Three recent laboratory-associated *Brucella* incidents resulting in >70 exposures, New York City, 2015

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Brucella

- Small, slow-growing Gram negative coccobacilli
- Primary human pathogens: *B. melitensis*, *B. abortus*, and *B. suis* (*B. canis* rarely causes infection)
- Readily aerosolized during routine lab work (e.g., opening plates, subculturing)

Brucellosis

- Common zoonotic disease in much of world
  - Rare in the US; 2 – 3 cases annually in NYC.
- Risk factors
  - Consumption of unpasteurized milk or milk products (typically in endemic country)
  - Exposure to infected farm animal or feral pig
  - Lab work with unrecognized *Brucella* isolate on open bench
- Infectious dose extremely low
- Incubation period typically 2 – 4 weeks (can be as long as 5 months)
- Symptoms: intermittent or undulant fever; sweats; fatigue; joint pain
- If not treated early, can persist as chronic, debilitating illness

Hospital and Lab A
Initial Evaluation

- 4/15/15
  - Patient presents to NYC hospital, traveling directly from JFK Airport, with >1 week of severe neck pain
  - In Mauritania 6 – 9 months
  - EMR notes: denies fever, chills or night sweats
  - In ED, temperature increases to 101.9° F
  - Two days later, ID physician elicits history of 4 months of recurrent fever, 8 – 10 lb. weight loss and anorexia
- Differential dx includes HIV, leptospirosis, mosquito- and tick-related infections, but not brucellosis

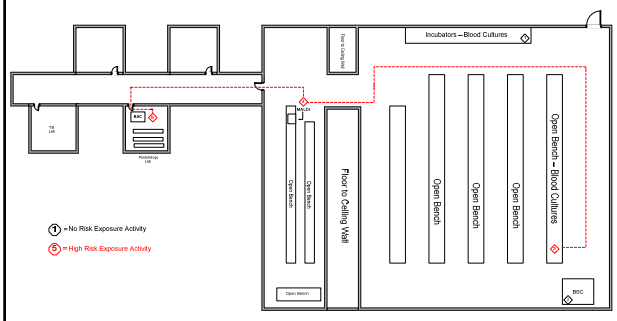
Hospital and Lab A
Illness Course

- After >70 hours of incubation, 2 blood culture sets flagged for growth
  - Bottles vented and Gram stained in biological safety cabinet (BSC)
  - Gram stain: small Gram negative coccobacilli
  - Work with isolate performed on open laboratory bench for one week
  - NYC Department of Health and Mental Hygiene (DOHMH) contacted after outside laboratory identifies presumptive *Brucella* sp.
  - Re-interviewed, patient reports consumption of raw cow, goat and camel milk when in Africa

Assessment of Exposure Risk After Laboratory *Brucella* Incident

- High-risk exposure
  - Direct personal exposure to isolate (e.g., sniffing; skin contact; pipetting by mouth; spraying into eyes, etc.)
  - Working with isolate on open bench
  - Being within 5 feet of laboratorian working with isolate on open bench
  - Being in laboratory at any time when procedure conducted on open bench that can aerosolize brucellae (e.g., venting blood culture bottles, catalase testing, or vortexing)
- Low-risk exposure
  - Being present in laboratory when others working with isolate, though not meeting high-risk definition

Lab A Visit – April 16, 2015



CDC *Brucella* spp. Post-Exposure Recommendations

		2008 Recommendations	2012 Recommendations
Antimicrobial PEP	High Risk	Doxycycline + rifampin x 3 weeks or TMP-SMX + rifampin x 3 weeks*	**No changes**
	Low Risk	Discuss PEP, make available	
Serologic Monitoring		Baseline, 2, 4, 6, 24 weeks post-exposure (after last known exposure)	Baseline, **6, 12, 18,** 24 weeks post-exposure (after last known exposure)
Symptom Surveillance		Regular (e.g., weekly) symptom watch for febrile illness through 24 weeks post-exposure (after last known exposure)	Regular (e.g., weekly) symptom watch and **daily self fever-checks** for febrile illness through 24 weeks post-exposure (after last known exposure)

* For exposures to *B. abortus* RB51 veterinary vaccine strain, rifampin *not* included

Incident Management Challenges

- Discerning risk is not clear-cut
  - Recalling when particular lab work took place and who may have been exposed
  - Assessing risk in persons who briefly traverse lab
  - Determining the shared air space
- Long-term commitment needed by hospital employee health to manage follow-up logistics
- Some at-risk employees (e.g., pregnant or immune suppressed) will refuse prophylaxis and serological surveillance

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Summary of Recent NYC Laboratory Incidents

	Lab A	Lab B	Lab C
Date DOHMH notified	4/15/2015	5/14/2015	7/20/2015
Travel history?	Yes	Yes	Yes
Travel history elicited?	Yes	Yes	Yes
Brucellosis symptoms?	Yes	Yes	**No**
Risk factors?	Yes	Yes	Yes
Brucellosis suspected?	**No**	**No**	No
Micro lab notified?	**No**	**No**	No
Hrs BCxs incubated before flagged	**>70**	**>100**	**~50**
BCxs vented on open bench?	No	Yes	Yes
BCxs Gram stained on open bench?	No	Yes	Yes
Gram stain results	Small GN coccobacilli	Small GP cocci	Small GN coccobacilli
Subcultured on open bench?	Yes	Yes	Yes
Catalase test on open bench?	Yes	No	No
Vortexed on open bench?	No	Yes	Yes
Used MALDI-TOF MS?	Yes	Yes	No
Used VITEK®?	No	Yes	Yes
Days isolate worked on open bench	**7**	**6**	**4**
Confirmed isolate	*B. melitensis*	*B. melitensis*	*B. melitensis*
Number of high risk exposures	24	15	11
Number of low risk exposures	11	3	10
Number prophylaxed (% high risk)	20 (80)	12 (80)	9 (82)
Number of infections as of 9/22/2015	0	0	0

Summary of Recent NYC Laboratory Incidents

	Lab A	Lab B	Lab C	Lab D
Date DOHMH notified	4/15/2015	5/14/2015	7/20/2015	8/28/2015
Travel history?	Yes	Yes	Yes	Yes
Travel history elicited?	Yes	Yes	Yes	Yes
Brucellosis symptoms?	Yes	Yes	**No**	Yes
Risk factors?	Yes	Yes	Yes	Yes
Brucellosis suspected?	**No**	**No**	No	**No**
Micro lab notified?	**No**	**No**	No	**No**
Hrs BCxs incubated before flagged	**>70**	**>100**	**~50**	**80**
BCxs vented on open bench?	No	Yes	Yes	**No**
BCxs Gram stained on open bench?	No	Yes	Yes	**No**
Gram stain results	Small GN coccobacilli	Small GP cocci	Small GN coccobacilli	Small GN cocci
Subcultured on open bench?	Yes	Yes	Yes	**No**
Catalase test on open bench?	Yes	No	No	**No**
Vortexed on open bench?	No	Yes	Yes	**No**
Used MALDI-TOF MS?	Yes	Yes	No	**No**
Used VITEK®?	No	Yes	Yes	**No**
Days isolate worked on open bench	**7**	**6**	**4**	**0**
Confirmed isolate	*B. melitensis*	*B. melitensis*	*B. melitensis*	*B. melitensis*
Number of high risk exposures	24	15	11	**0**
Number of low risk exposures	11	3	10	**0**
Number prophylaxed (% of high risk)	20 (80)	12 (80)	9 (82)	**0**
Number of infections as of 9/22/2015	0	0	0	**0**

Biosafety Steps to Prevent Exposure to *Brucella* spp.

- Vent all blood culture bottles in Class II or higher BSC
- Use BSC when working with unknowns, and especially slow-growing Gram negative organisms
- Review ASM protocols for ruling out and referring potential biological threat agents (BTA), including *Brucella* spp.
- Contact the Health Department when *Brucella* spp. cannot be ruled out
- Do not attempt identification of isolate with instruments or automated systems in lieu of referring a possible *Brucella* isolate to Public Health Laboratory

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APHL ASSOCIATION OF PUBLIC HEALTH LABORATORIES

LRN LABORATORY RESPONSE NETWORK

AMERICAN SOCIETY FOR MICROBIOLOGY

Recognize. Rule-Out. Refer.

Biothreat Agent Bench Cards for the Sentinel Clinical Laboratory

For questions, contact your designated LRN Reference Level Laboratory

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Brucella species

Gram Stain
- Faintly staining, tiny Gram-negative coccobacilli (0.4 x 0.8 µm)
- May be mistaken for cocci

Colony Morphology
- Growth on BAP and CHOC (CO_2 may be required by some strains); No growth on MAC (or EMB)
- Pinpoint colonies at 24h; Discrete, white colonies (0.5-1.0 mm) evident at 48h
- Non-hemolytic

Biochemical/Test Reactions
- Oxidase positive
- Catalase positive
- Urease positive
- Satellite negative

Additional Information
- Biosafety precautions: BSL-3 agent; perform all manipulations in a Class II BSC
- **Commonly misidentified as *Moraxella* spp., *Micrococcus* spp, *Corynebacterium* spp., "slow growing" *Staphylococcus* spp., *Oligella ureolytica*, *Bordetella bronchiseptica*, *Haemophilus* spp., or *Pasteurella* spp. by automated ID systems**
- Transmission: inhalation, consumption of unpasteurized dairy products, direct contact with skin
- **Common laboratory-acquired infection due to the generation of aerosols during manipulation**

Acceptable Specimen Types
- Bone marrow or whole blood in an appropriate blood culture bottle
- Joint or abdominal fluid in an appropriate blood culture bottle
- Spleen or liver abscesses
- Serum (≥1 mL, without anticoagulant)


Gram stain


48h growth on BAP


48h growth on CHOC

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Brucella species Algorithm

WARNING: See Additional Information Regarding Misidentification with Automated Systems

Tiny, Gram-negative coccobacilli (0.4 x 0.8 µm)

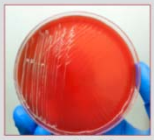
Poor growth at 24h on BAP and CHOC; Discrete colonies at 48h; Non-hemolytic; Non-pigmented; No growth on MAC (or EMB)

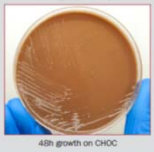
Perform all additional work in a certified Class II BSC

Oxidase positive
Catalase positive
Urease positive
Satellite negative

No → *Brucella* ruled out. Continue with routine identification.

Yes, STOP → *Brucella* not ruled out. Call the LRN Reference Level Laboratory and send suspect agent.


48h growth on BAP


48h growth on CHOC

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