IMMEDIATELY NOTIFIABLE 877-539-4344 or 206-418-5500

Washington State Department of HEALTH

Burkholderia

Signs and Symptoms	• Melioidosis (*B. pseudomallei*): localized (fever, ulcer, abscess), pulmonary (fever, chest pain, pneumonia), bacteremic (fever, respiratory distress, disorientation), or disseminated (fever, weight loss, stomach or chest pain, seizures). • Illness may be subclinical, acute, relapsing, or recurrent. • Rare human cases occur due to *B. mallei*, which is the cause of equine glanders.	
Incubation	Typically 1-21 days; median 4 days. may range from one day to many years.	
Case classification	**Clinical criteria**: In the absence of a more likely diagnosis, at least one symptom	
	Confirmed: isolation from any specimen, with or without clinical evidence	**Probable:** Clinically consistent with a presumptive laboratory result (paired sera or DNA detection), and either travel to an endemic region **or** known exposure (e.g., intentional release, laboratory exposure)
Differential diagnosis	Includes typhoid, tuberculosis, syphilis, erysipelas, lymphangitis; multiple causes of pneumonia, soft tissue or bone and joint infections, brain infections, pulmonary infections, sepsis	
Treatment	Appropriate antibiotic combination (IV followed by oral, up to 6 months of therapy) with relapses if incomplete. Up to 50% mortality with severe infection even when treated.	
Duration	Acute illness days to week, chronic infection can be relapsing or recurrent.	
Exposure	Through subcutaneous inoculation, ingestion, or inhalation of soil, dust, or fresh water in endemic region (tropical, subtropical: particularly South Asia, northern Australia, gulf coast of Mississippi), or from contact with contaminated imported products or pets. Person to person transmission is rare.	
Laboratory testing	Local health jurisdiction (LHJ) and Communicable Disease Epidemiology (CDE) arrange testing for individual cases • Washington State Public Health Laboratories can culture or confirm *Burkholderia* through culture or PCR; serology, PCR, culture, and whole genome sequencing available through CDC *Specimen shipping (Section 4):* • Once confirmed, *Burkholderia* isolates cannot be shipped • Ship sera, whole blood in EDTA, sputum, urine, or tissues **cold (freeze if arriving >72 hours from collection),** suspected culture at **ambient temperature**, with Bioterrorism or Serology form https://www.doh.wa.gov/Portals/1/Documents/5230/302-018-BioterrorismSpecimen.pdf https://www.medialab.com/dv/dl.aspx?d=1615463&dh=e4b87&u=69790&uh=0e2a1 • Specimen Collection and Submission Instructions https://www.doh.wa.gov/Portals/1/Documents/5240/SCSI-B-pseudomallei-V1.pdf	
Public health actions **URGENT**	Immediately report to CDE any cases with likely exposure in the United States • Identify exposures (agricultural or wildlife), particularly during travel • Identify others sharing the exposure and interview for symptoms • Identify potential laboratory exposures to specimens and isolates; assess risk; recommend symptom watch and sequential serum titers for all exposures, plus antibiotic prophylaxis for high risk exposures *Infection Control:* standard precautions; cultures are a risk for laboratory personnel	

Burkholderia (Melioidosis)

1. DISEASE REPORTING

A. Purpose of Reporting and Surveillance

1. To assist in the diagnosis and treatment of cases.
2. To identify potentially exposed healthcare and laboratory personnel and to provide counseling on post-exposure management.
3. To identify sources of transmission (e.g., travel exposure or imported products).
4. To raise the index of suspicion of a possible bioterrorism event when no natural exposure source is identified.

B. Legal Laboratory Reporting Requirements

1. Health care providers: **immediately** notifiable to local health jurisdiction.
2. Health care facilities: **immediately** notifiable to local health jurisdiction.
3. Laboratories: *Burkholderia* species **immediately** notifiable to local health jurisdiction; specimen submission required - cultures (2 business days). Any other specimens with results indicating *Burkholderia* infection should also be submitted (see Sections 3 and 4).
4. Veterinarians: animal cases notifiable to Washington State Department of Agriculture (see: http://app.leg.wa.gov/WAC/default.aspx?cite=16-70).
5. Local health jurisdictions: **immediately** notifiable to DOH Communicable Disease Epidemiology (CDE) 1-877-539-4344.

C. Local Health Jurisdiction Investigation Responsibilities

1. Conduct a rapid assessment to determine whether bioterrorism is a potential and whether laboratory exposure to a culture may have occurred. **If bioterrorism is suspected, immediately report the case to DOH: 1-877-539-4344 or 206-418-5500.**
2. Facilitate the transport of specimens to the Washington State Public Health Laboratories for confirmatory testing.
3. Identify possible locations and sources of exposure
4. Educate potentially exposed persons, including laboratory personnel, about signs and symptoms of disease; recommend antibiotic prophylaxis when needed.
5. Report all *probable* and *confirmed* cases to CDE (see definitions below). Complete the *Burkholderia* report form http://www.doh.wa.gov/Portals/1/Documents/5100/420-212-ReportForm-Burkholderia.pdf and enter the data in the Washington Disease Reporting System (WDRS).

2. THE DISEASE AND ITS EPIDEMIOLOGY

A. Etiologic Agent

Melioidosis is caused by gram-negative bacteria in the genus *Burkholderia*. Species known to cause disease in humans include *Burkholderia mallei* (glanders) and *B. pseudomallei* (melioidosis or Whitmore disease). Infection is associated with direct contact with contaminated soil and surface water, especially through skin abrasions. Infection can also occur through ingestion, inhalation or aspiration of contaminated soil or water, and predominantly occurs in tropical climates such as South Asia and northern Australia. In 2019, a Maryland resident tested positive for *B. pseudomallei* following exposure to a home freshwater aquarium stocked with fish and aquatic plants from South Asia. In 2021, a multistate cluster of melioidosis cases associated with aromatherapy spray imported from India was reported. In 2020 and 2022, two patients living in close proximity in the Gulf Coast region of southern Mississippi were diagnosed with melioidosis. Subsequently collected environmental samples documented presence of *B. pseudomallei* endemic in the United States for the first time. *Burkholderia* is a potential agent of bioterrorism. Even with appropriate antibiotic treatment, case fatality rates may reach 50%.

B. Description of Illness

Melioidosis may present in four general clinical forms:

- Acute or chronic localized infection which may or may not include symptoms of fever and muscle aches. Such infection often results in ulcer, nodule, or skin abscess. The infection may remain localized, or may progress rapidly through the bloodstream.
- Acute pulmonary infection presenting as bronchitis or pneumonia with symptoms of high fever, headache, chest pain, cough anorexia, and general muscle soreness. Cavitary lesions may be seen on chest X-ray.
- Bloodstream infection with symptoms of fever, headache, respiratory distress, abdominal discomfort, joint pain, muscle tenderness, and/or meningoencephalitis.
- Disseminated infection with symptoms of fever, weight loss, stomach or chest pain, muscle or joint pain, and/or headache or seizure. Abscesses in the liver, lung, spleen, and prostate are often observed in patients diagnosed with disseminated infections; less frequently, brain abscesses may be seen.

Disease may be more severe with pre-existing diabetes, cirrhosis, alcoholism, chronic renal disease, chronic lung disease, thalassemia, malignancy, or glucocorticoid treatment. Latent reactivation infection can occur months to years after exposure; this occurs in about 5% of recognized cases.

C. *Burkholderia* in Washington State

Four cases of melioidosis were reported over a decade, with exposures in Vietnam, Mexico, Thailand, and Malaysia. Twenty-five laboratory exposures were related to handling cultures for these cases.

D. Reservoirs

The organism occurs in contaminated soil and surface water. Globally the majority of cases are reported from South Asia and northern Australia. Cases in the United States are most often reported among returning travelers and immigrants or refugees.

E. Modes of Transmission

Exposure is through inhalation or aspiration of contaminated dust or water droplets, direct skin exposure especially through skin abrasions, or ingestion of contaminated water from endemic areas. Exposures to imported tropical plants, pet reptiles and freshwater fish imported from endemic areas, and imported products contaminated with *B. pseudomallei* have been previously reported.

F. Incubation Period

Typically 1-21 days with a median of 4 days; may range from one day to many years. Shorter incubation with higher inoculum. Latent reactivation infection can occur months to years after exposure.

G. Period of Communicability

There are only a few reports of person-to-person spread through blood or body fluids of an infected person. Transmission can also occur in utero or through breast feeding with mastitis.

H. Treatment

Treatment depends on the type of infection (localized, pulmonary, bacteremic, or disseminated.) *Burkholderia* is intrinsically resistant to many antibiotics, so correct choice of treatment regimen is essential. In general *Burkholderia* is susceptible to beta-lactams, carbapenems, trimethoprim-sulfamethoxazole, and doxycycline. Consultation with infectious disease specialists is strongly recommended. Microbial treatment generally starts with intravenous therapy for 10-14 days (acute phase), followed by 3-6 months of oral therapy (eradication phase). Relapses can occur with incomplete treatment, especially treatment <3 months.

3. CASE DEFINITIONS

A. Clinical Criteria

In the absence of a more likely diagnosis, at least one of the following signs or symptoms:

- Fever (temperature > 38.0°C [100.4°F])
- Muscle aches
- Ulcer
- Nodule
- Skin abscess
- Pneumonia
- Headache
- Chest pain
- Anorexia
- Respiratory distress
- Abdominal discomfort

- Joint pain
- Disorientation
- Weight loss
- Seizure
- Organ abscess (liver, lung, spleen, prostate, or brain)
- Encephalomyelitis/meningitis/extra-meningeal disease

B. Laboratory Criteria

Confirmatory:

Isolation of *B. pseudomallei* from a clinical specimen.

Presumptive:

1. Evidence of a fourfold or greater rise in *B. pseudomallei* antibody titer by IHA between acute- and convalescent-phase serum specimens obtained greater than or equal to 2 weeks apart, OR
2. Evidence of *B. pseudomallei* DNA (for example, by LRN-validated nucleic acid amplification test) in a clinical specimen.

Supportive:

Single *B. pseudomallei* total antibody titer of greater than or equal to 1:40 by serology in one or more serum specimens

C. Epidemiologic Linkage, Vital Records Criteria, Other Criteria

Epidemiologic Linkage: A person with at least one of the following findings:

- History of travel to or residence in a region endemic for melioidosis, OR
- Known exposure to *B. pseudomallei* as a result of intentional release or known product/source exposure (outside of laboratory), OR
- Known exposure to *B. pseudomallei* as a result of an occupational risk (i.e., laboratory exposure)

Vital Records Criteria: A person whose death certificate lists melioidosis as a cause of death or a significant condition contributing to death

Other Criteria: A person whose healthcare record contains a recent diagnosis of melioidosis

D. Case Classification (2023)

Confirmed:

Meets confirmatory laboratory evidence.

Probable:

- Meets clinical criteria AND presumptive laboratory evidence AND epidemiologic linkage.
- Meets vital records criteria AND presumptive laboratory evidence AND epidemiologic linkage.

- Meets other criteria AND presumptive laboratory evidence AND epidemiologic linkage.

Suspect:

- Meets clinical criteria AND supportive laboratory evidence AND epidemiologic linkage.
- Meets vital records criteria AND supportive laboratory evidence AND epidemiologic linkage.
- Meets other criteria AND supportive laboratory evidence AND epidemiologic linkage.

Note: Recurrent melioidosis can be defined as a re-presentation with *B. pseudomallei* culture-positive clinical disease occurring <18 months following initial diagnosis and after the time designated for treatment completion (both intravenous and oral phases) for the previous episode, irrespective of whether the patient was adherent to the therapy or initially lost to follow-up. Recurrent cases will not be counted as a new case for surveillance purposes. Epidemiological and exposure information can be used to determine if it is a new or recurrent infection, as can whole genome sequencing, if an isolate is available.

4. DIAGNOSIS AND LABORATORY SERVICES

A. Laboratory Diagnosis

Burkholderia can be isolated from blood, urine, sputum, wound swabs, and other tissues/fluids. Infection can also be diagnosed through DNA detection or through paired acute and convalescent serology; however, PCR has low sensitivity. A single serology test provides inconclusive results; paired sera are required for presumptive evidence.

Laboratory automated identification algorithms (e.g. MALDI-ToF or VITEK-2) may misidentify *B. pseudomallei* as *B. cepacia* or *thailandensis*. If suspicion is high for melioidosis, isolates suspected to be *B. pseudomallei* should be confirmed.

The organism presents a risk to laboratory workers. Alert laboratory personnel when specimens are sent from a suspect melioidosis case. Laboratories should use caution to avoid exposure within the laboratory by aerosol. If bacterial growth is suspicious for *Burkholderia,* contact PHL immediately to arrange for confirmatory testing.

B. Services Available at PHL

PHL Microbiology identifies *Burkholderia* species from pure isolates as well as culturing clinical specimens (sputum, tissue, urine). PHL Microbiology also performs rapid diagnostic testing using nucleic acid amplification methods (e.g., polymerase chain reaction) on EDTA-preserved blood, and can provide immediate testing in suspected bioterrorism situations.

PHL does not perform serologic tests; serum samples will be forwarded to Centers for Disease Control and Prevention (CDC) for testing. Call Communicable Disease Epidemiology at 206-418-5500 for approval before collecting and shipping specimens. Also see: https://www.doh.wa.gov/Portals/1/Documents/5240/SCSI-B-mallei-V1.pdf

Note that PHL requires all clinical specimens have two patient identifiers, a name **and** a second identifier (e.g., date of birth) both on the specimen label and on the submission form.

Due to laboratory accreditation standards, specimens will be rejected for testing if not properly identified. Also include specimen source and collection date.

C. Specimen Collection

1. **Isolates:** Submit isolates with a completed PHL Bioterrorism requisition form (https://www.doh.wa.gov/Portals/1/Documents/5230/302-018-BioterrorismSpecimen.pdf). Ship at ambient temperature.
2. **Culture:** Submit fluids (sputum, urine) or tissue in sterile leak-proof container with a completed PHL Bioterrorism requisition form (https://www.doh.wa.gov/Portals/1/Documents/5230/302-018-BioterrorismSpecimen.pdf). Ship cold, not frozen except if unable to ship urine or tissue within 72 hours, freeze urine or tissue and then ship frozen on dry ice.
3. **PCR:** Collect whole blood in lavender-top EDTA tube with a completed PHL Bioterrorism requisition form (https://www.doh.wa.gov/Portals/1/Documents/5230/302-018-BioterrorismSpecimen.pdf). Ship cold, not frozen unless unable to ship within 72 hours, then freeze and ship frozen on dry ice.
4. **Serology:** Collect 1–2 ml of both acute and convalescent sera (collected at least two weeks apart). If the specimen is freshly collected or still refrigerated, then ship cold, not frozen, on regular cold packs. If the specimen is already frozen, keep it frozen during transport by shipping on dry ice. Include a completed PHL serology submission form (https://www.medialab.com/dv/dl.aspx?d=1615463&dh=e4b87&u=69790&uh=0e2a1).

For questions regarding shipping and handling, laboratories can call PHL (206-418-5400).

5. ROUTINE CASE INVESTIGATION

Interview the case and others who might be able to provide pertinent information.

A. Evaluate the Diagnosis

Review the clinical presentation and laboratory results. **Confirmatory laboratory testing should be performed by a reference laboratory such as Washington State Public Health Laboratories (PHL).** Facilitate submission of laboratory specimens to PHL for confirmation. Proceed with investigation after preliminary or confirmatory laboratory results are available for sporadic cases. During an outbreak or a potential bioterrorism event, start the investigation before laboratory results are available.

B. Identify Potential Sources of Infection

Reservoirs are soil and water; exposures could include bare skin contact with soil or muddy water, walking through flood water or working with soil during/following severe weather events, or drinking contaminated water. Investigate possible exposures during the period 1 to 28 days before illness onset, including:

1. Travel to *Burkholderia*-endemic areas including tropical and subtropical regions, particularly Thailand and northern Australia. In the US, Gulf Coast States are considered potential melioidosis-endemic areas;
2. Work with animals (glanders) or acquisition of pets (including fish) from international sources;

3. Work in a microbiology laboratory.

Rare cases associated with imported products and pets have been identified. If no recent travel or occupational exposure is identified, consider the potential for imported pets, plants, or products. Consult with Communicable Disease Epidemiology: 206-418-5500.

C. Infection Control Recommendations/Case Management

Hospitalized patients should be cared for using standard precautions. Alert laboratories that might receive specimens from a person with suspected *Burkholderia* infection.

D. Identify Potentially Exposed Persons

1. Identify and interview persons who participated with the case in any risk activities or who may have been exposed to contaminated products or other sources. Inform ill persons (or their physician) of possible exposure, in order to facilitate proper diagnosis and treatment.
2. Identify laboratory workers who handled specimens or laboratory isolates. If cultures are still pending, laboratory workers should be reminded of appropriate handling of suspected *Burkholderia* cultures, i.e. do not work with cultures on an open bench.
3. See below for recommended antibiotic prophylaxis and serologic monitoring of exposed persons.

E. Management of Exposed Persons

All laboratory staff handling specimens with confirmed *Burkholderia* should undergo a risk assessment to determine their needs for post-exposure prophylaxis and follow-up. Similarly, persons with reported exposure to an animal known to be infected with *Burkholderia* should have a risk assessment to determine their needs for post-exposure prophylaxis and follow-up.

The site of any contamination or inoculation should be immediately washed and disinfected. High risk exposures include: inhalation, inoculation (puncture) or aerosols into the eye. These include events such as a bite or scratch by an experimental animal infected with *Burkholderia*, a needlestick or other penetrating injury with contaminated implement, a splash event leading to contamination of mouth, eyes, or broken skin, or the generation of aerosol outside of a biological safety cabinet. In addition, a worker with any predisposing condition (diabetes, chronic liver or kidney disease, alcohol abuse, long-term steroid use, hematologic malignancy, neutropenia or neutrophil dysfunction, chronic lung disease, thalassemia, or any other form of immunosuppression) working without proper PPE should be considered high risk. Low risk exposures include the inadvertent opening of a plate growing *Burkholderia* outside a biologic safety cabinet, inadvertent sniffing of an agar plate in the absence of contact between the worker and bacterium, the contamination of intact skin with culture, or a splash or spill event either without evidence of aerosol or inside a functioning biologic safety cabinet. All exposed persons should be educated about the symptoms of illness and told to seek care if fever develops. Self-recording of temperature twice daily for 21 days should be performed for all persons after exposure.

Persons with high risk exposures should begin post-exposure prophylaxis (PEP); PEP should be offered to persons who had low-risk exposures. PEP is trimethoprim-sulfamethoxazole or amoxicillin-clavulanic acid for 3 weeks. Persons with any exposure type should have serial serum titers assessed at baseline (as soon as possible following exposure) and at 1, 2, 4, and 6

weeks following the exposure. Note that serum should be collected for persons exposed to *B. mallei* but no validated serologic test currently exists.

In the event of seroconversion, further clinical evaluation and an extended course of treatment is recommended. In the event of a febrile illness, development of a cough, or progressive inflammation at the site of an inoculation event, blood culture, sputum culture, throat swab, and urine culture should be performed, as well as a chest radiograph.

Call Communicable Disease Epidemiology (206-418-5500) to discuss exposure classifications, the need for PEP for other persons exposed, and to request serologic testing. Please provide a summary report of the number of persons exposed, their exposure categories (high vs. low risk), initiation and completion of PEP, and any pregnant or otherwise immunocompromised persons.

Note that *Burkholderia* are considered select agents. Any laboratory exposure will require the laboratory to complete forms documenting an "accidental release" of a select agent. This is coordinated by the CDC Select Agent Program. See:

https://wwwnc.cdc.gov/eid/article/14/7/07-1501_article

https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5342a3.htm

F. Environmental Evaluation

DOH CDE (206-418-5500) can assist in contacting other state agencies when necessary for environmental investigations.

6. MANAGING SPECIAL SITUATIONS

A. Bioterrorist Event

Burkholderia has been designated a potential agent for bioterrorism. An intentional release (bioterrorist event) should be suspected if unusual clusters are seen in otherwise healthy individuals or in people in buildings with common ventilation systems. **Call Communicable Disease Epidemiology immediately at 206-418-5500 if *Burkholderia* is suspected in an unusual cluster.**

7. ROUTINE PREVENTION

A. Prevention Recommendations

1. **Travelers should use personal protective equipment** such as waterproof boots and gloves to protect against contact with soil and water in endemic areas.
2. **Avoid exposures if at risk for severe disease.** Persons with chronic illnesses or open wounds should avoid contact with water and damp soil in endemic regions.
3. **Clean contaminated wounds.** Skin breaks exposed to soil or water in endemic areas should be thoroughly cleaned.
4. **Take safety precautions.** Laboratory workers should handle all specimens for *Burkholderia* testing under appropriate biosafety conditions.

ACKNOWLEDGEMENTS

This document is a revision of the Washington State Guidelines for Notifiable Condition Reporting and Surveillance

published in 2002 which were originally based on the Control of Communicable Diseases Manual (CCDM), 17th Edition; James Chin, Ed. APHA 2000. We would like to acknowledge the Oregon Department of Human Services for developing the format and select content of this document.

UPDATES

March 2018: Guideline created.

December 2022: Updated Section 1B Legal Reporting Requirements consistent with 2023 WAC changes, added 2023 CSTE standardized case definition, general updates.

To request this document in another format, call 1-800-525-0127. Deaf or hard of hearing customers, please call 711 (Washington Relay) or email civil.rights@doh.wa.gov.