# State of The Globe: Melioidosis: Diagnostic Caveats and Emerging Solutions

Melioidosis is an emerging, potentially fatal disease caused by Gram-negative saprophytic bacterium *Burkholderia pseudomallei*. This disease is highly endemic in Northern Australia and South east Asia. Due to lack of experience and validated diagnostic modalities, this disease remains misdiagnosed or underdiagnosed, especially in areas of low endemicity. The disease spectrum may vary from mild skin infection without sepsis to disseminated infection and sepsis with case fatality ranging from 14% to 40%. Mortality associated with this disease may reach up to 80% if effective antimicrobial drugs are not given.[1] Clinical diagnosis is difficult as the disease has no pathognomonic clinical features and is "a remarkable imitator" of various infectious as well as noninfectious diseases.[2] A high incidence of melioidosis has been reported in people who have underlying predisposing conditions such as diabetes mellitus, renal disease, alcoholism, malnutrition, and people with immunosuppression.[3]

For confirmation of clinical diagnosis, culture on a selective medium such as Ashdown's medium is still considered as gold standard. Culture has 100% specificity, but sensitivity may vary depending on the type of specimen, media used, and the expertise of the microbiologist. An oxidase-positive, Gram-negative bacilli showing bipolar staining exhibiting resistance to aminoglycosides, colistin and polymyxin but showing sensitivity to amoxyclav may be provisionally identified as *B. pseudomallei* in resource-poor laboratory settings.[4] Rapid identification from colonies can be done with latex agglutination assays utilizing monoclonal or polyclonal antibodies. Many such assays developed in-house have been described which are rapid, inexpensive, and accurate; however, they need to be validated first.[5]

Various commercially available identification systems showing variable accuracy in identification are also available such as API 20NE, VITEK 2, and BD PHOENIX automated microbiology system, but there accuracy relies on the size of the strain database used for identification. Geographical location also needs to be taken into consideration as *B. pseudomallei* is known to harbor a vast intraspecies genomic diversity causing misdiagnosis in the automated system as concluded by the author in this study. Furthermore, these commercial systems may fail to distinguish between *B. pseudomallei*, *Burkholderia thailandensis* (phonotypically similar but rarely virulent species), and members of *Burkholderia cepacia* complex.[6]

Molecular confirmation by polymerase chain reaction (PCR) based on type III secretion system gene and single-nucleotide polymorphism in conserved regions such as BurkDiff assay can be done in reference laboratories. 16S rRNA gene sequencing for the identification of bacteria can also be done. Newer rapid methods based on mass spectrometry, such as matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF-MS), are found potentially useful in the correct identification of *B. pseudomallei*. Direct rapid detection from clinical specimen has been tried with immunofluorescence assay, lateral flow assay, and PCR. Various serological tests such as indirect hemagglutination assay and enzyme-linked immune sorbent assay have been utilized in various studies showing variable sensitivity and specificity. Recently, techniques such as metabolomic profiling with help of ultra high performance liquid chromatography-electrospray ionization-quadruple-time of flight-mass spectrometry (UHPLC-ESI-Q-TOF-MS) are also being researched for identification of *B. pseudomallei* from culture supernatants and distinguishing them from *B. thailandensis* and *B. cepacia* complex.[7]

For antimicrobial susceptibility testing, Clinical and Laboratory Standard Institute recommends minimum inhibitory concentration (MIC) measurements, but disc diffusion susceptibility and E-test strips are commonly used in endemic regions.[8] Doubtful result of disc diffusion susceptibility test, especially for trimethoprim-sulfamethoxazole, should be confirmed by MIC method. Ceftazidime and amoxyclav have been used as empirical treatment for melioidosis, but in rare chances of nonresponsiveness, use of carbapenems is advocated. Antimicrobial drug susceptibility testing methods using quantitative PCR to rapidly evaluate susceptibility, by comparing the growth of bacteria exposed to varying concentration of antimicrobial drugs with that of unexposed bacteria, are being developed which will give result within 12 h.[1]

A confirmed diagnosis of *B. pseudomallei* is a challenge, especially in low-prevalence settings. *B. pseudomallei* is a potential category B bioterrorism agent and a misdiagnosis can put the laboratory personnel at high risk of acquiring this infection by inhalation, inoculation, or ingestion. Documented reports of melioidosis from India are limited, which can be due to lack of awareness and nonavailability of good laboratory services in peripheral areas.[9] Therefore, clinicians and microbiologists should be made aware about this pathogen and its frequent misdiagnosis. Availability of validated diagnostic reagents for immunological and molecular tests and expansion of databases of commercial identification systems will likely remove the major hurdles in correct identification of *B. pseudomallei*. Development of rapid point of care tests such as lateral flow immunoassay would also prove to be helpful in rapid identification of isolates and direct detection from clinical specimens, especially in low-resource settings.

In conclusion, a high level of suspicion on the part of clinicians along with vigilant microbiologists and availability of discerning diagnostic assays may help in identification, reporting, and subsequent management of this "mimicker of maladies."[10]

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## References

1. Hoffmaster AR, AuCoin D, Baccam P, Baggett HC, Baird R, Bhengsri S, *et al.* Melioidosis diagnostic workshop, 2013. Emerg Infect Dis 2015;21(2);2015.
2. Loveleena, Chaudhry R, Dhawan B. Melioidosis; the remarkable imitator: Recent perspectives. J Assoc Physicians India 2004;52:417-20.
3. Currie BJ, Jacups SP, Cheng AC, Fisher DA, Anstey NM, Huffam SE, *et al.* Melioidosis epidemiology and risk factors from a prospective whole-population study in Northern Australia. Trop Med Int Health 2004;9:1167-74.
4. Limmathurotsakul D, Jamsen K, Arayawichanont A, Simpson JA, White LJ, Lee SJ, *et al.* Defining the true sensitivity of culture for the diagnosis of melioidosis using Bayesian latent class models. PLoS One 2010;5:e12485.
5. Dharakul T, Songsivilai S, Smithikarn S, Thepthai C, Leelaporn A. Rapid identification of burkholderia pseudomallei in blood cultures by latex agglutination using lipopolysaccharide-specific monoclonal antibody. Am J Trop Med Hyg 1999;61:658-62.
6. Podin Y, Kaestli M, McMahon N, Hennessy J, Ngian HU, Wong JS, *et al.* Reliability of automated biochemical identification of *Burkholderia pseudomallei* is regionally dependent. J Clin Microbiol 2013;51:3076-8.
7. Lau SK, Sridhar S, Ho CC, Chow WN, Lee KC, Lam CW, *et al.* Laboratory diagnosis of melioidosis: Past, present and future. Exp Biol Med (Maywood) 2015;240:742-51.
8. Clinical and Laboratory Standards Institute. Methods for Antimicrobial Dilution and Disk Susceptibility Testing of Infrequently Isolated or Fastidious Bacteria. CLSI document M45-A2. Wayne, PA: The Institute; 2010.
9. Vidyalakshmi K, Shrikala B, Bharathi B, Suchitra U. Melioidosis: An under-diagnosed entity in Western Coastal India: A clinico-microbiological analysis. Indian J Med Microbiol 2007;25:245-8.
10. John TJ. Melioidosis, the mimicker of maladies. Indian J Med Res 2004;119:vi-viii.



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**Quick Response Code:**

**Website:** www.jgid.org

**DOI:** 10.4103/jgid.jgid_107_17

**How to cite this article:** Ranjan N, Ranjan KP. State of the globe: Melioidosis: Diagnostic caveats and emerging solutions. J Global Infect Dis 2018;10:1-2.