Iranian Journal of Clinical Infectious Diseases
***2011;6(1):1-4***


**EDITORIAL**

# Re-emergence of Glander in Iran

**Masoud Mardani[*], Monireh Kamali**
*Infectious Diseases and Tropical Medicine Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran*

Glanders, caused by infection with the bacterium *Burkholderia mallei* is a highly contagious and often fatal zoonotic disease of solipeds. It is an old disease, described as early as 400 BC by Hippocrates and 330 BC by Aristotle (1). 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).

Naturally occurring glanders has been eradicated in most countries, but is still found in parts of Africa, the Middle East, South America, and Eastern Europe. From 1998 to 2007, focal outbreaks in Brazil, Turkey, the former USSR, Eritrea, Ethiopia, Iran, Iraq, United Arab Emirates, and Mongolia were reported (2). In Iran, sporadic cases of glanders is reported in solipeds. There were no new cases from 2003-2006 in Iran. Due to transported horses from west provinces in Iran, three cases were reported in 2007.

In 2009, we had 37 horses with positive mallein test (3,4). Because of the fatal nature of the disease and its use as biological weapons, and also with respect to the increased number of infected horses in our country during the recent years and the report of two new confirmed cases in lions of Tehran zoo, it is necessary to pay special attention to the re-emergence of the disease in Iran. In this editorial, we briefly review the clinical presentation and diagnosis and treatment of glanders.

*B. mallei*, an immotile, non-sporulating, facultative intracellular, gram-negative bacillus is an obligate mammalian pathogen that could not grow in soil or water. The organism, named from the Greek melis, meaning "severe disease," and its Latin derivative, malleus, meaning "depicting a malignant disease, was first isolated by Loeffler and Schütz in 1882 and confirmed as the cause of glanders in 1886. 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 (5).

In humans and horses, disease progression and pathology are similar, but the clinical presentation, even if related by direct transmission, may vary significantly. Understanding of the pathogenesis of glanders is limited. Some virulence mechanisms that have been identified are an extracellular polysaccharide capsule, type III and type VI secretion systems, and quorum-sensing mechanisms (6,7).

Transmission to human is most often associated with contact with sick animals, contaminated objects, infected tissues, or bacterial cultures. Entry typically occurs through the mucous membranes or via small wounds and abrasions in the skin. Aerosolized *B. mallei* is highly infectious, and transmission via aerosols can rapidly lead to

*Received*: 15 October 2010 *Accepted*: 25 October 2010
**Reprint or Correspondence**: Masoud Mardani, MD.
Infectious Diseases and Tropical Medicine Research Center
Shahid Beheshti University of Medical Sciences, Tehran, Iran.
**E-mail**: mmardani@hotmail.com

respiratory disease and septicemia in humans. Rare cases of person-to-person transmission between family members who nursed sick individuals or through ingestion of *B mallei* have been reported; such cases were thought to have been sexually transmitted (8).

Constitutional signs and symptoms typically occur early in the course of disease, and some may persist through treatment and be severe, leaving the patient exhausted. Common signs and symptoms include fever or low-grade fever in the afternoon to evening, chills with or without rigors, severe headache, malaise, generalized myalgia (particularly of the limbs, joints, neck, and back), dizziness, nausea, vomiting, diarrhea, tachypnea, diaphoresis (including night sweats), altered mental status and fatigue. Other nonspecific signs, any of which may be present, include tender lymph nodes, sore throat, chest pain, blurred vision, splenomegaly, abdominal pain, photophobia, and marked lacrimation (9).

Cutaneous manifestations include multiple papular or pustular lesions that may erupt anywhere on the body. The infectious process through the oral, nasal, or ocular mucous membrane is similar to the cutaneous process. Cutaneous or mucosal infections may spread, leading to disseminated infections. Dissemination to internal organs produces abscesses in virtually any organ, most commonly the spleen, liver, and lungs. Disseminated infections are associated with septic shock and high mortality, although they may also produce a more chronic, indolent course of infection (9).

A pulmonary infection typically produces pneumonia, pulmonary abscess, pleuritis, and pleural effusion, with associated signs and symptoms such as cough, dyspnea, chest pain, and mucopurulent sputum. Septicemic glanders results from the seeding of *B. mallei* into the bloodstream, whether as a primary event, secondary to a local or pulmonary infection or as a relapse in chronic or latent infection. Septicemia may be passing and lead to protract disseminated infection or be fulminant and rapidly fatal. Without aggressive treatment, *B. mallei* septicemia runs an acute course and may lead to death in 7 to 10 days (9).

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. A cell-mediated hypersensitivity reaction test (mallein test) was used extensively to screen for glanders in past eradication campaigns. Measurable titers of serum antibody against *B. mallei* develop approximately1 week after infection. Serologic tests including complement fixation, rose bengal plate agglutination test, indirect hemagglutination, counter immunoelectrophoresis, immunoblotting, and indirect fluorescent testing may be used for diagnostic purposes in some areas. The use of rapid DNA tests, such as PCR assays, for the diagnosis of infectious diseases is of great interest (10).

Information regarding effective antimicrobial treatment in humans is limited. *B. mallei* is susceptible to several antimicrobials, including aminoglycosides, tetracycline, sulfonamides, trimethoprim, imipenem, ceftazidime, piperacillin, and doxycycline, but it is variably resistant to streptomycin, amoxicillin, ampicillin, penicillin G, bacitracin, chloromycetin, carbenicillin, oxacillin, cephalothin, cephalexin, cefotetan, cefuroxime, cefazolin, ceftriaxone, metronidazole and polymyxin B. 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.

Parenteral treatment with ceftazidime has been suggested for severe or septic forms of the disease. Supportive therapy may be needed for individuals with septicemia, and surgical drainage of localized infection is an important adjunct to antimicrobial administration in humans. A vaccine against glanders for use in humans is not presently available (11).

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, the Anglo Boer War in South Africa and World War I. The organism was also used during World War II by Japanese forces; horses, civilians, and prisoners of war were infected. 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. *B. 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 (12).

For disease control purpose, cases of glanders in animals must be reported to the Organization for Animal Health. The mallein test and complement fixation test are the approved assays recommended for international trade purposes. 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. Ill animals and those with positive results of mallein tests are euthanatized.

*B. mallei* is susceptible to many common disinfectants, including solutions of benzalkoniumchloride, 1% sodium hypochlorite, 70% ethanol, 2% glutaraldehyde, iodine, mercuric chloride in alcohol, and potassium permanganate and can also be destroyed by UV irradiation, direct exposure to sunlight, or heating to 55°C (131°F) for 10 minutes. In clinical and research laboratories, *B. mallei* requires biosafety containment level 3 accommodation (13).

Therefore, glanders is an important disease that affects equids and humans. Although this disease has been eradicated from several countries, outbreaks do occur; hence, vigilance is essential. Human cases are often associated with outbreaks among equids or with work in laboratory settings. 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.

## REFERENCES

1. Dance DAB. Melioidosis and glanders as possible biological weapons. In: Fong IW, Alibek K, eds. Bioterrorism and infectious agents: a new dilemma for the 21st century. New York: Springer, 2005;p:99–143.

2. Dvorak DG, Spickler RA. Glanders: zoonosis update. JAVMA. 2008;233:570-8.

3. Iranian Organization for Animal Health, Control of Veterinary Disease. Diseases transmitted from animals to man subpart. Tehran, Iran. 2001. (In Persian)

4. ProMED Mail. Glanders, Equine—Iran ex Iraq. November 29, 2007. Archive No. 20071129.3854. Available at: promedmail.org.

5. Groves MG, Harrington KS. Glanders and melioidosis. In: Beran GW, Steele JH, eds. Handbook of zoonoses. Section A: bacterial, rickettsial, chlamydial, and mycotic. 2nd ed. Boca Raton, Fla: CRC Press, 1994; p:149–55.

6. Balder R, Lipski S, Lazarus J, Grose W, Wooten MR, Hogan R, et al. Identification of *Burkholderia mallei* and *Burkholderia pseudomallei* adhesions for human respiratory epithelial cells. BMC Microbiol. 2010;10: 250-69.

7. Schell MA, Ulrich RL, Ribot WJ. Type VI secretion is a major virulence determination in *Burkholderia mallei*. Mol Microbiol. 2007; 64:1466–85.

8. Bossi P, Tegnell A, Baka A. Bichat guidelines for the clinical management of glanders and melioidosis and bioterrorism-related glanders and melioidosis. Euro Surveill. 2004;9:E17–E18.

9. Gilbert RO. Glanders. In: Foreign animal diseases. The gray book. Richmond VA, editor. United States Animal Health Association, 1998. Available at: www.vet.uga.edu/vpp/gray_book02/fad/gla.php.

10. Elschner MC, Scholz HC, Melzer F, Saqib M, Marten P, et al. Use of a Western blot technique for the serodiagnosis of glanders. BMC Veterinary Research. 2011;7:4-28.

11. Thibault FM, Hernandez E, Vidal DR, Girardet M, Cavallo JD, Hernandez E. Antibiotic susceptibility of 65 isolates of *Burkholderia pseudomallei* and *Burkholderia mallei* to 35 antimicrobial agents. J Antimicrob Chemother. 2004; 54:1134–38.

12. Rotz LD, Khan AS, Lillibridge SR, Ostroff SM, Hughes JM. Public health assessment of potential biological terrorism agents. Emerg Infect Dis. 2002;8:225–30.

13. Dance DAB. Melioidosis and glanders as possible biological weapons. In: Fong IW, Alibek K, eds. Bioterrorism and infectious agents: a new dilemma for the 21st century. New York: Springer, 2005; p:99–143.