STANDARD DEVIATIONS: Noticing the Neglected

Greetings,

Would you rather be overlooked or overheard?

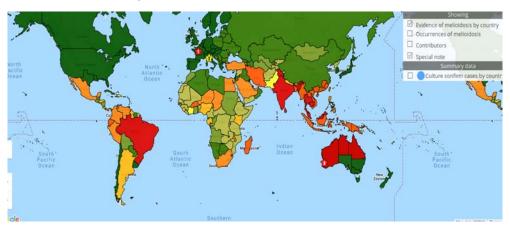
Would you rather be neglected or well-known?

You're probably more popular if you're well-known and often overheard than if overlooked and mostly neglected, right?

Melioidosis is a neglected tropical disease we don't hear enough about.

Melioidosis, also called Whitmore's disease, is an infectious disease that can infect humans or animals. The disease is caused by the bacterium *Burkholderia pseudomallei*.

It is predominately a disease of tropical climates, especially in Southeast Asia and northern Australia where it is widespread. It's estimated that **there are 165,000 human melioidosis cases per year worldwide**, of which **89,000 will be fatal** (like measles and far greater than dengue infection). Its mortality is 20-50% even with treatment (~90% untreated!).

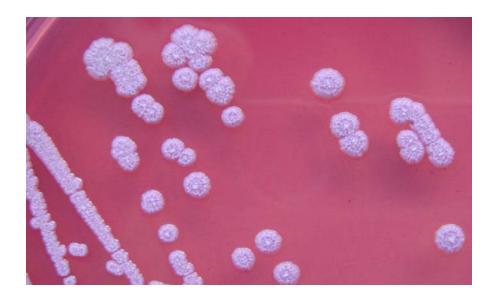


The bacteria causing melioidosis are found in contaminated water and soil. *Burkholderia* pseudomallei is a non-fermenting Gram-negative bacillus that is oxidase positive.

B. pseudomallei frequently does not show bipolar staining on Gram stain, but it is often pleomorphic and usually stains slightly unevenly.

B. pseudomallei colonies are usually cream colored with a metallic sheen and may become dry and wrinkled after >24 hours' incubation on blood agar, although considerable variation is seen. On MacConkey agar, *B. pseudomallei* colonies will initially be colorless and opaque with a metallic sheen but become pink after 48 hours (thought to be due to the uptake of dye from the medium), frequently with a central umbo. *B. pseudomallei* on Ashdown's agar grows as pinpoint colonies by 18 hours, which are usually purple, flat, dry and wrinkled after 48 hours of incubation.





People can get Melioidosis through direct contact with contaminated soil and surface waters. Melioidosis has a wide range of signs and symptoms that can be mistaken for other diseases such as tuberculosis or more common forms of pneumonia. It has been dubbed "the Great Imitator" due to the absence of a pathognomonic clinical syndrome and the ability to exhibit clinical manifestations that mimic other diseases, such as cancer or tuberculosis. Treatment generally starts with intravenous antimicrobial therapy for 10-14 days (Ceftazidime or Meropenem), followed by 3-6 months of oral antimicrobial therapy (Trimethoprimsulfamethoxazole or Amoxicillin/clavulanic acid).

Humans and animals are believed to acquire the infection by inhalation of contaminated dust or water droplets, ingestion of contaminated water, and contact with contaminated soil, especially through skin abrasions. It is rare, but not unheard, for people to get the disease from another person. The time between an exposure to the bacteria that causes the disease and the emergence of symptoms is not clearly defined, but may range from one day to many years; generally, symptoms appear two to four weeks after exposure but it has been found in veterans of the Vietnam War, years after exposure. There is a significant disparity between reported and estimated disease, and many consider melioidosis a major neglected tropical disease.

Besides humans, many animal species are susceptible to melioidosis, including: Sheep, goats, swine, horses, cats, dogs, and cattle.

Ubiquitous and dangerous, this is a Federal Select Agent. As a biothreat, it's capability for weaponization has been explored and developed by several countries because of the ease with which strains may be obtained from the environment, the ability to engineer strains that are resistant to multiple antibiotics, and the lack of a vaccine. This is a Risk Group 3 organism (NIH, BMBL) and should be handled with BSL-3 safety practices.



Detection requires good microbiological technique, attention to travel history and respect for safety protocols. Any culture suspicious for this organism must be referred to the State Laboratory for confirmation. Throwing this bug on the MALDI-TOF will result in having to complete the dreaded CDC Federal Select Agent Program **Form 3**, and possibly post-exposure prophylaxis. Microbiologists should treat unfamiliar, non-fermenting gram-negative rods with the characteristics described in the Sentinel procedures with caution and suspicion. **NOTE**: Suitable analogs of this bacterium are used in proficiency testing for sentinel Microbiology laboratories and it should be a component of the algorithms used in your differentials.

Once submitted to the State Laboratory for confirmation, we'll attempt to isolate and confirm the identification through several confirmatory tests. UPHL performs motility, Maltose, Oxidase, Gentamicin inhibition, Arginine dehydrogenase (decarboxylase), and PCR for 4 specific targets. I'm including our test algorithm in a post-script for the curious minded.

Although Melioidosis is not endemic to our area, we should not relax our safety awareness when travel history, clinical presentation, culture observation and risk assessment suggest the possibility of any biohazardous organism.

Have a great week and be safe,

Bryan

p.s. Here's the algorithm:

<u>Confirmation of Burkholderia mallei and Burkholderia pseudomallei</u>

To be considered as **confirmed** *B. mallei* or *B. pseudomallei*, an organism must meet the criteria listed in the following tables.

NOTE: Samples/specimens tested via biochemical and culture results alone or PCR results alone are considered **presumptive** for *B. mallei* or *B. pseudomallei*.

Confirmation requires a combination of culture, biochemical, and PCR results. PCR as part of the confirmatory algorithm must be performed on a culture isolate.

Table 1. CONFIRMATION of B. mallei

Arginine	Oxidase	Motility	Maltose	Gentamicin	PCR*
positive	variable	non-motile	negative	≥15 mm	MP1 positive
					MP2 positive
					MP3 positive
					PT1 negative



Table 2. CONFIRMATION of *B. pseudomallei*

Arginine	Oxidase	Motility	Maltose	Gentamicin	PCR*
positive	positive	motile	positive	≤12 mm	MP1 positive
					MP2 positive
					MP3 positive
					PT1 positive

^{*}For instructions on performing PCR assays and interpreting results, see <u>Detection of Burkholderia mallei</u> and <u>Burkholderia pseudomallei</u> DNA by Fluorogenic 5' Nuclease Assay using the [Specific Instrument].

References:

 $\underline{www.melioidosis.info/info.aspx?pageID=104\&contentID=1040206}$

 $www.cdc.gov/melioidosis/bioterrorism/threat.html\\ weathereffect\%20on\%20burk.pdf\\ www.cdc.gov/melioidosis/symptoms/index.html\\ jcm.asm.org/content/54/12/2866\\ www.centerforhealthsecurity.org/our-work/publications/glanders-and-melioidosis-fact-sheet csams.cdc.gov/LRN/Documents.aspx?location=tree&node=355\\$

