



Glanders and Melioidosis Backgrounder

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Causative agent

Glanders is caused by *Burkholderia mallei*, a Gram-negative, aerobic (requires oxygen), nonspore-forming, and nonencapsulated bacillus (rod-shaped bacterium). The organism has previously been named *Pseudomonas mallei*, *Malleomyces mallei*, *Actinomyces mallei*, *Loefflerella mallei*, *Actinobacillus mallei*, and *Pfeifferella mallei*.

Melioidosis (also called Whitmore's disease) is caused by *Burkholderia pseudomallei* (formerly *Pseudomonas pseudomallei*), which has the same characteristics as *B. mallei*. The bacterium is approximately 70% homologous to *B. mallei* using DNA hybridization. Because of this similarity, many consider the two bacteria to be biotypes or isotypes.

Natural distribution

B. mallei infection occurs primarily in horses, donkeys, and mules. Goats and carnivores are less susceptible to infection. Swine and cattle are resistant to infection. Glanders has been recognized since 400 BC. Three thousand horses and mules in the Confederate stables died from *B. mallei* infection in 1863. A major outbreak occurred during the Anglo-Boer War in 1899 to 1902 in South Africa, causing the death of 240,000 horses. Sporadic outbreaks occur in endemic areas.

B. mallei was eradicated from the United States in 1929. The organism survives in parts of Europe, Southeast Asia, Middle East, India, China, Mongolia, South America, and Africa. Infected animals are the source of infection for susceptible animals; *B. mallei* is not found in water, plants, or soil.

B. pseudomallei occurs most often in swine, goats, and sheep, but a limited number of infections have developed in other animals. The organism is endemic in Africa, Southeast Asia, Northern Australia, the South Pacific, India, China, and the Middle East. *B. pseudomallei* thrives in tropical and subtropical climates. Isolated cases have been reported in South America and the states of Hawaii and Georgia. The organism can be found in soil and water.

Transmission

Transmission of *B. mallei* is via ingestion, direct contact, or aerosol. Risk of transmission is increased by shared water and feed sources. Fomites, such as tack, can spread disease by transferring infectious discharges to a susceptible animal. Once introduced into a stable, the disease spreads rapidly.

Nasal discharges and pus from cutaneous ulcers are highly infective, but urine, saliva, tears, and feces may also transmit disease. Ingestion of contaminated horse meat has caused glanders in captive carnivores; cats may be more susceptible than dogs. Apparently recovered animals can be asymptomatic carriers, and are considered to be important sources of disease transmission.

Humans are highly susceptible to *B. mallei* infection. Biosafety Level 3 containment precautions are indicated for activities that are likely to produce aerosols, droplets, or high quantities or concentrations of the bacteria. Following infection by inhalation or through skin wounds or abrasions, there is usually a two- to five-day incubation period; longer incubation periods may occur. Veterinarians, caretakers, equine slaughterhouse workers, and laboratory staff are at higher risk of exposure to the disease.

B. pseudomallei is transmitted by ingestion of contaminated water or inhalation of contaminated dust. Poor sanitation in endemic areas places travelers and deployed military personnel at increased risk of exposure to *B. pseudomallei*. The incubation period ranges from two days to many years. Animal-to-human transmission is common. Human-to-human transmission is rare, but has resulted from contact with infective blood or body fluids. A human carrier state has not been identified, but animals may become carriers.

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Due to its historical significance and use as an agent of biological warfare in World Wars I and II and again in the 1980's, *B. mallei* is classified as a Category B bioterrorism agent by the Centers for Disease Control and Prevention (CDC). The potential for human infection from animals and the potential for substantial negative effects on the international trade of animals and animal products have resulted in its classification as a notifiable animal disease by the World Organization for Animal Health (OIE). Although *B. pseudomallei* is not considered a notifiable disease by the OIE, it is classified as a Category B bioterrorism agent.

Clinical Signs

Donkeys are more susceptible to *B. mallei*, and are therefore more likely to develop the acute form of disease. Horses are more resistant than donkeys, and tend to develop the chronic form of the disease. Mules are intermediate in susceptibility. Immunocompromised or undernourished animals and those kept in unsanitary conditions are at higher risk of developing disease.

Acute glanders results more commonly from ingestion of infected material. High fever, yellow-green or bloody nasal discharge, coughing, lymphadenopathy (enlarged lymph nodes), swelling of the mucous membranes of the nasal passages, and formation of ulcerative nodules in the nasal mucosa are observed. Nodular lesions may also develop in the lungs and other internal organs. Orchitis (infection and inflammation of the testes) may develop. Progressive debilitation is also observed. Septicemia and bacteremia are important features of the acute form of glanders, and death usually occurs within one to two weeks.

The cutaneous manifestation of glanders is called farcy. Nodules up to 2.5 cm in diameter develop in the skin of the legs, chest, and ventral abdomen—frequently along lymphatic vessels. The nodules rupture and ulcerate, discharging infectious fluid. Lymphatic vessels may become filled and distended with pus, and may be referred to as “Farcy pipes.”

Chronic glanders is more common in horses and in endemic areas. Horses with the chronic form of glanders may show mild clinical signs that are overlooked. Coughing and dyspnea (labored breathing) may be intermittently observed. Lymph nodes may harden, and legs may become thickened.

The pulmonary form of glanders results in coughing and labored breathing. Firm, gray or white nodules form within the lungs, and may become calcified. This form may require several months to develop. Affected horses also usually develop ulcerated nodules on the skin and nasal mucous membranes.

Nasal glanders results in increased mucus production and inflammation of the nasal mucous membranes. The disease progressively worsens, and greenish-yellow, thick, sometimes bloody, nasal discharge develops. Yellowish-gray nodules develop in the nasal mucosa, which then slough the epithelial surface and ulcerate. Once healed, scars are distinct and stellate (star-shaped).

Clinical glanders in equids has features that resemble *Streptococcus equi* infection (“strangles”), epizootic lymphangitis (*Histoplasma farciminosum* infection), ulcerative lymphangitis (*Corynebacterium pseudotuberculosis* infection), melioidosis, pneumonia, sinusitis, guttural pouch empyema, dermatophilosis (“rain rot”), and sporotrichosis (*Sporothrix schenckii* infection). Observation of progressive debilitation, combined with clinical signs and diagnostic tests, facilitates diagnosis.

Humans infected with *B. mallei* may exhibit purulent (pus-forming) skin infection, respiratory infections, fever, muscle aches, chest pain, headaches, muscle soreness, excessive tearing of the eyes, increased light sensitivity, swollen lymph nodes, and diarrhea. Septicemia will result in death within seven to 10 days. Abscesses may form in the liver, spleen, and/or muscles of the arms and legs. Chronic human glanders may result in the development of ulcerated and purulent nodules in the joints and muscles.

B. pseudomallei infection of animals results in purulent lesions in the lymph nodes and/or organs. Affected animals may harbor abscesses without exhibiting clinical signs of disease. Clinical signs vary with the location of the lesions, and include fever, loss of appetite, lymphadenopathy, lameness, rear limb weakness, nasal discharge, encephalitis (inflammation of the brain), coughing, emaciation, abdominal pain, and mastitis. Swine are more likely to develop chronic, asymptomatic infection. Skin lesions observed with the cutaneous form of glanders are not generally observed with *B. pseudomallei* infection.

Humans infected with *B. pseudomallei* exhibit clinical signs that are very similar to those associated with *B. mallei* infection, and accurate diagnosis relies on bacterial culture. Symptoms include respiratory distress, headache, fever, diarrhea, pustular lesions on the skin, and abscesses throughout the body. As with *B. mallei*, an overwhelming and fatal septicemia may develop. Humans with renal disease, chronic pulmonary disease, diabetes mellitus, or immunosuppression are at increased risk of developing severe disseminated septicemia.

Diagnosis

The mallein test can be performed to identify *B. mallei* carriers. Mallein contains endotoxins and exotoxins produced by *B. mallei*. Infected animals will demonstrate an allergic reaction to mallein inoculation, similar to the process of testing for tuberculosis using tuberculin inoculation. A 0.1 ml dose of mallein is injected into the skin of the lower eyelid, and the area is examined at 24 and 48 hours. A positive mallein test is characterized by marked swelling and edema of the injected eyelid, purulent conjunctivitis, light sensitivity, pain, and depression. Although a less desirable test, mallein can also be instilled into the conjunctival sac via an eyedrop; severe, purulent conjunctivitis will occur within six to 12 hours in affected animals. Larger volumes of mallein can be injected subcutaneously (under the skin), resulting in fever, swelling, and pain in positive animals; this is the least desirable form of mallein testing. The mallein test may stimulate the animal's immune system, resulting in the production of antibodies that may cause a positive complement fixation (CF) test, leading to false positive results.

Whole lesions, sections of lesions, abscess fluids, or other body fluids can be submitted for microscopic examination and bacterial culture. Serum samples should be cooled and shipped on ice. The CF test is reportedly 90 to 95% accurate, and is considered superior to the mallein test for identification of *B. mallei* infections. A dot enzyme-linked immunosorbent assay (ELISA), competitive ELISA (CELISA), and a counter-immunoelectrophoresis test have been developed, but have not yet been validated. A rose bengal plate agglutination test has been validated in Russia.

Injection of infectious *B. mallei* (in the form of infective body fluids) into the abdominal cavity of guinea pigs results in localized peritonitis and enlarged, painful testes; this is referred to as the Strauss reaction. This method of testing is only used when isolation in a laboratory animal is necessary and unavoidable.

As with *B. mallei*, microscopic examination and culture can be performed in cases of *B. pseudomallei* infection. Agglutination tests, indirect hemagglutination, immunofluorescence, and ELISA can be used for diagnosis of *B. pseudomallei* infection in some animal species.

Identification of *B. mallei* or *B. pseudomallei* is by culture and isolation of the organism. Due to cross reaction between *B. mallei* and *B. pseudomallei*, serologic testing is not of value in distinguishing the cause of infection. Distinguishing *B. mallei* and *B. pseudomallei* is possible only with microbial culture techniques and polymerase chain reaction (PCR).

Treatment

In the United States, **glanders and melioidosis are reportable**. State or Federal health officials should be notified immediately if either disease is suspected.

Traditionally, *B. mallei* has been susceptible in vitro to sulfamethoxazole-trimethoprim combinations, ceftazidime, imipenam, ciprofloxacin, some aminoglycoside antibiotics (streptomycin, gentamicin) and tetracyclines (including doxycycline). Affected animals are euthanatized; therefore, efficacy of treatment is unknown.

Human cases of melioidosis may require long-term therapy with multiple antimicrobials, including sulfamethoxazole-trimethoprim combinations, tetracyclines, and chloramphenicol. Surgical intervention to remove severely affected lung tissue or to facilitate abscess drainage may be necessary.

Morbidity and Mortality

Equine morbidity rates for glanders can be high, especially when animal populations are concentrated and/or maintained in unsanitary conditions. Because clinically affected horses are usually euthanatized to control the disease, case fatality rates (the number of affected cases that die from the disease) are unknown.

Human glanders is 95% fatal when not treated, but treatment reduces the case fatality rate to approximately 50%. Approximately 50 to 70% of chronic human cases die from the disease.

Sheep exhibit higher case fatality rates than other species with *B. pseudomallei* infection. Extensive abscessation and disseminated septicemia are associated with higher mortality, but septicemia is observed less often in animals than humans.

Septicemia associated with human melioidosis has a case fatality rate approaching 90%, with death occurring within 24 to 48 hours. Immunosuppressed patients exhibit higher case fatality rates. Without septicemia, mortality is less than 10%.

Prevention and Control

B. mallei can survive in clean water for approximately 20 days and up to six weeks in stables. The organism is destroyed by direct sunlight, phenol, potassium permanganate, copper sulfate, formalin, and chlorine. In damp conditions, bacteria can survive for three to five weeks. Decomposing material may harbor the bacteria for up to one month.

Strict quarantine of all infected and exposed animals is indicated. Clinically ill animals and animals with positive results of a mallein test are euthanatized, and the carcasses, contaminated bedding, and feed are burned or buried. Exposed equids that tested negative to mallein are isolated and retested two to three weeks later; if test results are positive at that time, they are euthanatized.

B. pseudomallei can survive for months to years in soil and water, but is readily destroyed by heat. The organism is susceptible to glutaraldehyde, formaldehyde, 70% ethanol, and 1% sodium hypochlorite. Animals affected with *B. pseudomallei* are generally isolated; mandatory euthanasia is not uniformly recommended.

There is no vaccine for *B. mallei* or *B. pseudomallei*.