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Short Communication

A Case-Study of Implementation of Improved Strategies for Prevention of Laboratory-acquired Brucellosis

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ABSTRACT

Background: In 2012, the Alaska Section of Epidemiology investigated personnel potentially exposed to a *Brucella suis* isolate as it transited through three laboratories.
Methods: We summarize the first implementation of the United States Centers for Disease Control and Prevention 2013 revised recommendations for monitoring such exposures: (1) risk classification; (2) antimicrobial postexposure prophylaxis; (3) serologic monitoring; and (4) symptom surveillance.
Results: Over 30 people were assessed for exposure and subsequently monitored for development of illness. No cases of laboratory-associated brucellosis occurred. Changes were made to gaps in laboratory biosafety practices that had been identified in the investigation.
Conclusion: Achieving full compliance for the precise schedule of serologic monitoring was challenging and resource intensive for the laboratory performing testing. More refined exposure assessments could inform decision making for follow-up to maximize likelihood of detecting persons at risk while not overtaxing resources.

1. Introduction

Laboratory-acquired brucellosis (LAB) cases have been previously reported in the United States. Anecdotally, clinical labs periodically misidentify or fail to anticipate the presence of *Brucella* spp., which creates a risk of episodic exposure at both clinical and reference laboratories. *Brucellae* are Gram-negative intracellular coccobacilli. There are several different species of *Brucella*, which have different host specificities and clinical manifestations. *Brucellae* are facultative and grow slowly, which sometimes contributes to their misidentification. Brucellosis can be a very debilitating and serious disease with symptoms that range in severity from fevers and body aches to arthritis and endocarditis. Because symptoms can be vague, brucellosis may not be immediately diagnosed and people can progress toward chronic brucellosis.

In 2012, an isolate collected from a blood culture taken on February 8, 2012, was presumptively identified as *Haemophilus* spp. at Laboratory A (an Alaska hospital laboratory) and was forwarded to Laboratory B (Arctic Investigations Program, a referral laboratory) for confirmation. Laboratory A uses a Siemens Microscan (Siemens Healthcare Diagnostics, Inc., Tarrytown, NY, USA) and Laboratory B uses culture-based methods for bacterial identification. On March 6, 2012, the Alaska Section of Epidemiology (SOE) received a call from Laboratory B that the isolate was suspected as *Brucella* spp. Subsequently, *Brucella suis* was confirmed by Laboratory C [Alaska State Public Health Laboratory (ASPHL)] on March 9, 2012. Alaska records an average of one case of brucellosis biennially. Locally-acquired cases are *B. suis* biovar 4 and historically have been associated with contact to infected reindeer or caribou carcasses [1].

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The blood specimen was drawn from an adult male patient in rural Alaska who had presented several times to a regional hospital emergency department (ED) for non-specific systemic illness of 6–8 weeks' duration. History and specific exposures elicited during ED visits were unremarkable. Following diagnosis and more extensive interviews, no further discrete exposures were revealed. Brucellosis typically results from contact with infected animals or animal products contaminated with the bacteria, with the most commonly infected animals including sheep, cattle, goats, pigs, and dogs [2]. Although patient occupation did not put him in close contact with animals, he lived in a rural area where hunting and a subsistence lifestyle are common. Therefore, patient exposure was presumed to be zoonotic.

Secondary exposures to, and ultimately disease from, *Brucella* spp. in a laboratory setting have been published [3–9], although no exposures were specific to *B. suis* biovar 4. In 2012, the United States Centers for Disease Control and Prevention (CDC) had begun revising recommendations for monitoring such exposures, including a change to the schedule for serial serologies, and published updated prevention strategies to prevent LAB, including: (1) risk classification; (2) antimicrobial postexposure prophylaxis (PEP); (3) serologic monitoring; and (4) symptom surveillance [10]. In this brief report, we describe implementation of these strategies to manage a laboratory exposure to an isolate of *B. suis* in Alaska.

2. Materials and methods

We implemented steps published in Traxler et al [10] as follows.

2.1. Risk classification

Alaska SOE staff consulted with the CDC *Brucella* spp. subject matter experts to develop a plan for assessing exposures of any affected laboratory workers and implementing a health monitoring schedule. Staff at each of the three laboratories were administered a questionnaire to assess specific practices performed with the specimen/isolate and the presence of appropriate personal protective equipment (PPE) or engineering controls in place during execution of those practices. Examples of risk classification criteria included assessing whether isolates were manipulated on an open bench without using the appropriate level of biosafety precautions and whether other staff were within a 1.5 meters radius of someone who was performing those activities [10]. Staff that had been present in the laboratories were then classified as either "High" or "Low" risk based on their participation in the work-up of the specimen/isolate or proximity to the work [10]. If specimen handling occurred with adequate PPE in the biological safety cabinet (BSC) as required [11], exposure was classified as "None". Additionally, laboratory practices at each facility were evaluated to ensure that future exposures could be minimized.

2.2. Antimicrobial PEP

Persons identified as being at high risk were recommended to receive the standard dosages of doxycycline (100 mg) twice daily and rifampin (600 mg) once daily for 3 weeks [10].

2.3. Serologic monitoring

Baseline serum samples as well as follow-up serological testing from blood collected at 6 weeks, 12 weeks, 18 weeks, and 24 weeks after last known exposure was recommended. ASPHL evaluated serum samples using the *Brucella* spp. micro-agglutination test (BMAT). In general, testing was batched for efficiency, although time for a single test may take a minimum of 1–2 days.

2.4. Symptom surveillance

Laboratory personnel identified through the investigation process were monitored for development of symptoms and referred to care and/or testing as appropriate.

3. Results

3.1. Risk classification

During the > 4 weeks from specimen collection to final confirmation of the isolate, a total of 32 people were identified who had either worked with the specimen or isolate or had been in the vicinity of the work, with most being associated with Laboratory B (Table 1).

3.2. Antimicrobial PEP

Six microbiologists who directly participated in the testing of the specimen or were in the immediate vicinity were identified as "High" risk and were recommended to receive the standard prophylaxis. Because of the delay in final confirmation and the

Table 1
Summary of serologic testing and postexposure monitoring for persons exposed to a *Brucella* spp. isolate at three laboratories, stratified by risk

Laboratory	No. of persons assessed	Risk categories, *n* (%)	Testing* intervals from exposure (wk)	Postexposure monitoring
A	4	High: 2 (50)	2 staff: B†, 8, 12, 20, 26	Doxycycline/rifampin postexposure antibiotics Fever watch
		Low: 2 (50)	1 staff: B†, 12, 26	Fever watch
			1 staff: B†, 8, 12	
B	27	High: 4 (15)	1 staff: 0‡, 2, 6, 12, 20	Doxycycline/rifampin postexposure antibiotics
			3 staff: 0‡, 6, 12, 20	Fever watch
		Low: 23 (85)	13 staff: 0‡, 6, 12, 20	Fever watch
			9 staff: 0‡, 6, 12	
			1 staff: 0‡	
C	1	None§	—	Fever watch

* Testing via the BMAT (*Brucella* spp. micro-agglutination test).
† The first follow-up blood draw for persons working in Laboratory A was in early March, ~1 month after the specimen had been manipulated by microbiologists. Therefore, the baseline or Day 0 interval listed here as 1 is actually 4 weeks from exposure. The other intervals were calculated based on the exact interval from exposure.
‡ Because the specimen had originally arrived in Laboratory B ~3–4 weeks prior to suspicion of *Brucella* spp. identification, the timing intervals for some of the exposed people may actually indicate an additional 3–4 weeks from exposure.
§ At Laboratory C, the isolate had been handled in a biological safety cabinet from the outset.
B, baseline.