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Brucella Exposure Risk Events in 10 Clinical Laboratories, New York City, USA, 2015 to 2017

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ABSTRACT From 2015 to 2017, 11 confirmed brucellosis cases were reported in New York City, leading to 10 *Brucella* exposure risk events (*Brucella* events) in 7 clinical laboratories (CLs). Most patients had traveled to countries where brucellosis is endemic and presented with histories and findings consistent with brucellosis. CLs were not notified that specimens might yield a hazardous organism, as the clinicians did not consider brucellosis until they were notified that bacteremia with *Brucella* was suspected. In 3 *Brucella* events, the CLs did not suspect that slow-growing, small Gram-negative bacteria might be harmful. Matrix-assisted laser desorption ionization–time of flight mass spectrometry (MALDI-TOF MS), which has a limited capacity to identify biological threat agents (BTAs), was used during 4 *Brucella* events, which accounted for 84% of exposures. In 3 of these incidents, initial staining of liquid media showed Gram-positive rods or cocci, including some cocci in chains, suggesting streptococci. Over 200 occupational exposures occurred when the unknown isolates were manipulated and/or tested on open benches, including by procedures that

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could generate infectious aerosols. During 3 *Brucella* events, the CLs examined and/or manipulated isolates in a biological safety cabinet (BSC); in each CL, the CL had previously isolated *Brucella*. Centers for Disease Control and Prevention recommendations to prevent laboratory-acquired brucellosis (LAB) were followed; no seroconversions or LAB cases occurred. Laboratory assessments were conducted after the *Brucella* events to identify facility-specific risks and mitigations. With increasing MALDI-TOF MS use, CLs are well-advised to adhere strictly to safe work practices, such as handling and manipulating all slow-growing organisms in BSCs and not using MALDI-TOF MS for identification until BTAs have been ruled out.

KEYWORDS biosafety, brucellosis, laboratory-acquired infection, risk assessment

Human brucellosis is a common zoonosis found throughout the Near East, Mediterranean Basin, southeastern Europe, Asia, Africa, South and Central America, and the Caribbean (1–4). Most human cases of brucellosis in the United States result from exposure to infected feral swine populations, travel to or residence in a country where the disease remains endemic, occupational exposure, or consumption of unpasteurized (raw) and contaminated dairy products (3, 4).

Brucellosis is immediately reportable to the New York City (NYC) Department of Health and Mental Hygiene (DOHMH) by laboratories and medical providers. From 2000 to 2014, 28 cases of brucellosis (median, 2 cases/year) were reported, including 6 *Brucella* exposure risk events (*Brucella* events) in clinical laboratories (CLs), resulting in more than 80 occupational exposures to *Brucella* spp. From 2015 to 2017, 11 confirmed cases (median, 4 cases/year) were reported to the NYC DOHMH, leading to 10 *Brucella* events in 7 CLs and over 200 occupational exposures.

Laboratory-acquired brucellosis (LAB) can result from inhalation of aerosolized brucellae when unrecognized isolates are manipulated by clinical laboratory workers (CLWs) on open benches (5–8). LAB cases are preventable if clinicians suspect brucellosis and alert CLs when clinical specimens are submitted for culture. However, CLWs are not consistently notified when brucellosis is a diagnostic consideration. Without implementation of appropriate engineering and administrative controls to prevent occupational exposures, CLs are vulnerable to *Brucella* events.

Since 2015, NYC DOHMH's Public Health Laboratory (PHL) has conducted in-person visits with 34 CLs to distribute and review bench cards published by the Association of Public Health Laboratories (APHL), the Laboratory Response Network (LRN), and the American Society for Microbiology (ASM) that contain recommended algorithms to rapidly and safely recognize potential biological threat agents (BTAs), including *Brucella* spp., and to refer them to PHL for confirmatory testing (9, 10). A mean of 25 CLs also participated from 2015 to 2017 in each of 6 biannual College of American Pathologists laboratory proficiency tests for recognition and referral of potential BTAs.

Centers for Disease Control and Prevention (CDC) guidance for the management of laboratory incidents with exposure to *Brucella* was first published in 2008 and was updated in 2013 (11–14). Recommendations include CLW exposure risk stratification as high, low, or minimal (but not zero) risk, depending on the proximity to potentially aerosolized brucellae; a 3-week, postexposure prophylaxis (PEP) regimen of doxycycline and rifampin for high-risk exposures (trimethoprim-sulfamethoxazole if doxycycline or rifampin is contraindicated or not tolerated); and 24 weeks of serological monitoring and symptom watch for both high- and low-risk exposures.

MATERIALS AND METHODS

Case ascertainment and investigation. Cases were identified when clinical isolates were referred by CLs to the NYC Public Health Laboratory (PHL) and the isolates were confirmed to be *Brucella* spp. with CDC-developed procedures. Species identification was determined with a New York State Clinical Laboratory Evaluation Program-approved conventional PCR assay and confirmed by culture-based methods (15).

Data collected for each confirmed case included clinical presentation, diagnostic workup, clinical management, clinicians' query for known brucellosis risk factors, and whether the clinicians suspected brucellosis and informed the CLs when submitting cultures.

TABLE 1 Clinical and epidemiologic features of 10 brucellosis patients in New York City, 2015 to 2017^e

Patient no.	Symptoms ^a	Duration of illness (wk)	Temp (°F) in ED	Abnormal laboratory tests ^b	DDx	Country(ies) of travel ^c	Br RF ^d
1	Recurrent fever, chills, night sweats, weight loss, anorexia, neck pain	16	97.9–101.9	A, D, E, F, G, H	PNA	Mauritania, Senegal	UPM
2	Recurrent fever, night sweats, weight loss, fatigue, cough, arthralgia	8	102	A, D	TB, MAL, BRN	Saudi Arabia	UPM
3	Fever, cough	2	102.9	A, C	BRN	Syria, Jordan, Lebanon	LC
4	Fever, nausea, abdominal and testicular pain	<1	103.4	A, B, D	E-O	Uzbekistan	LC
5	Fever, night sweats, severe bitemporal headache	<1	98.2	B, C, D	VS	Saudi Arabia	UPM, LY
6	Dyspnea, weakness, polydipsia, polyuria	4	98.1	C, D, E	NODM	Mexico	UPM, LC
7	Weakness and tremors	1	96.8	A, E	ESRD, MA	Mexico	UPM, LC
8	Fever, profuse sweats, headache, eye pain	<1	100.6–102.8	C, D	PNA	Saudi Arabia	Unk
9	Fever, night sweats, weight loss, weakness, cough	5	99.4	A, C, D, E	TB	Denied	Unk
10	Recurrent fevers, chills, sore throat, ankle pain	<1	99–101.2	A, D, E	MAL	Kuwait	UPM

^aCommon brucellosis symptoms are recurrent and intermittent fever, night sweats, cough, chills, anorexia, weight loss, fatigue, weakness, testicular pain, and arthralgia.

^bCommon brucellosis clinical findings are thrombocytopenia, mild anemia and leukopenia, elevated hepatitis transaminases and inflammatory markers, and hepatosplenomegaly.

^cIn each of these 10 instances, providers elicited the travel histories from each of the patients.

^dIn each of these 10 instances, providers did not suspect brucellosis and did not elicit brucellosis risk factors from any of the patients.

^eAbbreviations: ED, emergency department; A, anemia; B, leukocytosis; C, thrombocytopenia; D, elevated hepatitis transaminases; E, elevated alkaline phosphatase; F, elevated erythrocyte sedimentation rate; G, elevated C-reactive protein; H, elevated creatine phosphokinase; DDx, differential diagnosis; PNA, pneumonia; TB, tuberculosis; MAL, malaria; BRN, bronchitis; E-O, epididymo-orchitis; VS, viral syndrome; NODM, new-onset diabetes mellitus; ESRD, end-stage renal disease; MA, metabolic acidosis; Br, brucellosis; RF, risk factor; UPM, unpasteurized milk; LC, local cheese; LY, local yogurt; NT, not tested; Unk, unknown.

Initial incident management. Following NYC PHL confirmation, a conference call was held and included the NYC DOHMH, the New York State Department of Health (NYSDOH), CDC laboratory scientists and epidemiologists, and the hospital personnel managing the incident (e.g., laboratory directors and supervisors, occupational health providers, infection prevention and infectious disease specialists). Its aim was to review CDC recommendations for the prevention of brucellosis in exposed CLWs, to assign a presumptive risk classification to all persons potentially exposed per CDC criteria (13, 14), and to schedule an on-site laboratory walkthrough.

Laboratory risk assessment. The submitting CL detailed how the blood culture isolate(s) was manipulated, including whether it was in a type II biological safety cabinet (BSC) or on an open bench; the Gram stain and growth characteristics of the isolate(s); and analytical tests performed and platforms used.

During the laboratory walkthrough, biosafety experts and medical epidemiologists from the NYC DOHMH and the NYSDOH documented the CL layout and work flow; the locations where all isolate manipulations, specimen preparation, and testing occurred; the personal protective equipment worn; and the proximity of persons in the CL to the laboratory activities. These observations were used to refine the initial CLW risk stratifications and to inform recommendations for laboratory risk mitigation.

Exposure management. Persons determined to have high-risk exposures and those with low-risk exposures and conditions causing them to be more susceptible to infection were offered PEP (13, 14). Serum samples were collected from exposed persons at the baseline and every 6 weeks for 24 weeks after exposure and were submitted to CDC for analysis with a *Brucella* microagglutination test (BMAT) (16). Exposed persons were instructed to self-monitor and report any symptoms in the 24 weeks following the incident and were assessed weekly by each facility's occupational health providers.

Laboratory risk mitigation. CL directors considered and instituted engineering and/or administrative controls to address the hazards identified during the laboratory risk assessment.

RESULTS

Case ascertainment and investigation. From 2015 to 2017, 10 isolates referred to the NYC PHL were confirmed to be *Brucella* spp. Nine were identified as *Brucella melitensis*, and each was cultured from patients who reported travel to a country where brucellosis is endemic. A *B. abortus* isolate was cultured from a patient who denied recent travel yet reported consuming unpasteurized cheese from Mexico approximately 3 years before the current illness (Table 1).

Of the 10 microbiologically confirmed cases, 7 presented with histories and symptoms consistent with brucellosis; 4 reported symptoms of a week or less. All cases had laboratory abnormalities commonly seen with brucellosis (Table 1). However, in all 10 instances, clinicians did not ask about brucellosis risk factors or consider the diagnosis. Consequently, no CLs were alerted by clinicians that the blood culture bottles might yield a *Brucella* sp.

Laboratory risk assessment. Ten *Brucella* events occurred in laboratories A, B, C, D, E, F, and G during the time period. Four CLs were in academic medical centers, two CLs were in community hospitals, and one was a core CL for a hospital network. Though they had multiple *Brucella* events during the study period, walkthroughs were conducted at laboratories A and B only once, as public health authorities were already familiar with their layouts and implemented mitigations.

Means of 73 h (range, 50 to 98 h) and 43 h (range, 24 to 72 h) of incubation were needed before growth was detected in liquid media and on solid media, respectively. Four of the Gram stains performed directly from liquid media showed Gram-positive rods or cocci, including some cocci in chains, suggestive of streptococci or diphtheroids (Fig. 1). In contrast, Gram stains of each of the 10 isolates grown on solid media were more suggestive of *Brucella* spp.: 9 read as Gram-negative or Gram-variable coccobacilli, and 1 read as small Gram-negative cocci (Table 2). However, in two instances, matrix-assisted laser desorption ionization (MALDI)–time of flight (TOF) mass spectrometry (MS) or an automated identification and antibiotic susceptibility test (ID/AST) system was used before the colony Gram stains were performed (Table 3).

Unrecognized *Brucella* isolates were examined and manipulated on open benches for a median of 2 days (range, 2 to 7 days). A median of 3 days (range, 0 to 23 days) elapsed from the time of the initial Gram stain to the time of notification of the NYC DOHMH.

Table 2 lists the identified risk factors for *Brucella* events. Four CLs, accounting for 5 (50%) of the *Brucella* events, conducted on open benches procedures known to potentially aerosolize brucellae. Of these 5 *Brucella* events, 3 (60%) occurred with specimens that were initially thought to contain Gram-positive organisms. In one large CL with an open design, catalase testing and vortexing of the unknown isolate, procedures that can generate infectious aerosols, were conducted on an open bench, leading to 100 *Brucella* sp. exposures. In 3 *Brucella* events, CLWs conducted all examinations and manipulations of the isolates in BSCs. In each case, CLWs had previously experienced a *Brucella* event.

MALDI-TOF MS was used by 4 CLs during 6 of the *Brucella* events. Four of these incidents accounted for 84% (183/219) of the exposures in this series. The Bruker MALDI Biotyper was used by laboratories A and B, and bioMérieux's Vitek MS was used in laboratories E and G. Both systems failed to identify a *Brucella* sp. In one case, the Bruker MALDI Biotyper generated a low score for an *Ochrobactrum* sp. Laboratories B and G also used an ID/AST system to identify the isolate, but that effort was unsuccessful.

Two principal types of hazards led to exposure risks. First, CLWs failed to recognize suspicious isolates even when clues were present, such as prolonged incubation times in liquid media and/or on solid media and Gram stains consistent with *Brucella* spp. Second, manipulations of the unknown isolates, including procedures that could aerosolize brucellae, leading to many CLW exposures, occurred on open benches (Table 3).

Exposure management. Of the 219 exposed CLWs, 213 (97%) agreed to serological monitoring. One hundred twelve (51%) incurred high-risk exposures, and 71 (63%) of these agreed to receive PEP. Of those for whom data were available, PEP was prescribed within 1 to 6 days of exposure, though in one incident with a delayed diagnosis, PEP began 5 weeks after exposure (data not shown). No exposed CLWs reported symptoms, and there were no documented *Brucella* seroconversions.

Laboratory risk mitigation. Table 3 lists the hazards identified by laboratory risk assessments and environmental and administrative controls used to mitigate risk.

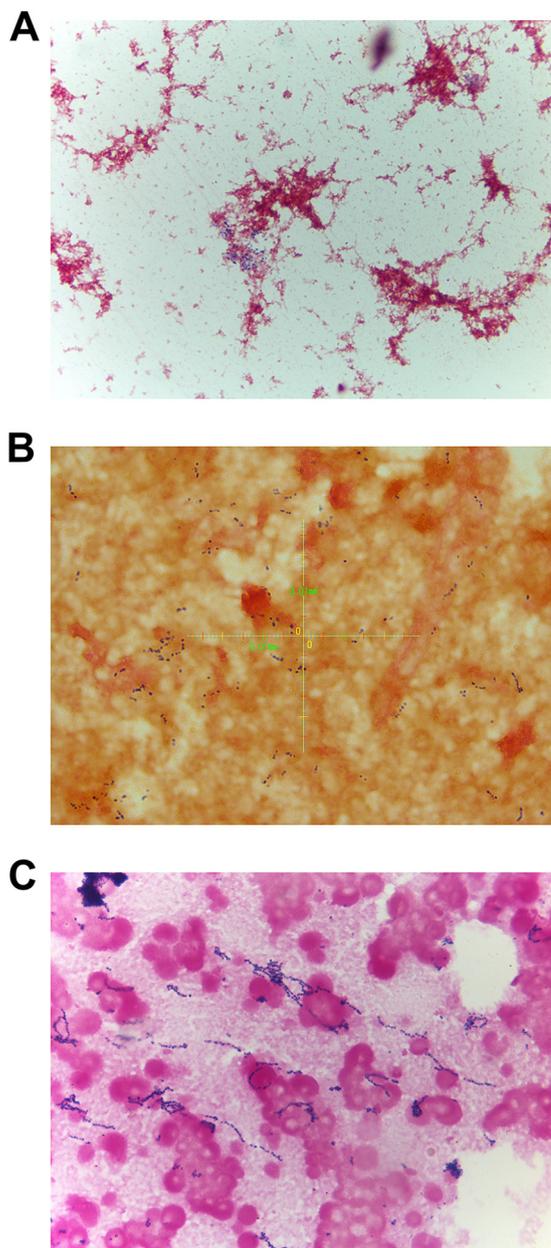


FIG 1 Gram stains of *Brucella* spp. growing in blood culture broth may be mistaken for common Gram-positive organisms. Gram stains from three clinical laboratories of blood culture bottles that ultimately yielded *Brucella* spp. The slow-growing Gram-positive bacilli (A), Gram-positive rods and Gram-positive cocci in chains (B), and Gram-positive cocci in pairs and chains (C) were mistaken initially for streptococci or diphtheroids. Following streaking of blood culture broth on agar plates, Gram stains of colonies yielded small, Gram-negative organisms more typical of *Brucella* (Table 2).

Four of the incidents took place in 3 CLs with prior experience managing *Brucella* events. In laboratory D, all work with the isolate was conducted in a BSC, as the director had experienced a *Brucella* event elsewhere and suspected *Brucella*; there were no exposures (Table 2). Laboratories A and B managed 2 and 3 *Brucella* events, respectively. After the 2015 incident, laboratory A established a new category of “higher risk” for blood culture isolates with certain Gram stain characteristics, for which enhanced biosafety procedures were required and automated ID/AST and MALDI-TOF MS use was limited. These measures, however, proved insufficient to prevent exposures during a second *Brucella* event in October 2017, when a slow-growing blood culture isolate appeared to be a Gram-positive coccus and was handled on an open bench. In

TABLE 2 Summary of laboratory details and public health impacts in 10 *Brucella* exposure risk events, New York City, 2015 to 2017^d

Brucella event no.	Date	CL (type)	No. of BC sets/mo	BCB		SGM		High-risk activities on open bench												Total no. of CLWs			
				Time (h) to detection ^a	Time (h) to detection bench ^b	GS result	GS result	MT	O/M	CT	SMT	MM	VGS	VS	KB	OU	BE	Past HREs	Total no. of HREs	Receiving PEP	In SS LAB	With Brucella sp. detected	
1	March 2015	A (A)	6,000	>70	24	SGNCB	SGNCB	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	24	11	20	35	0	<i>B. melitensis</i>
2	May 2015	B (A)	5,300	83, 97	48	SGNC	SGNC	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	15	3	13	16	0	<i>B. melitensis</i>
3	July 2015	C (C)	900	50	48	SGNCB	SGNCB	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	11	10	8	21	0	<i>B. melitensis</i>
4	August 2015	D (C)	1,500	80	24	SGNC	SGNC	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	0	0	0	0	0	<i>B. melitensis</i>
5	February 2016	E (A)	4,500–6,000	75	48	SGNCB	SGNCB	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	8	1	6	9	0	<i>B. melitensis</i>
6	May 2016	B (A)	5,300	93	48	GVCB	GVCB	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	0	2 ^c	0	2	0	<i>B. melitensis</i>
7	May 2016	B (A)	5,300	72, 98	72	SGNB	SGNB	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	0	0	0	0	0	<i>B. melitensis</i>
8	January 2017	F (A)	3,200	55, 58	48	GPR, GPCP	GVCB	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	2	2	2	4	0	<i>B. melitensis</i>
9	March 2017	G (N)	14,000	52, 66	24	GPR, GPCC	SGNCB	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	32	68	18	100	0	<i>B. abortus</i>
10	October 2017	A (A)	6,000	73, 76	50	GPC	GNCB	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	20	10	6	26	0	<i>B. melitensis</i>

^aNumber of hours of blood culture incubation before microbial growth was detected by an automated blood culture system.

^bNumber of days that personnel worked with the unknown isolate on an open bench.

^cSpecimens were prepared in a type II biological safety cabinet for MALDI-TOF MS and testing in an automated identification system.

^dAbbreviations: CL, clinical laboratory; (A), academic medical center; (C), community hospital; (N), hospital network laboratory; BC, blood culture; GS, Gram stain; BCB, blood culture bottle; SGM, solid growth media; SGNCB, small Gram-negative coccobacilli; SGPC, small Gram-positive cocci; PAC, pairs and chains; SGNC, small Gram-negative cocci; GVCB, Gram-variable coccobacilli; SGNB, small Gram-negative bacilli; GNCB, Gram-negative coccobacilli; GPR, Gram-positive rods; GPC, Gram-positive cocci; GPCC, Gram-positive cocci in chains; GPCP, Gram-positive cocci in pairs; HREs, high-risk exposures; LREs, low-risk exposures; PEP, postexposure prophylaxis; CLWs, clinical laboratory workers; SS, serosurvey; LAB, laboratory-acquired brucellosis; O/M, opening/manipulating plates; CT, catalase test; MT, matrix-assisted laser desorption/ionization time of flight mass spectrometry (MALDI-TOF MS); SMT, spotting MALDI-TOF MS test grid; MM, qualitative micromethod test; VGS, BCB venting, Gram stain, and subculture; VS, vortexing of specimen for testing on an automated identification system; KB, Kirby-Bauer test; OU, oxidase and urease tests; BE, *Brucella* event.

TABLE 3 *Brucella* exposure hazards identified and mitigations implemented by microbiology laboratories, New York City, 2015 to 2017^a

Hazard identified	Mitigation	
	Engineering	Administrative
Clinicians consistently fail to suspect brucellosis prior to laboratory diagnosis	Purchase and install BSC in which all manipulations of BCBs and isolates are conducted until BTA is ruled out	Training to enhance consideration of brucellosis when clinically and epidemiologically appropriate
Clinicians consistently fail to warn CLs that specimens may contain <i>Brucella</i> spp.	Automate CL notifications of BCBs with slow-growing organisms (planned)	Consider all Gram-variable organisms to be presumptive <i>Brucella</i> spp.
BCBs vented, opened, and manipulated on open bench	Automate CL notifications when tests are ordered by clinicians for highly infectious pathogens, such as <i>Brucella</i> , <i>Francisella</i> , and <i>Coccidioides</i> (planned)	Gram stain whenever inconsistent growth is seen on a plate
Slow-growing bacteria in BCBs, including some with suspicious GSs, not recognized as a possible biological hazard		Designate a new category for BCBs, increased risk, in which BCBs are labeled as such, incubated in a separate risk rack, and opened/manipulated in a BSC until a more routine organism is identified, with approval of a supervisor, for (i) BCB organisms that require at least 48 h of incubation before growth is detected; (ii) BCBs with SGNRs, GNCR, GNDC, SGPC, or SGVC or if no organisms are seen; (iii) solid medium plates from BCBs that show no growth after 24 h; and (iv) BCBs and plates associated with patients identified with possible brucellosis or disease caused by other highly infectious organism
GSs from BCBs with <i>Brucella</i> growth can yield Gram-positive organisms that can be mistaken for streptococci		Revise laboratory procedures
Growth on plates not always Gram stained prior to automated ID/AST or MALDI-TOF MS use		Training to review and reinforce proper use of ASM/APHL/LRN biothreat bench cards
Automated ID/AST and MALDI-TOF MS used before BTAs ruled out		Unannounced biosafety proficiency testing, using BCBs spiked with known GNRs and GNCR
<i>Brucella</i> not considered when isolate grows on CNA media		Automated ID/AST or MALDI-TOF MS not used until BTA or some other highly infectious organism is ruled out; if a BTA cannot be ruled out, refer to HD

^aAbbreviations: BCB, blood culture bottle; GS, Gram stain; ID/AST, identification and antibiotic susceptibility test system; MALD-TOF MS, matrix-assisted laser desorption–ionization time of flight mass spectrometry; CNA, Columbia nalidixic acid; BSC, biological safety cabinet; BTA, biological threat agent; CL, clinical laboratory; SGNR, small Gram-negative rods; GNRs, Gram-negative rods; GNCR, Gram-negative coccobacilli; GNDC, Gram-negative diplococci; SGPC, small Gram-positive cocci; SGVC, small Gram-variable cocci; ASM, American Society for Microbiology; APHL, Association of Public Health Laboratories; LRN, Laboratory Response Network; HD, health department.

response, laboratory A then expanded the “higher risk” blood culture category to include all blood culture isolates requiring at least 48 and 24 h of incubation in liquid medium and on solid medium, respectively, for growth to be detected.

Following the *Brucella* event in 2015, laboratory B installed an additional BSC where all blood culture work was to be conducted. It also decided to consider all Gram-variable organisms as presumptive *Brucella* spp. When another *Brucella* sp. isolate was handled there in May 2016, two low-risk exposures occurred when a CLW deliberately countermanded operating procedures, using an automated ID/AST and MALDI-TOF MS before reporting the isolate to NYC DOHMH. When a second *Brucella* isolate passed through laboratory B in May 2016, established procedures were followed and no occupational exposures resulted.

DISCUSSION

From 2015 to 2017, the incidence of brucellosis reported in New York City doubled, leading to 10 distinct CL incidents with potential exposure to *Brucella*. To our knowl-

edge, this may be one of the largest, if not the largest, jurisdictional series of *Brucella* events reported in the United States.

Of the 10 patients from whom *Brucella* spp. were isolated, 9 had traveled from regions where brucellosis is endemic, 8 consumed unpasteurized dairy products, and 7 presented with typical symptoms and clinical syndromes for the disease (3, 4). Even though the patients had recognized risk factors and clinical presentations, brucellosis was not considered diagnostically in any of the 10 culture-confirmed cases until the CL identified a putative *Brucella* sp. Consequently, the clinicians did not alert the CLs that clinical specimens might yield a hazardous pathogen.

Of note, this occurred during a period when, due to the emergence of zoonoses and mosquito-borne diseases with public health significance, including Middle East respiratory syndrome, Zika virus disease, avian influenza, and, most notably, Ebola virus disease, substantial resources were expended training frontline clinicians to consider travel as a critical factor when evaluating and managing febrile illnesses (17). It follows that additional strategies are needed to protect CLWs from potentially hazardous clinical specimens. For example, health care data management systems could be configured to automatically notify CLs when serological testing for potential CL hazards is ordered, allowing CLWs to ensure that any blood culture isolates are handled with appropriate precautions.

The *Brucella* events resulted in 219 exposed CLWs. One hundred twelve (52%) were CLWs with high-risk exposures, and 71 (67%) were of these were administered PEP; no LAB cases were detected.

One-third of CLWs with high-risk exposure ($n = 41$) chose not to take PEP. Of those individuals, 26 (63%) worked in laboratories A and G. In laboratory G, the exposure incident occurred in a large, open-design CL where CLWs may have decided that exposure or LAB was unlikely, comparing their work locations to where the aerosol-generating procedures were conducted. Of the CLWs with high-risk exposures following laboratory A's 2015 and 2017 *Brucella* events, 83% and then 30%, respectively, agreed to PEP. Perhaps some tolerated the PEP poorly in 2015 and, consequently, were uninterested in 2017. Others may have surmised that since no CLWs seroconverted in 2015, they could forego PEP in 2017. Ultimately, whether or not to go forward with a nontrivial, 3-week PEP regimen is a personalized decision best facilitated in consultation with a health care provider, taking into account underlying conditions affecting the CLW's vulnerability to LAB, potential adverse reactions to the antibiotics, proximity to the *Brucella* sp. isolate when benchwork was conducted, and the extent to which one is comfortable living with unquantifiable risk.

Serological monitoring and symptom watch for 6 months are recommended for both high- and low-risk exposures (13, 14). Compliance with this brucellosis surveillance strategy becomes especially salient for CLWs with high-risk exposure who opt out of PEP, as they would benefit most from the early detection of seroconversion or symptomatic infection and the prompt start of a regimen of treatment against brucellosis. In this series, only 5 (2%) of the exposed CLWs did not participate in these surveillance measures.

This series also demonstrated that it is inadvisable for CLWs to rely solely on a Gram stain of blood culture broth to determine whether or not to work with unknown isolates in a BSC. Sixty-eight percent (152/219) of *Brucella* sp. exposures occurred when Gram stains of blood culture media were mistaken for streptococci or diphtheroids and subsequent work was done on open benches. Most exposures occurred when this involved catalase testing or isolate vortexing, both of which may generate infectious aerosols. Another 30% (65/219) of *Brucella* events took place when Gram stains and growth characteristics more typical of *Brucella* spp. (i.e., slow-growing, small Gram-negative or Gram-variable organisms) were not recognized by CLWs. In this regard, some institutions may benefit from additional in-house CLW training.

MALDI-TOF MS has become increasingly common and was used by 4 CLs during 6 *Brucella* events; none of the isolates were successfully identified. MALDI-TOF MS will

consistently misidentify *Brucella* spp. until spectra for biological threat agents (BTAs) are included in commercially available optical libraries (18, 19). Recently, the manufacturer of the Vitek MS updated the system's database to include reference spectra for *Brucella* spp. (20, 21). CLs will also have access to other, sufficiently comprehensive MALDI-TOF MS databases, such as CDC's MicrobeNet (22), which can now identify *Brucella* spp. (23). In time, CLs may grow confident that MALDI-TOF MS will reliably and rapidly identify unrecognized BTAs that need immediate confirmatory testing at a public health reference laboratory.

As MALDI-TOF MS becomes more accessible to CLs, pressures will likely mount on CLWs to omit steps that can delay identification, such as consideration of growth characteristics, Gram stain, and colony morphology, before using the instrument. In one *Brucella* event, Gram stain of an isolate on solid medium, which would have yielded small Gram-negative coccobacilli, was not performed prior to MALDI-TOF MS analysis. Had this happened, the CLWs might have reconsidered the blood culture broth Gram stain, possibly leading to safer subsequent handling of the isolate. In busy, high-throughput laboratories with complex work flows or in laboratories where MALDI-TOF MS analyses are done directly from blood culture broth (24), unanticipated occupational risks from unknown clinical isolates may become evident.

Operating procedures will need to adjust accordingly. For example, the same CLW who reviews a Gram stain before preparing blood culture liquid media for MALDI-TOF MS by lysis-centrifugation/lysis-filtration could be responsible for reviewing any colony isolate Gram stain before inactivating it and preparing MALDI-TOF MS test grids (23). That said, the risk associated with MALDI-TOF MS usage is not well understood, and current exposure management recommendations should be reevaluated as more information becomes available (25).

Laboratory A's handling of two *Brucella* events demonstrates that iterative cycles of laboratory risk assessments are central to effective biorisk management systems and may be needed to successfully identify facility-specific corrective actions and to fine-tune mitigations (26). The steps taken by laboratory A in response to the 2015 *Brucella* event did not prevent the 2017 exposure incident from occurring, and additional mitigations were then put into place.

It has been argued previously that CLs might consider handling all slow-growing and/or suspect pathogens in a BSC until BTAs and other highly infectious pathogens are ruled out (11). Based on the evidence in this series, it would be prudent for all CLs to consider implementing this, regardless of blood culture throughput. In this regard, it is important to note that *Brucella* events result in lengthy and costly impacts on affected institutions and for responding government agencies. We did not quantify costs. However, the time invested by facility providers, CLs, occupational health programs, and public health agencies was substantial.

Brucellosis is a common zoonosis worldwide. Even in American hospitals, where brucellosis is rarely encountered, and especially in locales with diverse ethnic communities and where international travelers are common, *Brucella* spp. persist as biological hazards to CLWs manipulating unknown clinical isolates. Providers are advised to assess patients for risk factors when patients present with histories of travel to areas where brucellosis is endemic and illnesses compatible with brucellosis and to alert CLs when this diagnosis is considered.

CLs are well-advised not to eliminate steps that might alert CLWs that BTAs have not been ruled out and to continue using the diagnostic protocols of APHL, LRN, and ASM for potential BTAs. In this way, suspicious isolates will be recognized rapidly and safely and referred expeditiously to PHLs for confirmatory testing (9, 10). This series also underscores that a comprehensive biorisk management strategy (26) and consistent adherence to safe work practices are absolute requirements to mitigate *Brucella* event-associated CLW exposure risks in this rapidly changing diagnostic environment.

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