

Zoonosis Update

Glanders

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Glanders is a highly contagious bacterial disease of horses, mules, and donkeys that is characterized by respiratory, cutaneous, and lymphatic nodular lesions. The disease is zoonotic, affecting persons in close contact with infected animals or those working with the organism in laboratory settings. Once prevalent worldwide, glanders has been eradicated from most countries; however, focal outbreaks do still occur. *Burkholderia mallei*, the causative organism of glanders, is considered a potential bioterrorism agent and has been used historically for this purpose. Control and prevention measures for glanders involve evaluation of susceptible equids, quarantine measures, depopulation of infected animals, and disinfection of premises and equipment. Awareness of the disease and collaboration between veterinary and human health professionals is essential for the early detection and protection of equids and humans.

The Causative Organism

Glanders is caused by *B mallei*, a nonmotile, nonsporulating, facultative intracellular, gram-negative bacillus.¹⁻⁴ The organism, named from the Greek *mellis*, meaning “severe disease,” and its Latin derivative, *malleus*, meaning “depicting a malignant disease,”^{2,3} was first isolated by Loeffler and Schütz in 1882 and confirmed as the cause of glanders in 1886.^{1,5,6} Since then, this organism has been classified in a number of genera and was most recently named *Pseudomonas mallei* before being reclassified into the new genus *Burkholderia* in 1992.⁷ *Burkholderia mallei* is an obligate mammalian pathogen; growth of this organism in soil or water has never been reported.^{1,5} This is somewhat surprising because *B mallei* is very closely related to and may have evolved from the saprophytic soil bacterium *Burkholderia pseudomallei*, the cause of melioidosis.⁸⁻¹² Unlike *B pseudomallei*, which is genetically highly diverse, *B mallei* is genetically homogeneous.^{8,10,12,13} These 2 organisms also differ in their survival in the environment. Whereas soil is the natural habitat for *B pseudomallei*, *B mallei* is not resistant to inactivation in the environment, and it is not thought to persist outside equine hosts for long periods of time.^{5,6} Limited environmental survival of the latter organism, particularly in wet, humid, or dark conditions, may be possible for 3 to 5 weeks.^{1,5} *Burkholderia mallei* can remain viable in room-tem-

ABBREVIATION

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perature water (20° to 25°C [68° to 77°F]) for as long as a month.^{1,14} It is inactivated by heat, direct sunlight, and commonly used disinfectants, including hypochlorites.^{5,14,15}

Understanding of the pathogenesis of glanders is limited; however, recent research involving genetic techniques¹⁶⁻²² and experimental induction of *B mallei* infections in hamsters and mice^{19,23,24} are providing some new insights into this disease. Some virulence mechanisms that have been identified are an extracellular polysaccharide capsule,^{16-19,22} type III^{20,21} and type VI¹⁸ secretion systems, and quorum-sensing mechanisms.²² Studies of *B mallei* virulence, the associated host response, and the feasibility of vaccine development have been reviewed.²⁵

Epidemiology

Glanders is an old disease, described as early as 400 BC by Hippocrates and 330 BC by Aristotle.^{1,5,26} In the past, *B mallei* was an important equine pathogen worldwide. Its spread was facilitated by the use and transport of horses, especially when animals were housed under crowded conditions (eg, during military campaigns).^{1,3,5,9} In some instances, these confinement situations resulted in major epidemics among equids.^{1,3,9}

At present, glanders is associated with limited geographic areas. Aided by the decline in the use of equids for transport, control programs eradicated this disease by 1965 from several countries, including the United States, Australia, Canada, and western Europe.^{4,26-31} No naturally occurring cases of glanders have been reported in North America in the past 60 years.^{1,5} The disease is still endemic in parts of the Middle East, Asia, Africa, and South America.^{4,15,27,32-34} From 1998 to 2007, focal outbreaks in Brazil, Turkey, the former USSR, Eritrea, Ethiopia, Iran, Iraq, United Arab Emirates, and Mongolia were reported.^{4,26,35-39} Glanders may also occur naturally in Pakistan.^{3,15,27} However, the geographic distribution of *B mallei* can be difficult to determine precisely because in serologic surveys, cross-reactions with *B pseudomallei* occur.¹⁵ Because of the substantial impact of this disease on international trade in animals and animal products, as well as the potential for zoonotic disease, glanders is listed as a notifiable animal disease by the World Organization for Animal Health (OIE).⁴⁰

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Glanders as a Bioterrorism Weapon

Glanders has a long association with military conflicts. When horses were extensively used for transportation and cavalry troops were common, epizootics often developed following the movement of horses to new areas or during their confinement under crowded conditions. Death or euthanasia of large numbers of equids occurred during the US Civil War,^{4,9,41} the Anglo-Boer War in South Africa,⁵ and World War I.^{1,4,26}

Burkholderia mallei has also been used intentionally against horses and humans in the military services. In World War I, German agents are believed to have deliberately infected equids transported to Allied forces on the Eastern Front.^{4,9,26,42} The organism was also used during World War II by Japanese forces; horses, civilians, and prisoners of war were infected.^{26,42} More recently, it has been suggested that the former Soviet Union used *B mallei* on a limited basis against the mujahideen in Afghanistan in the 1980s.^{9,26} *Burkholderia mallei* has been classified as a Category B bioterrorism agent by the CDC on the basis of its potential for dissemination, its ability to cause human morbidity and death, and the need for enhanced diagnostic capacity and surveillance.^{43,44}

Species Affected by Glanders

Glanders primarily affects members of the soliped family (ie, horses, donkeys, mules); however, most mammals are susceptible to experimentally induced infection to some degree.^{3,24,45} Natural infections in species other than equids are rare, but cats, dogs, camels, goats, and sheep have been affected.^{1,3,23,24,26,32,45,46} Among carnivores, felids may be particularly susceptible.^{15,47} Glanders has developed in captive wild felids following consumption of contaminated horse meat.^{15,45,46,48,49} Several rodent species, in particular guinea pigs and hamsters, are highly susceptible to glanders and have been used for diagnostic testing or experimental studies.^{1,15,23,24,45,50,51} Cattle, pigs, rats, and birds are considered to be more resistant to the disease.^{1,3,26,45}

Humans are also susceptible to glanders, but are considered accidental hosts.^{5,9} Most infections develop in individuals who are in close contact with infected animals (eg, veterinarians and animal caretakers) or those working in laboratories with *B mallei* bacterial cultures or infected tissues.^{3-5,9,15,42,52-57} Development of glanders in laboratory workers has been documented; this population is considered at the highest risk for exposure.^{9,52,55} The most recently reported human case in the United States occurred in 2000, when a research microbiologist was unknowingly exposed while working with the organism.^{56,57} This was the first human case of glanders reported in the United States since 1945.^{56,57}

Transmission

Glanders is highly communicable among equids, especially under crowded, unsanitary, or stressful conditions.^{4,5,9,33} Skin exudates and respiratory secretions from infected animals contain large numbers of organisms, which can easily spread on fomites and in the environment.^{3,15,32} Horses with chronic or latent infections are often responsible for maintenance of the

disease in facilities or in geographic regions; the movements of these animals can contribute to the spread of the disease.^{3,15,27} Transmission among equids most commonly occurs via ingestion of the organism, entry through skin abrasions or mucous membranes, or aerosol exposure.^{3,5,15,27,53} Common sources of exposure for equids include contaminated food and water and contaminated equipment such as harnesses and grooming tools.^{3,15,27,32,33} Carnivores can be infected if they ingest meat from infected animals.^{46,48,49}

Human exposure is most often associated with contact with sick animals, contaminated objects, infected tissues, or bacterial cultures.^{3,9,27,42} Entry typically occurs through the mucous membranes or via small wounds and abrasions in the skin. Most reported laboratory-acquired infections have occurred via cutaneous injuries or inhalation of infectious aerosols during routine handling of cultures or samples.^{3,9,42,52,57} Aerosolized *B mallei* is highly infectious, and transmission via aerosols can rapidly lead to respiratory disease and septicemia in humans.^{9,58} Humans may also become infected through ingestion of *B mallei*, but this occurs less often than in other animals.⁹ Rare cases of person-to-person transmission between family members who nursed sick individuals have been reported⁵⁸; 2 such cases were thought to have been sexually transmitted.⁵⁸ The potential use of aerosolized *B mallei* as a biological weapon raises concerns about the possibility of widespread disease in the public during a bioterrorist attack.^{9,26,58}

Disease in Nonhuman Animals

In equids, glanders can be an acute or chronic disease. Mules and donkeys are considered most susceptible to acute disease.^{3,15,32} The incubation period is short; death often occurs in a few days to a few weeks.^{3,9,15,59} Horses, and also mules, may have chronic or latent infections.¹⁵ Chronic infections can develop over several weeks to months and may initially be subclinical.^{3,32} Latently affected animals may be ill for some months, then make an apparent recovery; however, the infection persists for years.^{15,53} Some chronically or latently infected animals have minimal signs of illness, and the diagnosis may not be made; these animals can serve as a pathogen reservoir for other healthy animals.

Clinically, glanders may affect the upper respiratory tract, pulmonary regions (lower portions of the respiratory tract), and skin.^{3-5,15,33} Multiple nodules and ulcers develop in the upper airways, including the nasal cavities, of some animals. Rupture of the nodules leads to the development of thick, hemorrhagic, mucopurulent nasal discharge, which may occur unilaterally or bilaterally.^{4,5,9,15,33,45} Bloody crusting may be seen on the nostrils, and there may be purulent ocular discharge.^{27,34} The nasal mucous membranes may be swollen and ulcerated; perforation of the nasal septum is possible.^{3,5,15,33,45} The regional lymph nodes become large and painful and may suppurate and drain.^{3,5,15,33,53} The submandibular lymph nodes can adhere to the skin and mandible and may be hard and knotty.^{5,15} If the nasal ulcers heal, characteristic stellate scars remain on the nasal mucosa.^{4,15,33,34}

Pulmonary glanders is associated with development of round, firm, grayish, encapsulated nodules throughout the lung tissues.^{33,60} Nodule centers may be caseous or undergo calcification.⁴ If the lesions are extensive, lung consolidation or pneumonia may develop. Equids with pulmonary disease typically have signs of depression and anorexia, with malaise, coughing, and fever (40°C [104°F]).^{3,33} In more advanced stages, dyspnea and rales may be detected.^{32,33} The pulmonary nodules can rupture, sometimes discharging their contents into the bronchioles and promoting extension of the infection to the upper portions of the respiratory tract. In some cases, pulmonary glanders can remain clinically inapparent for lengthy periods.

Cutaneous glanders, also known as farcy, develops following skin injury or secondarily to respiratory disease.^{5,33} It is characterized by superficial or deep subcutaneous abscesses with or without ulceration and lymphadenitis.^{4,33,45} The subcutaneous nodules can be as large as 2.5 cm (1 inch) in diameter and typically ulcerate and discharge a highly infective sticky pus.^{9,15,33} Nodules can develop on regions of the head, neck, thorax, or ventral portion of the abdomen.^{5,9,27,33,61} Lymphatic vessels become swollen and filled with purulent exudate (so-called farcy pipes) or develop nodules (farcy buds).^{4,5,15,33} This occurs most commonly in the extremities.^{3,33} In addition, nodules sometimes develop in internal organs including the liver, spleen, and testes.^{4,5,15,33,61} Recently, neurologic signs were reported for the first time in experimentally infected horses, possibly as a result of secondary bacterial infections that developed from a compromised blood-brain barrier.⁵⁹

Large cats and other carnivores (polar bears, lions, tigers, leopards, jackals, and hyenas) have been infected with *B mallei* following the consumption of infected horse meat.^{46,48,49} In infected cats, nodule and ulcer development was localized to the nasal mucous membranes and conjunctivae and was accompanied by purulent nasal discharge with blood.⁴⁶ Lymphadenopathy near the esophagus and respiratory passages also caused dyspnea.⁴⁶ Death occurred in 8 to 14 days after ingestion of the infected meat.⁴⁶

Disease in Humans

Glanders is uncommon in humans, but it is painful and life threatening; the mortality rate among untreated clinical cases is high.^{27,58} Persons with immunosuppressive conditions may be particularly susceptible to systemic spread of the organism.⁴² As in other animals, the incubation period and signs of disease reflect the route of entry and may include fever, localized cutaneous lesions, pulmonary infection, septicemia, chronic suppurative infection, or a combination of these syndromes.^{1,9,58} Any localized infection may disseminate throughout the body, resulting in septicemia.^{9,58} Subclinical cases have been identified during autopsies.^{9,27,53,55}

Cutaneous glanders (farcy) develops after entry of *B mallei* through a laceration or abrasion. After an incubation period of 1 to 5 days, nodules, abscesses, and ulcers develop in the skin, typically along the lymphatic vessels of the face, arms, or legs.^{1,15,54,58} Nodules may caseate or become calcified. Localized erythema

or cellulitis may also develop in the affected areas.^{1,27,42} Regional lymph nodes may become swollen.⁵⁸ Development and rupture of nodules in the ocular or respiratory mucous membranes results in mucoid or mucopurulent discharge.^{26,27,58}

Pulmonary signs of glanders become apparent following the inhalation of *B mallei*. The incubation period ranges from 1 to 14 days.^{42,58} Symptoms are usually nonspecific and may include fever, malaise, myalgia, coughing, pleuritic chest pain, and periods of sweating; a mucopurulent nasal discharge may also be evident.^{1,9,58} Pneumonia, pulmonary abscesses, and pleural effusions can develop.^{1,9,33,45,54,58} The pulmonary form of the disease often leads to or develops concurrently with septicemia.

In humans, systemic disease may develop via any route of exposure. Multiple systems can be affected, and multiorgan failure may occur.^{9,55,58} Symptoms include sudden onset of fever, chills, myalgia, malaise, sensitivity to light, lacrimation, and headache.^{1,9,56} Erythroderma or skin nodules and abscesses may be widely disseminated on the body.^{9,42} Regional lymph nodes may be swollen; cellulitis or lymphangitis can also develop. Ulcerated and purulent nodules or abscesses may form in the liver, the spleen, or the joints and muscles of the arms and legs.^{1,9,26,53,54} Fatal cases culminate in respiratory distress, delirium, shock, and death.^{1,26,58} Without appropriate treatment, septicemic glanders leads to death within 24 to 48 hours after the onset of symptoms and has a case fatality rate as high as 95%.^{1,9,45,58}

Chronic infections may also develop in humans.^{1,9,27,45,53} Nodular lesions may develop in many organs, including the lungs, liver, spleen, skin, or muscles. Weight loss and lymphadenopathy are also evident. Chronic glanders may remain latent in afflicted individuals and is characterized by exacerbations and remissions over many years.^{1,9}

Diagnosis of Glanders in Nonhuman Animals

The differential diagnoses for glanders include strangles (*Streptococcus equi* infection), epizootic lymphangitis (*Histoplasma farciminosum* infection), sporotrichosis (*Sporothrix schenckii* infection), ulcerative lymphangitis (*Corynebacterium pseudotuberculosis* infection), and melioidosis (*B pseudomallei* infection).³³ Melioidosis is particularly difficult to differentiate because *B pseudomallei* is closely related to *B mallei* and the 2 species cross-react in serologic and hypersensitivity tests.^{8,15,17,62,63} One consequence is that the 2 diseases might be confused during diagnosis; melioidosis in horses, which can resemble glanders, has been described occasionally.⁶³ Cross-reactivity can also cause complications in countries where *B mallei* is not endemic. Horses that have been sensitized to *B pseudomallei*³⁰ or related nonvirulent organisms such as *Burkholderia thailandensis* could have false-positive results in glanders screening tests.¹⁶

Postmortem lesions in equids can raise the index of suspicion for glanders. Glanders is characterized by the development of granulomas and ulcers in a variety of tissues. Nodules and confluent ulcers with irregular borders may be evident on mucous membranes, including those of the nasal passages, nasal septum, larynx,

and upper lip.^{5,15,34,35,59} Submucosal nodules in the nasal passages may be necrotic and ulcerated; lesions that have healed will appear as stellate scars.^{5,15,34} Nodular foci (as large as 1 cm in diameter) may be detected within lung tissues and beneath the pleura.^{5,15,33,35} Nodules in an early stage of development are encircled by a reddened border, whereas more developed lesions may have a caseous or calcified center and can be surrounded by white or gray fibrous tissue.²⁷ Equids with acute pulmonary glanders may have diffuse miliary pneumonic foci (2 to 10 mm in diameter) rather than nodules.^{15,34,60} Severe diffuse pulmonary edema may be evident in all lung lobes.⁵⁹ Bloody purulent exudate may fill the nasal cavity, paranasal sinuses, and trachea.^{35,59} In experimentally infected horses, pulmonary edema (possibly secondary to airway obstruction by exudates) and foci of congestion or pneumonia have been reported.³⁴ The mandibular, cervical, and mediastinal lymph nodes are often large and firm; some of these nodes may be congested and fibrotic and may contain abscesses.^{15,32,59} Swollen lymphatic vessels with chains of nodules are sometimes detected in the skin.^{15,34,60} Some skin nodules may be ulcerated or crusted, with matting of the hair where their oily contents were discharged.^{15,60} Similar nodules may also be identified in many other organs, including the liver, spleen, or testes.^{5,15,33,59}

In equids with glanders, histopathologic lesions may include vasculitis and thrombosis of the vessels of the nasal mucous membranes, accompanied by neutrophilic granulocyte infiltration.³⁵ Areas of ulceration contain large numbers of disintegrated neutrophilic granulocytes and macrophages in the submucosa.³⁵ Nodules are encapsulated and necrogranulomatous and are surrounded by numerous inflammatory cells, including neutrophils, lymphocytes, and macrophages.^{5,34}

In equids, a diagnosis of glanders can be made when *B mallei* is isolated from samples or an immunologic reaction to the organism is detected serologically or on the basis of hypersensitivity test results. The gold standard for diagnosis is the isolation and identification of *B mallei* in cultures of samples from lesions or various exudates, including respiratory secretions. *Burkholderia mallei* can be stained with methylene blue, Wright, or Gram stains, but the staining can be weak or irregular; bipolar staining of the organism may be observed.^{1,58} These organisms are gram-negative. They can be pleomorphic in older cultures, but in clinical samples and young cultures, they typically form straight or slightly curved rods that are 0.3 to 0.8 μm in width and 2 to 5 μm in length.^{1,6,32,58} Microscopic examination may reveal abundant bacteria in smears from fresh lesions, but *B mallei* can be difficult to detect in more chronic lesions.³² Although organisms are often present in tissue sections, they can have a beaded appearance and may not be readily identified.^{23,32} Some authors report that, in tissues, this organism is identified best with Giemsa stain.²³

Burkholderia mallei can be grown on routine culture media, including nutrient, blood, and MacConkey agars; growth is slow, but colonies are usually visible within 48 hours.^{6,32} Optimal growth occurs at 37°C (98.6°F).^{6,32} The organism is aerobic and facultatively anaerobic only in the presence of nitrate.³² Glycerol enrichment is often used for isolation. A viscid, smooth, slightly cream-colored, confluent layer is seen on gly-

erol agar after a few days; this layer eventually becomes thicker, tougher, and darker brown.^{5,32} *Burkholderia mallei* also grows well on glycerol-potato agar or in glycerol broth, with less luxuriant growth described on nutrient agar.³² A selective medium has been developed.⁶⁴ *Burkholderia mallei* ferments some carbohydrates under the appropriate conditions, and it can be identified by its cell and colony morphology, lack of motility (which differentiates it from other members of the genus), and biochemical reactions.^{1,6,32} Automated bacterial identification systems do not always correctly identify this organism,^{57,65} which can be a particular problem when the index of suspicion for *B mallei* infection is low. Inoculation into laboratory animals, particularly guinea pigs (the Strauss reaction) or hamsters, was used for isolation of *B mallei* in the past,^{5,27} but this technique is now rarely practiced.³²

A cell-mediated hypersensitivity reaction test (mallein test) was used extensively to screen equids for glanders in past eradication campaigns. This test is still used to certify equids as negative for glanders during importation to some countries. It may also be used in the diagnosis of clinical cases, although it has some limitations as a diagnostic test.^{5,32,66} The mallein test is based on a hypersensitivity reaction to mallein, a commercially available, purified protein derivative of *B mallei*. The test is performed most often by intrapalpebral injection.³² In reactors, marked eyelid swelling develops within 24 to 48 hours; it is accompanied by fever and occasionally by purulent ocular discharge.³² No reaction or minimal swelling of the lower eyelid develops in unsensitized animals.³² Mallein can also be administered in topical ophthalmic preparations or via SC injection at nonocular sites; conjunctivitis develops after administration of such ophthalmic solutions, and firm, painful swellings with raised edges develop at the sites of SC injection within 24 hours.³² The latter 2 methods are considered less desirable than intrapalpebral injection, and the SC injection method may not be accepted by some countries for international trade.³² Although the mallein test is considered to be sufficiently specific and sensitive for detection of *B mallei* infection as part of eradication programs and import evaluations,³² its sensitivity for diagnosis in clinical cases may be limited.^{32,61,67,68} In some studies,^{61,67} as few as 46% to 75% of horses with clinically apparent glanders were identified by this test. False-positive reactions can occur in animals that are sensitized to other closely related *Burkholderia* spp, including *B pseudomallei*, and cross-reactions with *Streptococcus equi* have been described.⁶⁹ In addition, the injection of mallein stimulates an immune response that can interfere with future serologic testing.^{32,66,70} Although this reaction is transient in some instances, subsiding within a few weeks, permanent sensitization could develop in some animals.⁶⁶

Serologic tests are sometimes used to screen equids for importation to glanders-free countries or to identify clinically affected animals. Measurable titers of serum antibody against *B mallei* develop approximately 1 week after infection.⁷¹ Complement fixation was the preferred serologic test in past eradication programs because of its ability to detect subclinically or chronically infected animals.³⁰ This test was most useful when

the prevalence of disease was high; only a few animals, such as pregnant or old horses, yield false-negative reactions.³⁰ Complement fixation is still used to assess imported equids for glanders³²; however, its use has some drawbacks in populations with a low prevalence. False-positive results are frequently reported,³⁰ and the natural anticomplementary activity in the sera of some equids can interfere with the test.^{66,67} Several accurate ELISAs have been developed and are also used to screen animals for international trade.^{32,70} Other serologic tests including indirect hemagglutination, counterimmunoelectrophoresis, immunoblotting, and indirect fluorescent testing may be used for diagnostic purposes in some areas^{30,67}; these tests are not approved by the OIE for use in international trade.³² In Russia, rose bengal plate agglutination test results are sometimes used for diagnosis.³² In a recent evaluation,⁶⁷ this test was able to identify 90% of horses with positive bacterial culture results, whereas the mallein test identified 75% of those horses. The rose bengal test could eventually become a useful assay for identification of some glanders suspects that do not react in the mallein test.⁶⁷ Most serologic tests for glanders use crude preparations of *B mallei*; consequently, those tests have some limitations in sensitivity or specificity.^{30,72} These limitations may be mitigated by use of more specific test reagents.³⁰ In addition, serologic tests cannot distinguish *B mallei*-specific reactions from reactions to *B pseudomallei*.

The use of rapid DNA tests, such as PCR assays, for the diagnosis of infectious diseases is of great interest. However, the close genetic relationship between *B mallei* and *B pseudomallei*, together with the high genetic variability in *B pseudomallei*, complicates the differentiation of these organisms via DNA testing.^{7,8,10,12,62} Some PCR techniques can identify the organisms only to the Pseudomallei group, a group that includes both organisms.⁷³ However, other recently developed PCR assays can distinguish *B mallei* from *B pseudomallei*.⁷⁴⁻⁷⁶ Other genetic techniques, including PCR-restriction fragment length polymorphism, pulsed-field gel electrophoresis, 16S rRNA sequencing, variable number tandem repeat polymorphism, and multilocus sequence typing, have also been used to specifically identify *B mallei*.^{63,77-80}; these specialized techniques are available mainly in research laboratories. Newer testing methods such as polysaccharide microarrays are also being explored.⁸¹

Treatment of Nonhuman Animals

Treatment of animals that have glanders is often not advised because they may remain subclinically infected and shed *B mallei*.^{3,15,33} Animals may be treated with antimicrobials in countries where glanders is endemic; however, the currently available agents are usually not particularly effective.³³ Although some clinical improvement (eg, increase in feed intake, drying of ruptured cutaneous nodules, or marked reduction in nasal discharge) may be evident initially, antimicrobials penetrate poorly into nodules, and animals may relapse once treatment is discontinued.⁶¹ The risk for zoonotic transmission also discourages treatment.

Treatment of Humans

Information regarding effective antimicrobial treatment in humans is limited, although some attempt has been made recently to fill this gap.⁸² *Burkholderia mallei* is susceptible to several antimicrobials, including aminoglycosides, tetracyclines, sulfonamides, trimethoprim, imipenem, ceftazidime, piperacillin, and doxycycline, but it is variably resistant to streptomycin and penicillin.^{5,61,82-85} Oral administration of amoxicillin-clavulanate potassium, doxycycline, or trimethoprim-sulfamethoxazole for prolonged periods (60 to 150 days) has been suggested for treatment of localized disease.^{42,58} Parenteral treatment with ceftazidime has been suggested for severe or septic forms of the disease.³³ Supportive therapy may be needed for individuals with septicemia, and surgical drainage of localized infection is an important adjunct to antimicrobial administration in humans.¹ A vaccine against glanders for use in humans is not presently available.⁵²

Prevention and Control

Cases of glanders in animals must be reported to the OIE.⁴⁰ The occurrence of this disease in a country can result in restrictions on international trade in horses and other affected animals. The mallein test and complement fixation test are the approved assays recommended by the OIE for international trade purposes.³²

Glanders is exotic to the United States; suspected cases must be reported immediately to either the USDA Area Veterinarian in Charge or the State Veterinarian. Once officials have been notified, government veterinarians who are trained in the diagnosis of exotic diseases investigate and confirm whether glanders is present. Prompt recognition of glanders-affected animals will reduce the risk that this disease will spread. Equids in the United States are not expected to have any preexisting immunity and would be highly susceptible to infection. Import evaluation and quarantine requirements for equids are used to minimize the risk of disease introduction.^{9,86}

If glanders is detected, control measures include strict quarantine of all infected and exposed animals, diagnostic testing of animals with clinical signs indicative of glanders, and assessment of apparently normal equids with the elimination of those that react positively in screening tests.^{5,27,32,66} Ill animals and those with positive results of mallein tests are euthanized. Equids exposed to *B mallei* that yield negative results in mallein tests are isolated and retested 2 to 3 weeks later.³ Carcasses or contaminated bedding and feed should be burned or buried in accordance with state regulations.^{3,15} Equipment or other items in contact with infected animals should be disinfected.^{3,15,27}

Burkholderia mallei is susceptible to many common disinfectants, including solutions of benzalkonium chloride, 1% sodium hypochlorite, 70% ethanol, 2% glutaraldehyde, iodine, mercuric chloride in alcohol, and potassium permanganate.^{1,5,9,14} *Burkholderia mallei* can also be destroyed by UV irradiation, direct exposure to sunlight, or heating to 55°C (131°F) for 10 minutes.^{5,14} These methods have been previously successful in controlling the disease.^{1,28,31}

People who handle tissues from infected animals, bacterial cultures, or contaminated fomites should implement strict precautions to prevent infection.⁵² Protective clothing including surgical masks, gloves, face shields, and gowns should be worn.^{3,42} In clinical and research laboratories, *B mallei* requires biosafety containment level 3 accommodation.^{14,42} Precautions are indicated for activities that are likely to produce aerosols, droplets, or high quantities or concentrations of the bacteria.^{3,52} Currently, there is no commercial vaccine against glanders for use in humans or any other animal species; research into host immune responses to *B mallei* has been initiated, but results have been limited.^{17,23,50,51,75}

Public Health Implications

Glanders is an important disease that affects equids and humans. Although this disease has been eradicated from several countries, outbreaks do occur; thus, vigilance is essential. Human cases are often associated with outbreaks among equids or with work in laboratory settings. Although the risk of introduction into the United States is low, *B mallei* could be introduced accidentally through the importation of infected horses and contaminated fodder or equipment. It could also be introduced intentionally by bioterrorists. Either scenario could have serious public health implications. Given the efficient transmission of glanders in settings where horses are in close contact with each other, such as those encountered within the racing industry, and the high case fatality rate associated with *B mallei* infection in humans, early detection of the disease is essential for the health of humans and other animals. This will require increased awareness and collaboration between veterinary and human health professionals to facilitate the early detection of cases.

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