Virginia Department of Health
Glanders: Guidance for Healthcare Providers
Key Medical and Public Health Interventions after Identification of a Suspected Case

Table of Contents

1. Epidemiology

Glanders is a zoonotic disease caused by the bacterium *Burkholderia mallei*. Glanders is primarily a disease of horses, donkeys, and mules, but other animals (e.g., camels, cats, dogs, rabbits, goats, guinea pigs, field mice, hamsters, monkeys, bears, wolves) can become infected if they contact infected animals or consume infected meat. Human infection occurs through direct contact with tissues or body fluids of infected animals. The bacteria enter the body through cuts or abrasions in the skin and through mucous membranes (e.g., eye, nose, or mouth). It may also be inhaled via infected aerosols or dust contaminated by infected animals, and by ingestion of contaminated food or water. Person-to-person transmission is rare but could potentially occur through sex or care of infected patients. Cases of person-to-person transmission have not been reported in the U.S.

Sporadic reports of glanders occur globally, with enzootic foci existing in Asia and the eastern Mediterranean. In April 2010, Bahrain reported their first occurrence of the disease; in Brazil, the disease reappeared in 2009. No naturally occurring cases of equine or human glanders have been reported in the United States since the 1940s. People who care for infected animals or handle infected specimens are at increased risk of becoming infected, including veterinarians, horse caretakers, laboratorians, equine butchers, and abattoir workers. Laboratory-acquired glanders infections have been reported and these have occurred following aerosol or cutaneous exposures; these occupational infections are more likely to have occurred when processing enriched material (e.g., *B. mallei* cultures) rather than clinical specimens. In 2000, one case occurred in a research laboratory worker in the U.S. after accidental exposure.

If a case of glanders is suspected, it is critical to identify the individual's occupation (e.g., laboratory worker, veterinarian, or any job or recreation involving equids) and travel history to assess possible exposures. If the patient's history does not indicate a possible source of exposure, bioterrorism should be suspected. *B. mallei* is designated as a Category B bioterrorism agent (i.e., one with

moderate ease of transmission and lower morbidity and mortality than category A agents). *B. mallei* is also designated as a select agent, which means that it could be developed as a bioterrorism agent and that possession, use, or transfer of this organism requires registration with the Centers for Disease Control and Prevention (CDC) or the U.S. Department of Agriculture (USDA) through the Federal Select Agent Program.

2. Clinical Manifestations

The clinical spectrum of human glanders ranges from asymptomatic infection to life-threatening septicemia and varies depending on the mode of infection, dose, and host factors. Illness can generally be characterized into one of four clinical syndromes: localized, pulmonary, septicemic (bloodstream), or chronic. One form can progress to another, and combinations of syndromes occur. Some patients have had a biphasic illness, separated by remissions lasting a few days to several weeks.

Localized Form

- Incubation Period: 1–5 days
- Signs and symptoms of localized cutaneous infections often include nodules, abscesses, and/or ulcers in the mucus membranes or skin at the site of inoculation. The initial lesion may begin as a blister and then evolve into an ulcer. Lymphatic involvement near the site of inoculation can occur, resulting in lymphangitis with multiple suppurative foci. If mucus membranes are involved (e.g., eyes, nose, oral cavity), there may be mucopurulent, blood-tinged discharge, as well as swelling and local tissue destruction. Systemic signs may occur, including fever, rigors, headache, fatigue, and myalgia. Swelling and abscesses in regional lymph nodes can occur. Dissemination to other locations in the body may occur 1–4 weeks after infection. With treatment, the fatality rate of localized infection is 20%.

Pulmonary Form

- Incubation Period: 10–14 days (could be as short as 1–2 days)
- Signs and symptoms might include cough, fever, dyspnea, chest pain, and mucopurulent discharge. Pulmonary abscesses, pleural effusion, and pneumonia are characteristic. Skin abscesses may develop after several months. Untreated it often progresses to sepsis (see below). Chest radiographs might show segmental or lobar pneumonia, bilateral bronchopneumonia, miliary nodules, or cavitating lesions; consolidation might be present. The fatality rate can be 90%–95% without treatment and ~40%–50% with treatment.

Septicemic Form

- Incubation Period: 1–4 weeks
- Signs and symptoms of the septicemic form of glanders might occur at any point in the illness and are consistent with a typical sepsis syndrome. Fever, chills, myalgias, headache, pleuritic chest pain, and flushing may be present. Additional signs and symptoms may include jaundice, cyanosis, photophobia, diarrhea, a generalized papular (progressing to pustular) rash, multiple abscesses involving spleen, liver, and lungs, or granulomatous or necrotizing lesions in any organ. Multiorgan failure is common, and death can occur rapidly. Untreated septicemia is usually fatal within 7–10 days. Blood cultures might be negative. The fatality rate can be 95% or higher without treatment and ~40%–50% with treatment.

Chronic Form

- Signs and symptoms might include multiple abscesses, nodules and ulcers in various tissues characterized by remission and exacerbation that can persist for years (reported to last up to 25 years). Weight loss, lymphadenopathy, and lymphangitis are common. It is difficult to treat, and the fatality rate can be as high as 50% even with treatment.

Fatality rates are estimated based on historical records; mortality may be lower with modern medicine (e.g., supportive care and antibiotics.)

3. Laboratory Testing and Diagnosis

Notification when Glanders is Suspected

If glanders is suspected, the healthcare provider should immediately report the case to the local health department per Virginia's disease reporting regulations and the unusual occurrence of disease of public health concern. The local health department will discuss options for public health testing. If VDH approves public health testing, specimens may be sent to the Division of Consolidated Laboratory Services (DCLS). The health department will facilitate notification and shipment to DCLS. Specimens potentially containing *Burkholderia mallei* should never be shipped to DCLS without prior approval.

Laboratory Biosafety

Laboratory personnel **must** be alerted if glanders is suspected so that they can take appropriate precautions. Laboratory work should be performed using biosafety level (BSL) 3 precautions or BSL 2 with BSL 3 precautions, which includes PPE (gown, gloves, face/eye protection) and respiratory protection. All patient specimens and culture isolates should be handled while wearing gloves and PPE in a biosafety cabinet (BSC). Subcultures should be performed in a Class II BSC. Plates should be taped shut when incubating. All further testing should be performed only in the BSC while wearing gloves to protect from infections through the skin. Any procedure that can generate an aerosol, such as preparing standard inoculums for identification systems, must be performed in a BSL 2 BSC with BSL 3 precautions. Centrifugation and vortexing should be avoided. If *B. mallei* is suspected, samples should be submitted to DCLS for further testing, as soon as possible.

Because *B. mallei* is rarely isolated in the United States, its characteristics are unfamiliar to many clinical microbiologists. Automated bacterial identification systems used by clinical laboratories might misidentify *B. mallei* as another bacteria, such as *Burkholderia cepacia*, *Chromobacterium violaceum*, *Pseudomonas stutzeri*, *Bacillus* spp., *Pandoraea* spp., or *Ralstonia* spp. Therefore, the clinical laboratory should forward any isolate to DCLS (after consultation with DCLS) if it meets a combination of the criteria outlined below for suspected *B. mallei* based on clinical suspicion or available laboratory testing:

- Any clinical suspicion of suspected *B. mallei* infection
- Colony morphology on sheep blood agar: at 24 hours of incubation, there is poor growth or pinpoint to small grey colonies; at 48 hours of incubation, colonies appear smooth, gray, or translucent. *B. mallei* will grow without any inhibition around the colistin or polymyxin B disk.
- Gram stain morphology: Gram negative, faintly staining, straight or slightly curved coccobacilli
- Oxidase test: variable (e.g., positive or negative test result)

- Motility test: nonmotile. Note: the motility test should only be performed if the laboratory has the appropriate motility media; a wet preparation of any suspected *B. mallei* isolate should **not** be performed
- No growth at 42 degrees Celsius on sheep blood agar
- Triple Sugar Iron (TSI): nonfermenter

Sample Collection

Sample collection instructions for testing at DCLS (and potentially at CDC) are shown in Table 1. Because of the highly infectious nature of this organism, consultation with DCLS about specimen collection and handling is required. The DCLS Emergency Officer can be reached 24 hours a day/7 days a week at 804-335-4617.

Table 1. Sample Collection Instructions for Testing Suspected Glanders*

Test and Turnaround Time	Acceptable samples	Amount	Instructions
Burkholderia mallei identification and genotyping (at DCLS and CDC) Estimated turnaround time: 5–7 business days for culture confirmation (at DCLS) upon specimen receipt and 14 days for genotyping (at CDC) upon specimen receipt.	Blood (for culture)	10 mL	Collect before antibiotic use if possible. Use blood isolator tube. If isolator tube is not available, then blood culture should be incubated on the instrument at the local lab and then the isolate should be forwarded if it "flags" positive. Ship isolate at room temperature. Transport to lab within 16 hours.
	Blood (for tests other than culture)	2 mL (or more)	Collect blood in red top or purple top (EDTA) blood tube. Ship refrigerated with cold packs. Transport to lab as soon as possible.
	Urine	10 mL (or more)	Collect in sterile screw-capped container or sterile urine container. Ship refrigerated with cold packs. Transport to lab as soon as possible.
	Abscess, tissue aspirate, or purulent discharge	3 mL, or as much material as possible (avoid swabs)	Aspirate with a syringe and transfer material to a sterile screw-capped leak-proof container, if possible. Aspirate can remain in collection syringe if needle is removed, and syringe is capped to prevent leakage. Ship refrigerated with cold packs. Transport to lab as soon as possible.
	Sputum or bronchoscopy specimens	3 mL (or more)	Collect in sterile screw-capped leak-proof container. Ship refrigerated with cold packs. Transport to lab as soon as possible.
	Tissue biopsy	1 gram	Collect in sterile container. Moisten sample with sterile broth or saline. Ship refrigerated with cold packs. Transport to lab as soon as possible.
	Culture isolate	N/A	Contact the DCLS Bioterrorism Response Coordinator or Emergency Officer directly when a suspected isolate is identified.* Send culture on an agar slant, or a plate if slant is not available. Isolates should be shipped at room temperature. Transport to lab as soon as possible.
Burkholderia mallei molecular detection (PCR at CDC and DCLS) Estimated turnaround time at DCLS: 1 business day upon specimen receipt.	Testing at DCLS: Whole blood, serum or isolate. Testing at CDC: Whole blood, serum, urine, abscess, sputum, or tissue	0.5–1mL (or more)	Whole blood specimens should be collected in purple top (EDTA) tube; green top (heparin) tube is not acceptable. Other specimens should be collected as described above or below. Agar slants should be shipped at room temperature and clinical specimens should be shipped refrigerated with cold packs. Transport to lab as soon as possible.
	Serum (serological testing is performed at CDC)	2mL (or more)	Collect acute and convalescent serum (>14 days apart) in red top or tiger top tubes. Remove serum and place in sterile tube. Acute and convalescent specimens can be shipped together (freeze acute specimen until convalescent specimen has been collected and is ready for shipment; ship both specimens on dry ice); if shipping separately, ship refrigerated with cold packs.
	Culture isolate	N/A	Contact the DCLS Bioterrorism Response Coordinator or Emergency Officer directly when a suspected isolate is identified.* Send culture on an agar slant, or a plate if slant is not available. Isolates should be shipped at room temperature. Transport to lab as soon as possible.

*Adapted from American Society for Microbiology's Sentinel Level Clinical Laboratory Guidelines for Suspected Agents of Bioterrorism and Emerging Infectious Diseases: *Burkholderia* (2016). If glanders is suspected, notify the local health department immediately to discuss the case. If VDH approves public health testing, specimens may be sent to Division of Consolidated Laboratory Services (DCLS) with the DCLS Test Request Form; include the name of the test on the form. For questions about collecting specimens or for notifying DCLS when submitting specimens, contact the DCLS Emergency Officer available 24/7 at 804-335-4617.

Diagnosis

The definitive diagnosis of glanders is based on isolating and identifying *B. mallei* in a clinical sample in conjunction with clinically compatible signs and symptoms. Of note, blood cultures often remain negative, even in patients with septicemia. PCR and other molecular tests have been developed, but they are not widely available.

4. Treatment

The U.S. Public Health Emergency Medical Countermeasures Enterprise held a workshop in 2010 for subject matter experts to develop consensus recommendations for treatment and postexposure prophylaxis against *B. pseudomallei* and *B. mallei* (Lipsitz 2012). The recommendations focus primarily on treatment of melioidosis caused by *B. pseudomallei*; however, experts agreed that recommendations would be similar for glanders because antibiotic susceptibility profiles for *B. mallei* resemble those of *B. pseudomallei* and clinical experience with melioidosis treatment might be applicable to glanders. Of note, *B. pseudomallei* is naturally resistant to many antimicrobial drugs, and this resistance must be taken into account when selecting the appropriate treatment. Treatment of both glanders and melioidosis consists of an intensive phase with intravenous therapy lasting for at least 10–14 days (Table 2) and an eradication phase with oral therapy to reduce the chances of relapse (Table 3).

Table 2. Initial intensive-phase therapy for *Burkholderia pseudomallei* and *B. mallei* infections during a public health emergency*

Patient Group	Drug	Regimen for Suspected or Confirmed Clinical Cases (10–14 day duration)†
With no complications	Ceftazidime	50 mg/kg (up to 2 g) intravenous every 8 hours, **or** 6 g/d by continuous infusion after a 2-g bolus
With neuromelioidosis or persistent bacteremia or in intensive care unit	Meropenem	25 mg/kg (up to 1 g) intravenous every 8 hours

*For additional information on dosing, please consult the package inserts and the source: Lipsitz R, Garges S, Aurigemma R, et al. Workshop on treatment of and postexposure prophylaxis for *Burkholderia pseudomallei* and *B. mallei* infection, 2010. Emerg Infect Dis. 2012; 18 (12). Available at http://wwwnc.cdc.gov/eid/article/18/12/12-0638_article.htm (Accessed April 12, 2023).

†Duration of intensive therapy is generally 10–14 days; however, ≥4 weeks of parenteral therapy may be necessary in cases of more severe disease (e.g., septic shock, deep seated or organ abscesses, extensive lung disease, osteomyelitis, septic arthritis, or neurologic melioidosis). Consider adding trimethoprim-sulfamethoxazole for patients with severe infection involving the brain, prostate, or other privileged site (same dosing as described for eradication therapy below). Can be administered by intravenous infusion over 30–60 min every 12 hours, or nasogastric, or oral, as appropriate. If trimethoprim-sulfamethoxazole is included, continue for the entire duration of the intensive phase. Switching to meropenem is indicated if patient condition worsens while receiving ceftazidime (e.g., organ failure, development of a new focus of infection during treatment, or if repeat blood cultures remain positive). Depending on the severity of infection, the dose for patients ≥3 months of age can be ≤40 mg/kg; not to exceed 2 g/dose.

Table 3. Oral eradication-phase therapy for *Burkholderia pseudomallei* and *B. mallei* infections during a public health emergency*

Drug	Patient Group	Regimen for Suspected or Confirmed Clinical Cases (minimum 12-week duration)†
Trimethoprim-sulfamethoxazole§	Adult, >60 kg	160 mg/800 mg tablets: 2 tablets every 12 hours
	Adult, 40–60 kg	80 mg/400 mg tablets: 3 tablets every 12 hours
	Adult, <40 kg	160 mg/800 mg tablets: 1 tablet every 12 hours **or** 80 mg/400 mg tablets: 2 tablets every 12 hours
	Child	8 mg/40 mg/kg; maximum dose 320 mg/1,600 mg every 12 hours

---OR---		
Amoxicillin/clavulanic acid (co-amoxiclav)	Adult, ≥60 kg	500 mg/125 mg tablets: 3 tablets every 8 hours[¶]
	Adult, <60 kg	500 mg/125 mg tablets: 2 tablets every 8 hours[¶]
	Child	20 mg/5 mg/kg every 8 hours; maximum dose 1,000 mg/250 mg every 8 hours

*For additional information on dosing, please consult the package inserts and the source: Lipsitz R, Garges S, Aurigemma R, et al. Workshop on treatment of and postexposure prophylaxis for *Burkholderia pseudomallei* and *B. mallei* infection, 2010. Emerg Infect Dis. 2012; 18 (12). Available at http://wwwnc.cdc.gov/eid/article/18/12/12-0638_article.htm (Accessed April 12, 2023).
[†]Recommended duration of therapy is a minimum of 12 weeks.
[§]If the organism is susceptible and the patient does not have a documented allergy to it, oral trimethoprim-sulfamethoxazole is the agent of first choice. If the organism is resistant to trimethoprim-sulfamethoxazole or the patient is intolerant, the second-line choice is co-amoxiclav. Co-amoxiclav is available in different ratios and formulations, depending on the source country. Co-amoxiclav at a ratio of 4:1 is preferred to ensure there is sufficient clavulanate (Cheng AC, 2008 cited in Lipsitz R et al, 2012). Preparations of co-amoxiclav are available in the United States, with ratios of amoxicillin to clavulanic acid ranging from 2:1 to 16:1, as follows: 22:1 (Augmentin 250 mg), 4:1 (Augmentin 125 mg and 250 mg suspension, Augmentin 125 mg and 250 mg chewable tablet, Augmentin 500 mg.), 7:1 (Augmentin 200 mg and 400 mg suspension, Augmentin 400 mg chewable tablet, Augmentin 875 mg oral tablet), 14:1 (Augmentin ES-600, Amoclan 600 mg suspension) and 16:1 (Augmentin XR).
[¶]Weight-based dosage based on 20 mg/5 mg/kg/dose.

5. Postexposure Prophylaxis

Consensus postexposure prophylaxis recommendations for *B. mallei* and *B. pseudomallei* are based on the 2010 workshop held by the U.S. Public Health Emergency Medical Countermeasures Enterprise (Lipsitz 2012) and are summarized in Table 4. As with the treatment for the eradication phase, oral trimethoprim-sulfamethoxazole is the agent of first choice for prophylaxis.

Table 4. Postexposure prophylaxis for *Burkholderia pseudomallei* and *B. mallei* infections during a public health emergency*[†]

Drug	Patient Group	Regimen for Suspected or Confirmed Clinical Cases (21-day duration)
Trimethoprim-sulfamethoxazole	Adult, >60 kg	160 mg/800 mg tablets: 2 tablets every 12 hours
	Adult, 40–60 kg	80 mg/400 mg tablets: 3 tablets every 12 hours
	Adult, <40 kg	160 mg/800 mg tablets: 1 tablet every 12 hours **or** 80 mg/400 mg tablets: 2 tablets every 12 hours
	Child	8 mg/40 mg/kg; maximum dose 320 mg/1,600 mg every 12 hours
---OR---		
Amoxicillin/clavulanic acid (co-amoxiclav)	Adult, ≥60 kg	500 mg/125 mg tablets: 3 tablets every 8 hours[§]
	Adult, <60 kg	500 mg/125 mg tablets: 2 tablets every 8 hours[§]
	Child	20 mg/5 mg/kg every 8 hours; maximum dose 1,000 mg/250 mg every 8 hours

*For additional information on dosing, please consult the package inserts and the source: Lipsitz R, Garges S, Aurigemma R, et al. Workshop on treatment of and postexposure prophylaxis for *Burkholderia pseudomallei* and *B. mallei* infection, 2010. Emerg Infect Dis. 2012; 18 (12). Available at http://wwwnc.cdc.gov/eid/article/18/12/12-0638_article.htm (Accessed April 12, 2023).
[†]Duration of postexposure prophylaxis is 21 days. If the organism is susceptible and the patient does not have a documented allergy to it, oral trimethoprim-sulfamethoxazole is the agent of first choice. If the organism is resistant to trimethoprim-sulfamethoxazole or the patient is intolerant, the second-line choice is co-amoxiclav.
[§]Weight-based dosage based on 20 mg/5 mg/kg/dose.

6. Vaccination

A vaccine to prevent glanders in humans or animals is not available. Prevention of glanders focuses on controlling the disease in the natural reservoir (e.g., horses, donkeys, mules) through early detection, humane culling, and safe removal of infected carcasses. People who handle infected animals, tissues, or body fluids should wear appropriate personal protective equipment. Laboratorians should be alerted when glanders is suspected so that they can implement the appropriate biosafety precautions to prevent exposure.

7. Infection Control

For infection control, Standard and Airborne Precautions are recommended for patients with glanders.

8. Decontamination

Under favorable, natural conditions (i.e., warm and moist environments), *B. mallei* can survive for up to several months. Hospital rooms of patients with glanders should receive terminal cleaning consistent with standard precautions, and clothing or linens contaminated with body fluids should be disinfected according to hospital protocol. Current practices to disinfect and sterilize patient-care equipment and environmental surfaces are sufficient for managing areas where glanders patients are evaluated, admitted, and treated.

9. Postmortem Practices

If glanders is suspected as a cause of death, the district Office of the Chief Medical Examiner (OCME) should be immediately notified (https://www.vdh.virginia.gov/medical-examiner/district-offices-contact-us/). Consultation should occur to determine if an autopsy should be conducted, the parties responsible for conducting the autopsy, and proper personal protective procedures to follow.

10. Public Health Measures

- Suspected or confirmed glanders cases should be reported immediately to the local health department. See https://www.vdh.virginia.gov/health-department-locator/
- Laboratory specimens should be sent to the state public health laboratory (DCLS) for confirmation of the agent and other studies after VDH approves testing. For questions about collecting specimens, the DCLS Emergency Officer can be reached 24 hours a day/7 days a week at 804-335-4617.
- The designated public health authority should begin an epidemiologic investigation.
    - Collect detailed information from the patient to attempt to identify the source of the exposure
    - Investigate contacts of the case-patient for compatible illness to investigate a potential common exposure
    - Notify Virginia Department of Agriculture and Consumer Services (VDACS) if animal exposures are identified
    - Implement control measures to prevent disease and additional exposures. For laboratorians or others potentially exposed who might have worked with the agent before identification, postexposure prophylaxis and monitoring might be recommended based on a risk assessment.
    - VDH will work with the CDC, Federal Bureau of Investigation and other state or federal agencies as necessary

11. References and Resources

American Society for Microbiology (ASM). Sentinel Level Clinical Laboratory Guidelines for Suspected Agents of Bioterrorism and Emerging Infectious Diseases. Glanders: *Burkholderia mallei* and Melioidosis: *Burkholderia pseudomallei*. Revised March 2016. Available at https://asm.org/ASM/media/Policy-and-Advocacy/LRN/Sentinel%20Files/Burkholderia-Marc2016.pdf (Accessed April 12, 2023).

Blaney, D. Melioidosis. In: Heymann DL, ed. Control of Communicable Diseases Manual. 21st ed. Washington, DC: American Public Health Association; 2022. Accessed online March 9, 2023.

Center for Food Security and Public Health, Iowa State University. Glanders Fact Sheet. Last updated February 2015. Available at https://www.cfsph.iastate.edu/Factsheets/pdfs/glanders.pdf. (Accessed April 12, 2023).

Center for Infectious Disease Research and Policy (CIDRAP). Infectious Disease Topics: Glanders & Melioidosis. Available at http://www.cidrap.umn.edu/infectious-disease-topics/glanders-melioidosis (Accessed April 12, 2023).

CDC. Airborne Precautions. Available at https://www.cdc.gov/infectioncontrol/basics/transmission-based-precautions.html#anchor_1564058235. (Accessed April 12, 2023)

CDC. Chosewood, LC and Wilson, DE eds. *Biosafety in Microbiological and Biomedical Laboratories*. 5th edition. HHS Publication No. (CDC) 21-1112, 2009. Available at https://www.cdc.gov/labs/BMBL.html (Accessed May 31, 2023).

CDC. Glanders. Available at https://www.cdc.gov/glanders/ (Accessed April 11, 2023).

CDC. Healthcare Response Activities (Glanders). Available at https://www.cdc.gov/glanders/bioterrorism-response-planning/healthcare-response-activities.html. (Accessed April 14, 2023.)

CDC. Laboratory-Acquired Human Glanders --- Maryland, May 2000. *MMWR*. 2000; 49 (24); 532-5. Available at http://www.cdc.gov/mmwr/preview/mmwrhtml/mm4924a3.htm (Accessed April 12, 2023).

Lipsitz R, Garges S, Aurigemma R, et al. Workshop on treatment of and postexposure prophylaxis for *Burkholderia pseudomallei* and *B. mallei* infection, 2010. *Emerg Infect Dis*. 2012; 18 (12). Online report available at http://wwwnc.cdc.gov/eid/article/18/12/12-0638_article.htm (Accessed April 11, 2023).

World Organisation for Animal Health. Glanders. Available at https://www.woah.org/en/disease/glanders/. (Accessed April 12, 2023).