DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

Centers for Disease Control
and Prevention (CDC)
Atlanta GA 30333

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To: National Association of State Public Health Veterinarians

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Subject: Melioidosis in Imported Nonhuman Primates

Dear Interested Party:

Due to recent cases of melioidosis in imported nonhuman primates (NHPs), the Centers for Disease Control and Prevention Division of Global Migration and Quarantine (CDC DGMQ) is providing information to CDC-registered NHP importers and other stakeholders who may have occupational exposure to imported NHPs. Since 2021, three separate cases of melioidosis were diagnosed in NHPs imported from Cambodia. Two of the infected NHPs developed subcutaneous abscesses in the lumbosacral region weeks to months after importation. In both cases, treatment with antibiotics resulted in clinical improvement, but humane euthanasia was elected upon diagnosis of melioidosis. Post-mortem testing showed evidence of persistent systemic infection in both NHPs. The third NHP developed facial swelling four weeks after importation and was euthanized due to poor response to treatment; at necropsy, multiple abscesses were noted in the abdomen. Despite initial isolate misidentification by commercial laboratories in two of the cases (as *Burkholderia cepacia, Escherichia coli,* and *Enterococcus* spp.), the etiologic agent in all cases was ultimately confirmed to be *Burkholderia pseudomallei* by reference laboratories. Molecular diagnostics at CDC identified two genetically distinct lineages from the two isolates available for testing, both with origins in Southeast Asia.

Background

Melioidosis is a potentially fatal infectious disease of humans and animals caused by the Tier 1 Select Agent *B. pseudomallei.*[1] This bacterium is found in soil and water of tropical and sub-tropical regions, including Southeast Asia, Southern China, and parts of South America.[2,3] Occasionally, cases are identified in people in the U.S., typically after international travel to areas where the organism is endemic. Animals (including NHPs) imported from endemic regions of the world have also developed melioidosis after arriving in the United States.[3] *B. pseudomallei* has not been detected in environmental samples (e.g., soil, water) within the U.S.; but research has indicated that environmental conditions in the southern U.S.

[1] eCFR :: 42 CFR Part 73 -- Select Agents and Toxins
[2] Benoit TJ, Blaney DD, Doker TJ, Gee JE, Elrod MG, Rolim DB, Inglis TJ, Hoffmaster AR, Bower WA, Walke HT. 2015. A Review of Melioidosis Cases in the Americas. Am J Trop Med Hyg 93:1134-1139.
[3] Limmathurotsakul D, Golding N, Dance DA, Messina JP, Pigott DM, Moyes CL, Rolim DB, Bertherat E, Day NP, Peacock SJ, Hay SI. 2016. Predicted global distribution of Burkholderia pseudomallei and burden of melioidosis. Nat Microbiol 1:15008.

could promote establishment of the organism if it were introduced.[4,5] Approximately 60% of the NHPs imported to the U.S. originate in countries where melioidosis is endemic and *B. pseudomallei* is present in the environment.

Humans and NHPs can be infected through inhalation or ingestion of environmental *B. pseudomallei*, or by contamination of breaks in the skin, like cuts or scratches. Direct transmission between people and animals is rare, but people can be exposed through contact with infectious animal materials such as feces, bodily fluids, or exudates from wounds.[6] The incubation period in people is typically 1–21 days but is highly variable and can be much longer. In NHPs, the incubation period is not definitively known, but can also be prolonged; one report described a rhesus macaque that developed melioidosis 10 years after importation into the U.S.[7] Clinical features in people and NHPs are variable and include pneumonia, abscesses in skin and other organs, sepsis, central nervous system abnormalities, and death. In people, the case fatality rate ranges from 10%–50%.[8]

Melioidosis can be treated with antibiotics, although antimicrobial resistance does occur. Prolonged courses of intravenous (2–8 weeks) followed by oral (3–6 months) antibiotics are recommended, and infection can recur if not completely cleared when treatment is discontinued.[8] In animal melioidosis cases, euthanasia is generally recommended instead of treatment due to potential for antimicrobial resistance with prolonged treatment protocols, potential for recurrence, and concern over shedding of *B. pseudomallei* into the environment.[6]

Recommendations

- *CDC-Registered NHP Importers**
    - During the CDC-mandated post-importation quarantine period, follow your CDC-approved standard operating procedures (SOPs) for working with imported NHPs and diagnostic specimens.
    - If an animal develops clinical signs of bacterial infection (e.g., abscesses, draining tracts in the skin), or if lesions indicating bacterial infection (e.g., abscesses in abdominal organs, pneumonia) are noted at necropsy, submit specimens collected from lesions to a laboratory for bacterial culture.
        - Notify the laboratory that the material is from a recently imported NHP that is currently in quarantine, and you suspect an infectious agent. If the NHP was imported from an endemic region, notify the laboratory that *B. pseudomallei* is a possibility, and that precautions should be taken to avoid exposure to aerosols.[3]
        - **Note: 42 CFR 71.53 requires importers to retain any samples of tissues, blood, serum, or bodily fluids collected during necropsy until the NHP**

[4] Portacci K, Rooney AP, Dobos R. 2017. Assessing the potential for Burkholderia pseudomallei in the southeastern United States. J Am Vet Med Assoc 250:153-159.
[5] Hall CM, Busch JD, Shippy K, Allender CJ, Kaestli M, Mayo M, Sahl JW, Schupp JM, Colman RE, Keim P, Currie BJ, Wagner DM. 2015. Diverse Burkholderia Species Isolated from Soils in the Southern United States with No Evidence of B. pseudomallei. PLoS One 10:e0143254.
[6] The Center for Food Security and Public Health ISUCoVM. Melioidosis, pp. 220-224. In: Spickler AR, Roth JA, Galyon J, Lofstedt J editors. Emerging and Exotic Diseases of Animals, 4th Edition. Ames, Iowa: Iowa State University College of Veterinary Medicine.
[7] Fritz PE, Miller JG, Slayter M, Smith TJ. 1986. Naturally occurring melioidosis in a colonized rhesus monkey (Macaca mulatta). Lab Anim 20:281-285.
[8] Wiersinga WJ, Virk HS, Torres AG, Currie BJ, Peacock SJ, Dance DAB, Limmathurotsakul D. 2018. Melioidosis. Nature Reviews Disease Primers 4:17107.

shipment has been released from CDC-mandated quarantine, in case other testing is required by CDC. Importers should also retain diagnostic specimens collected from ill NHPs in case additional testing is required.

- Consider the possibility of melioidosis in NHPs imported from endemic regions with consistent clinical signs or necropsy findings.[3] If you suspect melioidosis, contact your local or state public health department for guidance on how to submit specimens or isolates to a Laboratory Response Network (LRN) laboratory for diagnosis or confirmatory testing.
  - Keep in mind that commercially available automated identification systems may misidentify *B. pseudomallei.*
- Communicate with CDC DGMQ if there are NHP morbidities or mortalities during quarantine, as required by 42 CFR 71.53.
- If melioidosis is confirmed in an imported NHP during CDC-mandated quarantine, work with your local or state health department and CDC DGMQ to determine appropriate actions regarding the affected NHP and other NHPs in the cohort. The health department can also assist in evaluating risk of exposure in quarantine facility and laboratory personnel.

- *Recipients of Imported NHPs that have cleared the CDC-mandated quarantine period (e.g., researchers, zoos)**
  - Consider melioidosis in NHPs imported from endemic regions of the world, regardless of the time that has passed since importation.[3] Keep in mind the incubation period can be prolonged (months to years).
  - If an NHP has clinical signs of infection or if lesions indicating infection are noted at necropsy (e.g., abscesses, draining tracts, pneumonia), submit specimens collected from lesions to a laboratory for bacterial culture.
    - Notify the laboratory that the material is from an imported NHP, and you suspect an infectious agent. If the NHP was imported from an endemic region, notify the laboratory that *B. pseudomallei* is a possibility, and that precautions should be taken to avoid exposure to aerosols.[3]
  - Consider the possibility of melioidosis in NHPs imported from endemic regions with consistent clinical signs or necropsy findings.[3] If you suspect melioidosis, contact your local or state health department for guidance on how to submit specimens or isolates to a Laboratory Response Network (LRN) laboratory for diagnosis or confirmation.
    - Keep in mind that commercially available automated identification systems may misidentify *B. pseudomallei.*
  - If melioidosis is confirmed in an NHP, contact your local or state health department immediately to determine appropriate actions.

- *Laboratorians*
  - Laboratory personnel are at increased risk for infection from clinical specimens because some laboratory procedures may aerosolize particles that could inadvertently release *B. pseudomallei* into the air.[9] Laboratory personnel can reduce their risk of exposure by

[9] Melioidosis Cases and Selected Reports of Occupational Exposures to Burkholderia pseudomallei--United States, 2008-2013. Benoit TJ, Blaney DD, Gee JE, Elrod MG, Hoffmaster AR, Doker TJ, Bower WA, Walke HT; Centers for Disease Control and Prevention (CDC). MMWR Surveill Summ. 2015 Jul 3;64(5):1-9.PMID: 26135734

following safe laboratory practices and using BSL3 protocols when handling specimens from NHPs and cultures if melioidosis is suspected. [10]

- Laboratory staff who may have been exposed to *B. pseudomallei* should refer to existing CDC guidance.[11]
- Melioidosis is diagnosed by culturing *B. pseudomallei* from clinical specimens. Automated identification systems commonly used by microbiology laboratories (e.g., MALDI-TOF, 16s, VITEK-2, API 20NE) may misidentify *B. pseudomallei* as another bacterium, including other *Burkholderia* spp. (e.g., *B. cepacia* and *B. thailandensis*), *Pseudomonas* spp., *Chromobacterium* spp., and *Aeromonas* spp.[12]
- If *B. pseudomallei* is suspected considering the clinical presentation, origin of the NHP, and potential for misidentification using automated systems, contact your state or local health department immediately. The health department can facilitate forwarding the isolate for confirmation to the closest reference laboratory and initiate a public health investigation.
- If *B. pseudomallei* is confirmed in a clinical specimen, it must be reported immediately to the Federal Select Agent Program.

For More Information:

- Melioidosis | CDC
- Melioidosis (iastate.edu)
- Treatment and postexposure prophylaxis:
  - Workshop on Treatment of and Postexposure Prophylaxis for Burkholderia pseudomallei and B. mallei Infection, 2010 (nih.gov)
  - Management of Accidental Laboratory Exposure to Burkholderia pseudomallei and B. mallei - Volume 14, Number 7—July 2008 - Emerging Infectious Diseases journal - CDC
  - 2020 Review and revision of the 2015 Darwin melioidosis treatment guideline; paradigm drift not shift (plos.org)
- Burkholderia Infections | Red Book: 2021–2024 Report of the Committee on Infectious Diseases | Red Book Online | American Academy of Pediatrics (aap.org)

[10] Biosafety in Microbiological and Biomedical Laboratories: Biosafety in Microbiological and Biomedical Laboratories—6th Edition (cdc.gov)

[11] Peacock SJ, Schweizer HP, Dance DAB, Smith TL, Gee JE, Wuthiekunan V, et al. Management of accidental laboratory exposure to *Burkholderia pseudomallei* and *B. mallei* [online report]. Emerg Infect Dis [serial on the Internet]. 2008 Jul [*date cited*]. Available from http://www.cdc.gov/EID/content/14/7/e2.htm

[12] Wu B, Tong X, He H, Yang Y, Chen H, Yang X, Xu B. 2021. Misidentification of *Burkholderia pseudomallei*, China. Emerg Infect Dis 27:964-966.

* Suggested diagnostic algorithm for imported NHPs when clinical signs/necropsy findings may indicate melioidosis