



Expansion of the *Brucella* Genus to include *Ochrobactrum*: Clinical Considerations (2022)

LRN Meeting

Bacterial Special Pathogens Branch
Zoonoses and Select Agent Laboratory

Caroline Schrodt, MD, MSPH

Rebekah Tiller, MPH

Agenda

- **Background/Context: Reclassification**
- **Definitions**
- **General Comparison**
- **Clinical Presentation & Treatment**
- **Scenarios**
- **Clinician Messaging**
- **Case definition considerations**
- **Reiteration of Recommendations**

Background: In 2020 *Ochrobactrum* spp. were re-classified to the *Brucella* genus.

- **Taxonomic nomenclature changed to align phylogenetic analysis***
- **Reflected in some rapid microbial ID systems**
- **Prompting changes in Laboratory, Clinical, Public Health management**

*Hordt A, Lopez MG, Meier-Kolthoff JP, Schleuning M, Weinhold LM, Tindall BJ, Gronow S, Kyrpides NC, Woyke T, Goker M. 2020. Analysis of 1,000+ Type-Strain Genomes Substantially Improves Taxonomic Classification of Alphaproteobacteria. *Front Microbiol* 11:468.

Brucella species: 2022

List of Prokaryotic names with standing in Nomenclature (LPSN)

Classical *Brucella* species

- 1 *Brucella abortus* (Schmidt 1901) Meyer and Shaw 1920 (Approved Lists 1980)
- 2 *Brucella canis* Carmichael and Bruner 1968 (Approved Lists 1980)
- 3 *Brucella ceti* Foster et al. 2007
- 4 *Brucella inopinata* Scholz et al. 2010
- 5 *Brucella melitensis* (Hughes 1893) Meyer and Shaw 1920 (Approved Lists 1980)
- 6 *Brucella microti* Scholz et al. 2008
- 7 *Brucella neotomae* Stoenner and Lackman 1957 (Approved Lists 1980)
- 8 *Brucella pinnipedialis* Foster et al. 2007
- 9 *Brucella ovis* Buddle 1956 (Approved Lists 1980)
- 10 *Brucella papionis* Whatmore et al. 2014
- 11 *Brucella suis* Huddleson 1929 (Approved Lists 1980)
- 12 *Brucella vulpis* Scholz et al. 2016

There are several novel *Brucella* strains that have been described from frogs, bats, Australian rodents and a sting ray that have not been designated as species.

New *Brucella* species, previously *Ochrobactrum*

- 13 *Brucella anthropi* (Holmes et al. 1988) Hördt et al. 2020
- 14 *Brucella ciceri* (Imran et al. 2010) Hördt et al. 2020
- 15 *Brucella cytisi* (Zurdo-Piñeiro et al. 2007) Hördt et al. 2020
- 16 *Brucella daejeonensis* (Woo et al. 2011) Hördt et al. 2020
- 17 *Brucella endophytica* (Li et al. 2016) Hördt et al. 2020
- 18 *Brucella gallinifaecis* (Kämpfer et al. 2003) Hördt et al. 2020
- 19 *Brucella grignonensis* (Lebuhn et al. 2000) Hördt et al. 2020
- 20 *Brucella haematophila* (Kämpfer et al. 2007) Hördt et al. 2020
- 21 *Brucella intermedia* (Velasco et al. 1998) Hördt et al. 2020
- 22 *Brucella lupini* (Trujillo et al. 2006) Hördt et al. 2020
- 23 *Brucella oryzae* (Tripathi et al. 2006) Hördt et al. 2020
- 24 *Brucella pecoris* (Kämpfer et al. 2011) Hördt et al. 2020
- 25 *Brucella pituitosa* (Huber et al. 2010) Hördt et al. 2020
- 26 *Brucella pseudintermedia* (Teyssier et al. 2007) Hördt et al. 2020
- 27 *Brucella pseudogrignonensis* (Kämpfer et al. 2007) Hördt et al. 2020
- 28 *Brucella rhizosphaerae* (Kämpfer et al. 2008) Hördt et al. 2020
- 29 *Brucella thiophenivorans* (Kämpfer et al. 2008) Hördt et al. 2020
- 30 *Brucella tritici* (Lebuhn et al. 2000) Hördt et al. 2020

Definitions: BBS & NBBS

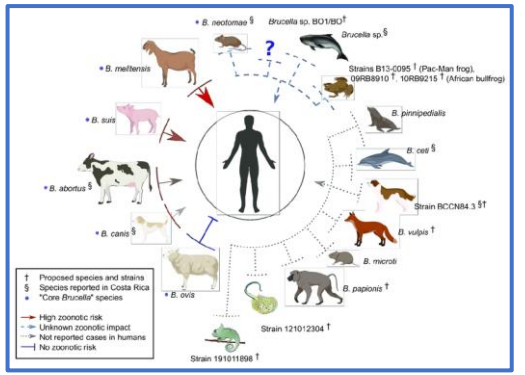
- **BBS**: Brucellosis-causing *Brucella* species (BBS) (including but not limited to *Brucella canis*, and select agents *B. melitensis*, *B. abortus*, and *B. suis*). The *Brucella* LRN PCR assay only detects BBS and does not detect NBBS.

- **NBBS**: Non-Brucellosis causing *Brucella* spp. (NBBS) include bacteria from the former *Ochrobactrum* genus that have been taxonomically combined into the *Brucella* genus. NBBS might cause disease in some patients but do not cause brucellosis and do not require manipulation in a BSL-3 laboratory.

BBS vs. NBBS

| | BBS (Brucellosis-Causing Brucella Species) | NBBS (Non-Brucellosis Causing Brucella Species) |
|--------------------------|--|---|
| Natural Habitat | Animal reservoirs, zoonotic | Soil and water or in hospital environment |
| Clinical significance | Insidious, invasion of multiple tissue types, development of chronic syndrome and focal complications | Rare, infections typically occur through use of contaminated equipment, or in hospital wounds from catheters, opportunistic |
| Reportable Disease | Brucellosis | No |
| Antimicrobial treatment | doxycycline + aminoglycoside or doxycycline + rifampin (6 weeks up to 6 months) [fluoroquinolones, ceftriaxone, or sulfamethoxazole-trimethoprim also have role] | imipenem, the newer fluoroquinolones and the aminoglycosides (amikacin or gentamicin) |
| Antimicrobial Resistance | Rare | Yes |
| Opportunistic Infection | No | Yes |

Brucella spp.



Ochrobactrum spp.





Recap: Not all *Brucella* spp. are the same!

- **Different reservoirs**
 - Zoonotic vs Environmental
- **Different patient susceptibility and exposure risks**
- **Different clinical manifestations**
 - Some symptom overlap
- **Different antimicrobial resistance patterns**
 - Resistance is common in NBBS.
- **Different first-line antibiotic choices**
 - Some medication overlap
- **Different length of treatment**

NBBS as Pathogens

Review

The Genus *Ochrobactrum* as Major Opportunistic Pathogens

Michael P. Ryan ^{1,2}  and J. Tony Pembroke ^{2,*} 

- Reviewed 128 articles describing 289 cases human infection with NBBS (*Ochrobactrum* spp.)
- 95.8% *Brucella anthropi* (*Ochrobactrum anthropi*)
- 92% Opportunistic, in people with underlying conditions or immunocompromise

• Infection Types



- 46% Bacteremia
- 12% Sepsis, Septicemia, Septic Shock
- Others include peritonitis, abscesses, pneumonia, endocarditis, endophthalmitis, keratitis

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NBBS as Pathogens

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- Highly resistant to beta-lactam and other antibiotics
- Susceptible to imipenem, fluoroquinolones like ciprofloxacin, aminoglycosides, and trimethoprim/sulfamethoxazole
- 96.5% Survival

Scenarios

- **Rapid ID Systems may show:**
 - Old nomenclature (i.e., *Ochrobactrum anthropi*)
 - New nomenclature (i.e., *Brucella anthropi*)
 - Combination old + new [i.e., *Brucella (Ochrobactrum) anthropi*]
 - Unspecified if BBS or NBBS
 - → All of the above should undergo ASM rule-out testing
- **ASM Rule out testing**
 - IF: Colony morphology and microbial testing aligns with NBBS
 - THEN: Report NBBS to clinician
 - IF: Colony morphology and microbial testing aligns with BBS
 - THEN: Submit to LRN laboratory as a suspect BBS
- **Brucella LRN testing**
 - IF: “*Brucella* spp.” is negative by the *Brucella* LRN PCR
 - THEN: Report "BBS DNA was not detected by RT-PCR"
- **Appropriate messaging to clinicians**

Considerations for Clinician Messaging



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Brucella and Ochrobactrum **Taxonomic Updates for Laboratories**

Frequently Asked Questions (FAQ) for Clinical Laboratories

Authors: Rosemary She, Carrie Anglewicz, Kurt Jerke, Ryan Relich, Mark Glazier,
Laura Filkins*, Audrey Schuetz*

**Co-corresponding authors*

On behalf of the American Society for Microbiology Clinical and Public Health Microbiology Committee,
Laboratory Practices Subcommittee

<https://asm.org/Guideline/Brucella-and-Ochrobactrum-Taxonomic-Updates-for-La>

Considerations for Clinician Messaging (adapted from ASM's "*Brucella* and *Ochrobactrum* Taxonomic Updates for Laboratories")

- If applicable: Convey that recent taxonomic revisions have reassigned *Ochrobactrum* species to the genus *Brucella*.
- NBBS are distinct from species that cause brucellosis.
- NBBS include bacteria from the former *Ochrobactrum* genus that have been taxonomically combined into the *Brucella* genus
- NBBS are not Select Agents of bioterrorism concern.
- ***When clinically indicated, **antimicrobial therapy recommendations** for infections with NBBS (formerly *Ochrobactrum*) **are unchanged**.
- ***Patients with infection due to NBBS **do not have brucellosis** and should not be reported as a brucellosis case

Brucellosis (*Brucella* spp.) 2010 Case Definition

Clinical Description

An illness characterized by acute or insidious onset of fever and one or more of the following: night sweats, arthralgia, headache, fatigue, anorexia, myalgia, weight loss, arthritis/spondylitis, meningitis, or focal organ involvement (endocarditis, orchitis/epididymitis, hepatomegaly, splenomegaly).

Laboratory Criteria For Diagnosis

Definitive

- Culture and identification of *Brucella* spp. from clinical specimens
- Evidence of a fourfold or greater rise in *Brucella* antibody titer between acute- and convalescent-phase serum specimens obtained greater than or equal to 2 weeks apart

Presumptive

- *Brucella* total antibody titer of greater than or equal to 160 by standard tube agglutination test (SAT) or *Brucella* microagglutination test (BMAT) in one or more serum specimens obtained after onset of symptoms
- Detection of *Brucella* DNA in a clinical specimen by PCR assay

Case Classification

Probable

A clinically compatible illness with at least one of the following:

- Epidemiologically linked to a confirmed human or animal brucellosis case
- Presumptive laboratory evidence, but without definitive laboratory evidence, of *Brucella* infection

Confirmed

A clinically compatible illness with definitive laboratory evidence of *Brucella* infection

Current Recommendations

| Level | Circumstance | Recommendation |
|----------------------|---|---|
| Clinical laboratory | Isolate identified as a NBBS [<i>Brucella (Ochrobactrum) anthropi</i> or <i>Brucella (Ochrobactrum) intermedium</i>] on a rapid identification system or genomic test | <ol style="list-style-type: none"> 1. Evaluate using the <u>ASM rule-out testing</u> 2. If unable to differentiate using microbiological methods, refer to LRN laboratory for rule-out testing |
| Clinical laboratory | Isolate identified as a " <i>Brucella</i> spp" on a rapid identification system | <ol style="list-style-type: none"> 1. Evaluate using the <u>ASM rule-out testing</u> 2. Refer to LRN laboratory for rule-out testing if unable to differentiate using microbiological methods |
| State PHL | Isolate is negative on the <i>Brucella</i> LRN PCR | <ol style="list-style-type: none"> 1. Report "BBS DNA was not detected by RT-PCR"- no further testing required 2. NOT REQUIRED; But if species identification is desired, submit isolate to CDC's Special Bacteriology Reference Laboratory |
| Clinical community | Patient is infected with NBBS [<i>Brucella (Ochrobactrum)</i> species (<i>i.e anthropi, intermedium, other</i>)] | Treat for NBBS (formerly <i>Ochrobactrum</i>) infection if clinically indicated |
| State Epidemiologist | Patient infected with NBBS [<i>Brucella (Ochrobactrum)</i> species (<i>i.e anthropi, intermedium, other</i>)] | Do NOT report as brucellosis |

Questions?

Bacterial Special Pathogens Branch: bzb@cdc.gov

Zoonoses and Select Agent Laboratory: zsal@cdc.gov

Special Bacteriology Reference Laboratory: sbri@cdc.gov

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

