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Public health response to an imported case of canine melioidosis

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Summary

Melioidosis in humans presents variably as fulminant sepsis, pneumonia, skin infection and solid organ abscesses. It is caused by *Burkholderia pseudomallei*, which in the United States is classified as a select agent, with “potential to pose a severe threat to both human and animal health, to plant health or to animal and plant products” (Federal Select Agent Program, http://www.selectagents.gov/, accessed 22 September 2016). *Burkholderia pseudomallei* is found in soil and surface water in the tropics, especially South-East Asia and northern Australia, where melioidosis is endemic. Human cases are rare in the United States and are usually associated with travel to endemic areas. *Burkholderia pseudomallei* can also infect animals. We describe a multijurisdictional public health response to a case of subclinical urinary *B. pseudomallei* infection in a dog that had been adopted into upstate New York from a shelter in Thailand.

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CONFLIC T OF INTEREST

None of the authors have any conflict of interests to declare.

Investigation disclosed three human contacts with single, low-risk exposures to the dog's urine at his residence, and 16 human contacts with possible exposure to his urine or culture isolates at a veterinary hospital. Contacts were offered various combinations of symptom/fever monitoring, baseline and repeat *B. pseudomallei* serologic testing, and antibiotic post-exposure prophylaxis, depending on the nature of their exposure and their personal medical histories. The dog's owner accepted recommendations from public health authorities and veterinary clinicians for humane euthanasia. A number of animal rescue organizations actively facilitate adoptions into the United States of shelter dogs from South-East Asia. This may result in importation of *B. pseudomallei* into almost any community, with implications for human and animal health.

Keywords

Burkholderia pseudomallei ; canine; dog importation; melioidosis

1 | CASE PRESENTATION

A 4-year-old male, mixed breed, disabled dog who had spent 21 months in a dog shelter in Thailand was adopted into a shelter in the United States. The dog arrived at John F. Kennedy International Airport in New York State near midnight on 19 April 2016, on a commercial airline flight, travelling in a crate in the cargo hold. He then travelled by car, confined to a crate, approximately 200 miles, to his new home at a shelter/sanctuary for chronically ill or disabled animals, arriving approximately 0300 on 20 April 2016. The shelter is in Broome County, NY, about 50 miles from Cornell University Hospital for Animals (CUHA) in Tompkins County.

He presented to CUHA on 21 April 2016 for evaluation of spinal trauma and inability to walk of approximately 2 years duration. He had been unable to ambulate since his arrival at the animal shelter in Thailand but had reportedly regained some function while there and was able to walk with assistance. He was incontinent of urine. He was up to date on his rabies vaccination. He was eating and drinking normally. Further medical history was unavailable.

On examination, the patient was bright, alert and responsive. He was briefly able to bear his own weight and ambulate once assisted into a standing position. There was marked muscle atrophy of both hindlimbs. The skin of the inguinal area was abnormally thickened, damp and malodorous, consistent with infection caused by urine scald related to incontinence.

Radiographs of the spine revealed damage to the cranial end-plate of the fourth lumbar vertebra. Absent lumbar puncture or magnetic resonance imaging (MRI), spinal infection could not be ruled out, but the radiographic changes appeared chronic and were more suggestive of trauma than of infection. Urinalysis was benign except for 5–20 red blood cells per high-power field, likely related to trauma during the cystocentesis by which the sample was acquired. The ptient was discharged to the care of his owners with appropriate nursing care and rehabilitation instructions. For the inguinal pyoderma, he was placed on oral cephalexin and a topical chlorhexidine spray. He returned a few days later for fitting of a hindlimb cart; urine cultures were pending at that time.

The bacteriology section at the Animal Health Diagnostic Center at Cornell University performed an aerobic culture on the urine sample following its standard operating procedures and using their automated identification system, Matrix-Assisted Laser Desorption Ionization Time-of-Flight (MALDI-TOF) mass spectrometry (Singhal, Kumar, Kanaujia, & Virdi, 2015) for identification of the bacterium. The fingerprint output revealed a close match with *Burkholderia*, precipitating additional biosafety precautions and reference to the New York State Biodefense Laboratory (NYSBDL) for definitive identification. All disposables and wastes generated from the case were secured pending results. After confirmation of *Burkholderia pseudomallei* at NYSBDL, all disposables and wastes associated with the case were destroyed by autoclaving with appropriate documentation. Cleaning and disinfection of hospital areas routinely used either accelerated hydrogen peroxide or an ammonium chloride-based neutral disinfectant; all areas the dog contacted were disinfected again using a 10% bleach solution.

2 | BURKHOLDERIA PSEUDOMALLEI

Burkholderia pseudomallei, a saprophyte and the causative organism of melioidosis, is found most commonly in soil and surface water in the tropics, especially South-East Asia and northern Australia. With increasing awareness and diagnostic capacity over the past two decades, melioidosis is being recognized more frequently elsewhere, including Taiwan, China, Brazil, Central America, India and the Caribbean (Benoit et al., 2015; Currie, Dance, & Cheng, 2008; Doker et al., 2015; Vandana et al., 2016). One model estimates 68,000–412,000 human cases annually worldwide, arising from an estimated 79 different countries (Limmathurotsakul et al., 2016).

In the United States, most human cases occur in travellers who have visited endemic areas or in immigrants from endemic countries; however, two cases have been reported in individuals without a history of travel outside of the United States (Doker et al., 2014; Stewart et al., 2011).

Melioidosis is acquired by inhalation, ingestion or transdermal inoculation from environmental sources such as soil or standing water. There are limited case reports of person to person and perinatal transmission (Abbink & Orendi, 2001; Fang, Chen, Zhu, & Mao, 2016; McCormick et al., 1975). Individuals with diabetes, thalassaemia, alcoholism and renal impairment are more susceptible to melioidosis (Cheng & Currie, 2005). In addition to environmental sources, there have been two outbreaks associated with contaminated potable water supplies (Currie et al., 2001; Inglis et al., 1999).

In humans, melioidosis can present in many forms (Wiersinga, Currie, & Peacock, 2012), including:

1. Bacteremia and fulminant sepsis
2. Pneumonia, often with abscesses
3. Cutaneous infection
4. Solid organ abscesses and granulomas

Some forms of melioidosis, particularly the cutaneous form, can become chronic and relapsing.

Burkholderia pseudomallei can also cause infection and disease in a number of animals (Sprague & Neubauer, 2004). Goats and sheep are particularly susceptible, with several epizootics reported in the literature (Choy, Mayo, Janmaat, & Currie, 2000; Sutmoller, Kraneveld, & Van Der Schaaf, 1957). Cattle, swine, dogs and cats are considered to have low susceptibility (Sprague & Neubauer, 2004). Cases of melioidosis have been seen in iguanas and non-human primates (Johnson et al., 2013; Zehnder et al., 2014). Imported canine culture-positive melioidosis has not been described in the United States. Several such cases, some fatal, were reported among military working dogs in the Republic of Vietnam (Moe, Stedham, & Jennings, 1972; Stedham, 1971), but it appears that the animals remained in country and thus did not present an importation risk to a non-endemic area. Some military working dogs returning to the United States demonstrated serologic evidence of subclinical infection (Alexander et al., 1972).

3 | FIELD INVESTIGATION

Personnel from the Broome County Health Department visited the animal shelter on 4 May 2016 and interviewed the owner/operator, who lives on the premises.

The facility is essentially a small farm. At the time of the site visit, it housed approximately 135 animals, which included dogs, cats, horses, livestock and fowl. The grounds were organized and well-kept, and the house and outbuildings were well-maintained.

It was customary at the facility for newly arriving dogs to be housed for a period of days in a private downstairs room in the house, which is where he remained at the time of the visit to the facility. The dog looked healthy and behaved normally, except for paralysis of his hindlimbs. He was wearing a diaper. His antibiotic had been changed from cephalexin to enrofloxacin after the preliminary urine culture report from CUHA indicated Gram-negative rods resistant to the former (MIC = 256 μg/ml) but sensitive to the latter (MIC = 0.25 μg/ml).

Except for the two trips to the hospital detailed above, he had remained in the private room. He had voided in the crate during the car ride from the airport, and this had been cleaned and disinfected with bleach upon arrival home. Another partially paralysed dog from the shelter had accompanied him on the initial visit to CUHA. Each had been in their own crate in the back seat of the car for the trip.

The owner/operator had already taken several actions upon receipt of the urine culture results: continuing confinement to the single room, limiting access to a single caregiver, the use of latex gloves for direct contact, double diapering, an environmental cleaning regimen with a bleach solution and placement of a bleach shuffle pit at the entrance to the dog’s room.

4 | MANAGEMENT OF HUMAN CONTACTS

In its endemic range, *B. pseudomallei* is acquired, by humans and animals, from soil and surface water, often in an agricultural setting. Although several cases of suspected animal-to-human transmission have been reported in the literature, none have been confirmed through genotyping, and evidence for zoonotic transmission is purely circumstantial (Fhogartaigh & Dance, 2015). Guidelines for the management of human exposures exist only within the context of laboratory settings (Peacock et al., 2008). The present case, however, included circumstances that complicated our interpretation and application of existing knowledge and exposure guidelines: *B. pseudomallei* culture-positive urine in an incontinent and paraplegic companion animal needing a high level of direct involvement by his human caregivers, all in the setting of a non-endemic area.

4.1 | AT THE VETERINARY HOSPITAL

The Tompkins County Health Department, Cornell University's Environmental Health and Safety Department, and the university's student health services collaborated to assess possible human exposures. For laboratory workers, assessments of risk were based on published guidelines (Peacock et al., 2008). Risk assessments for laboratory personnel were based on materials handled (e.g. urine, faeces, culture); activities performed (e.g. area cleanup, culturing, centrifugation, waste management, facilities maintenance); location of individual in relation to activities performed and travel routes of the affected dog; and the use of infection control measures (engineering controls and personal protective equipment.) Risk assessment in non-laboratory personnel is not well-addressed in existing literature; judgments were based on medical interviews, job duties, specific care activities performed, body fluids contacted and travel routes through the facility relative to those of the affected dog.

Twenty-seven possibly exposed individuals were assessed. Eleven were deemed to be at no risk, and no further actions were taken in their regard. Of the remaining 16, four were laboratorians, while twelve were clinic personnel, including veterinary faculty, residents, students and veterinary technicians. Fourteen were considered low-risk, and two were considered high-risk (due solely to preexisting chronic medical conditions that predispose to infection with *B. pseudomallei*.)

Six of the 16 at-risk contacts agreed to 3 weeks of symptom monitoring by Tompkins County Health Department staff nurses. Three contacts agreed to baseline and sequential serology for *B. pseudomallei*. While not without risk (Mitchell et al., 2016), post-exposure prophylaxis was discussed with the two high-risk contacts, in accordance with published guidelines (Peacock et al., 2008), and one agreed to the recommended 3-week course of trimethoprim-sulfamethoxazole.

4.2 | AT THE DOG'S RESIDENCE

Six human subjects with possible contact with the dog were identified from the animal shelter. They comprised staff and volunteers, another resident at the house, a family member of the owner/operator and a large-animal veterinarian from CUHA who periodically made

rounds at the facility. None of them had any immunocom-promising conditions or relevant chronic illnesses. In-depth interviews disclosed that only three had any direct contact with the dog's urine.

There are no published guidelines for management of humans potentially exposed to *B. pseudomallei* outside of the laboratory setting. In consultation with experts at the CDC Bacterial Special Pathogens Branch and the Royal Darwin Hospital in northern Australia, these one-time skin exposures to the dog's urine were considered to be less of a risk than even the low-risk exposures described in the guidelines for laboratorians (Peacock et al., 2008), as the concentration of organisms in voided urine was likely to be much lower than that in a laboratory culture. Thus, no antibiotic post-exposure prophylaxis was recommended. The three subjects were educated on symptom and fever monitoring, and they were asked to measure their temperatures twice a day for 3 weeks and send results weekly to the health department. Their primary care physicians were briefed. Baseline serologic testing for antibodies to *B. pseudomallei* was obtained from all three of the contacts.

5 | RESOLUTION

In the absence of any treatment regimen with demonstrated efficacy in eradicating *B. pseudomallei* from the canine urinary tract, and thus with an ongoing source of potential human exposure to a rare and serious infection, all clinicians and public health agencies involved recommended euthanasia, and the dog's owner agreed. This was accomplished at CUHA on 6 May 2016. In the light of stringent federal regulations regarding select agents, and the infrastructure necessary to do so safely, an autopsy was not performed. Disposal of the body was by alkaline hydrolysis.

All six monitored contacts from the veterinary hospital remained well throughout their monitoring periods. No reports of illness among the other 10 contacts were received. The individual undergoing antibiotic post-exposure prophylaxis completed the course without incident. One individual's sequential serology result doubled at week 4, rising from 1:20 to 1:40; this was considered indeterminate and non-actionable. All other serological results were negative.

By the end of their monitoring period, all three contacts at the animal shelter had remained well. Baseline serologic tests all returned negative.

6 | DISCUSSION AND IMPLICATIONS

Infection with *B. pseudomallei* is very rare in humans and animals in the United States, but it is endemic in many parts of South-East Asia, where an often-brutal dog meat trade motivates many dog rescue organizations to facilitate adoptions into the United States. This may result in importation of this rare select agent into almost any community, with implications for medical, veterinary and public health personnel.

It may be challenging for clinicians outside of endemic areas to recognize this unfamiliar illness; astute enquiry about travel history, for humans and for animals, can facilitate

diagnosis in both. Vigilance in the microbiology laboratory, with timely referral of suspect isolates to reference facilities, is also advised.

In the present case, urinary *B. pseudomallei* infection combined with incontinence, neither of which was likely to resolve, presented some unique concerns over minimal but ongoing exposure of the dog's human caretakers. Prospects for a good quality of life for the dog were also poor if he was faced with perpetual indoor confinement and separation from the many other animals on the premises. In the absence of a promising and practical treatment regimen, humane euthanasia was recommended. When such a recommendation is necessary, the animal and its owner deserve empathy and emotional support from clinicians and public health personnel. An empathetic approach also helps maintain important working relationships between local health departments and animal owners, shelters and boarding facilities.

Published guidelines regarding inadvertent exposure to *B. pseudomallei* pertain specifically to laboratory workers (Peacock et al., 2008). Clinical judgement is necessary when attempting to apply that guidance in non-laboratory settings (in assessment of the clinic and the household in this case). Expert consultation may be needed.

The question of environmental contamination also arises. Winters in upstate New York are probably not conducive to survival of the organism, but persistent soil contamination and associated cases have occurred in temperate climates, as described by Mollaret (Mollaret, 1988). Environmental conditions could con-ceivably be more favourable to *B. pseudomallei* in the southeastern United States (Limmathurotsakul et al., 2016; Portacci, Rooney, & Dobos, 2017).

Currently, animals imported to the United States are not screened for melioidosis. However, this dog had no signs referable to *B. pseudomallei* and would likely have escaped notice in any practicable import inspection regime. Thus, vigilance among veterinarians caring for animals from South-East Asia would be wise. Further research into the volume of international dog adoptions, and into the prevalence of *B. pseudomallei* infection in these animals, would be valuable.

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Impacts

- *Burkholderia pseudomallei* is a select bacterial agent that causes acute or chronic disease, sometimes life-threat-ening, in humans and other animals.
- *Burkholderia pseudomallei* is rare in the United States but endemic in other parts of the world, including South-East Asia and northern Australia.
- Worldwide, movement of animals is becoming more common. A thorough travel history and an awareness of global pathogens are important in the care of both humans and animals.