techniques, the appropriate isolation practices for patients who may be infected by these agents, and laboratory safety.

The microbiologist, who has insulin-requiring diabetes mellitus, was well until early March 2000, when he developed an increasingly painful mass in his left axilla. On March 16, he had a temperature of 101.5°F (38.6°C) and was seen by a primary-care provider. He was given one dose of ceftriaxone intramuscularly and was started on a 10-day course of cephalexin. Despite completing the therapy, episodes of fever increased, and he experienced marked fatigue, malaise, night sweats, and weight loss. A medical evaluation, which included blood and urine cultures and chest radiographs, was unrevealing. In early April, the patient started a 10-day course of clarithromycin, which improved the symptoms and coincided with resolution of the left axillary mass; however, four days after completing the regimen, his symptoms returned. He continued to lose weight and began to experience mid-epigastric abdominal pain. Multiple blood cultures were obtained

and were negative for bacteria.

An abdominal computerized tomography (CT) scan performed on May 2 revealed multiple hepatic and splenic lesions consistent with abscesses. Because of increased abdominal pain, hyperglycemia, and diabetic ketoacidosis, the patient was admitted to hospital A. An ultrasound-guided fine needle aspiration of a medial left hepatic lobe lesion was performed and yielded purulent-appearing material. Blood cultures again were obtained. Because of the patient's work history, occupationally acquired *Burkholderia* infection was considered, and one dose of piperacillin-tazobactam was administered intravenously. On the second hospital day, the patient developed respiratory distress requiring mechanical ventilatory support. He was placed in respiratory isolation, given intravenous tobramycin and doxycycline, and transferred to hospital B for further treatment.

At the time of transfer on May 4, hospital A identified small, bipolar, weakly-staining Gram-negative rods in cultures of the liver abscess fluid. On May 5, Gram-negative bacteria also were isolated from the blood cultures. An automated bacterial detection system at hospital A initially identified the bacteria as *Pseudomonas fluorescens/putida*. However, subsequent studies of the same isolate performed at hospital B and CDC, including motility studies, cellular fatty acid analyses, and 16S ribosome sequencing, identified the organism isolated from the liver abscess as *B. mallei*.

Because the patient worked with strains of *B. mallei* sensitive to imipenem and doxycycline, he was treated with those antibiotics and his symptoms rapidly improved. Repeat abdominal CT obtained after 10 days of therapy showed slight regression of the hepatic and

splenic abscesses. The patient was treated with intravenous imipenem and doxycycline therapy for two weeks. When he was switched to oral doxycycline and azithromycin, the patient's liver and spleen abscesses continued to resolve.

The patient reported no exposures to horses, mules, or donkeys. He neither reported nor recalled any laboratory mishaps, although on occasion he had handled without wearing gloves laboratory equipment containing live *Burkholderia* strains. No other persons with whom he lived or worked reported recent febrile illnesses. No health-care workers who came in contact with him while he was a patient have reported symptoms consistent with glanders.

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### Editorial Note

Glanders is a bacterial infection caused by the Gram-negative rod, *B. mallei* (formerly *Pseudomonas mallei*). Primarily a disease of equids (e.g., horses, mules, and donkeys), glanders also has been reported in carnivores that have fed on infected horse carcasses and, although rare, glanders has been reported in humans. The disease was eliminated from domestic animals in the United States during the 1940s (1) and the last reported human case in the United States occurred in 1945 (2). Glanders still occurs occasionally in equids and humans in central and southeast Asia, the Middle

East, parts of Africa, and possibly South America, and *B. mallei* is being researched in the United States because it is considered a potential agent of biological terrorism (3).

In humans, glanders usually is acquired through direct skin or mucous membrane contact with infected animal tissues. The incubation period usually is one to 14 days. The clinical presentation varies (4, 5); cutaneous inoculation can result in localized infection with nodule formation and lymphadenitis (4). The disease often manifests as pneumonia, bronchopneumonia, or lobar pneumonia, with or without bacteremia (4). As in this case, hepatic and splenic involvement has been reported (2). A few antibiotics have been used to treat humans. Sulfadiazine (25 mg/kg intravenous, four times a day) was efficacious in some cases (2). In mice, doxycycline and ciprofloxacin have been effective therapies (6; W. R. Byrne, USAMRIID, personal communication, 2000). The mortality of apparent infection was approximately 95% before the use of antimicrobial agents; however, except when bacteremia develops, better diagnosis and more appropriate therapy have lowered mortality (5). No vaccine against *B. mallei* infection is available.

Glanders has been reported as a laboratory-acquired infection. During World War II, six unrelated cases of laboratory-acquired infection with *B. mallei* occurred at Camp Detrick, Frederick, Maryland (3). Some of these cases were attributed to inhalation of infectious aerosols generated by spillages of liquid culture media containing the bacterium. Other cases were reported to have no obvious cause other than the routine handling of the organism. In this report, the patient did not recall an unusual incident while working with *B. mallei*; however, the presentation of unilateral lymphadenopathy suggests a cutaneous inoculation. Most laboratory-acquired infections are associated with routine handling of microbes and not with injuries (7).

This case raises issues concerning the ability of clinical laboratories to identify rare agents like *B. mallei* rapidly and accurately and the importance of considering occupational exposures among laboratory workers presenting with febrile illness. Serologic and DNA-based diagnostic assays are not standardized, widely available, or approved by the Food and Drug Administration. Automated bacterial identification systems used by most clinical laboratories may not cor-

rectly speciate *B. mallei*, as occurred in this reported case. Effective communication between clinic and laboratory is essential in cases such as this so that unusual pathogens may be considered in the laboratory diagnosis.

Standard precautions (8) (i.e., the use of disposable surgical masks, face shields, and gowns, when appropriate, to prevent splashing of mucous membranes and skin) are sufficient to prevent transmission of this disease to those caring for patients, and biosafety level three is recommended for laboratory staff handling *B. mallei* (9).

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