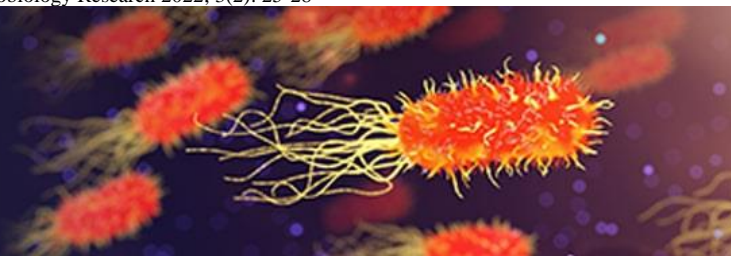


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## Glanders: A highly infectious re-emerging serious zoonotic bacterial disease

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### Abstract

Glanders is a highly infectious re-emerging zoonotic disease that produces serious disease in humans and animals, especially equines. The disease is caused by *Burkholderia mallei*, a gram-negative, facultative intracellular pathogen. It is mostly an equine disease that affects horses chronically and donkeys and mules acutely. Humans are affected when contacted with infected animals or contaminated environments. The disease is endemic in developing continents like Africa, Asia, and South America. By testing, destroying positive animals, and limiting the import of animals from foreign nations, the disease has been eradicated from many countries. However, it is seen when re-emerged in many parts of world. The bacteria cause nodules and ulcerations in the upper respiratory tract and lungs. Though *Burkholderia mallei* is susceptible to various antibiotics but it is difficult for early diagnosis. Early diagnosis and treatments are crucial. The gold standard approach for diagnosing glanders is the isolation and identification of *B. mallei* from clinical samples. Animal field diagnosis frequently involves the mallein test. Glanders has been identified as a biological threat agent of category "B" and is capable of being utilized as a biological weapon. Neither human nor veterinary vaccination is available in Glanders. As a result, it's crucial to adopt preventative measures, particularly by farmers, equine handlers, veterinarians, and anybody else who might be at danger. It's also necessary to raise knowledge of how to avoid and control it in endemic areas.

**Keywords:** *Burkholderia mallei*, glanders, re-emerging, zoonosis

### Introduction

World is facing great challenges today due to emerging and re-emerging diseases that affect humans and animals both in developing as well as in developed nations of the world (Pal, 2007; Pal and Gutama, 2022) <sup>[19,18]</sup>. Glanders is a highly zoonotic contagious and fatal disease of donkeys, mules and horses caused, which is caused by bacteria called *Burkholderia mallei* (Pal, 2016) <sup>[21]</sup>. The disease is one of re-emerging fatal bacterial disease (Pal and Gutama, 2022) <sup>[18]</sup>. The disease is characterized by nodules and ulcerations in the upper respiratory tract and lungs (Khan *et al.*, 2013) <sup>[10]</sup>. From many developed countries like North America, Europe and Australia the disease has been eradicated but in continents like Africa, Asia and Latin America there is sporadic cases. Glanders is eradicated by test and slaughter of positive animals' method (Anderson and Bokor, 2012; Malik *et al.*, 2012) <sup>[1, 14]</sup>.

Due to its ability to spread and cause infection through aerosols, *B. mallei* can be used as a biological weapon and thus has biological defense concern so it should be considered more important from practical point of view (Anderson and Bokor, 2012) <sup>[1]</sup>. When the Germans deployed glanders against horses in the Great War, it has also been claimed that it was the first modern attempt at biological warfare (Wheelis, 1998) <sup>[16]</sup>. Due to its economic impact on the global commerce in animals and byproducts, glanders is a transboundary animal disease that needs to be notified to the World Organization for Animal Health (OIE) (Bossi *et al.*, 2004) <sup>[4]</sup>. Infection on human presents as two forms as both acute and chronic forms, and affects mainly the respiratory system, the skin and subcutaneous soft tissues. The disease is a recognized occupational risk for veterinarians, equine butchers, stable handlers and laboratory workers, and it was more common during wars in which large numbers of horses were used (Pal, 2007; Pal, 2016) <sup>[19, 21]</sup>. Therefore objective of this review is to review on public health importance and general overview of Glanders.

### Etiology

Glanders is caused by *Burkholderia mallei*, which is bi-polar gram negative bacteria, straight

or slightly bent (2-5  $\mu\text{m}$  long and 0.3-0.8  $\mu\text{m}$  wide), non-spore forming and facultative intracellular, rod shaped bacterium (Pal, 2007) [19]. *Burkholderia mallei* is member of the genus *Burkholderia*, family *Burkholderiaceae*, and bacterial order *Burkholderiales* (OIE, 2016) [17]. The bacterium is an obligate aerobic (except in media containing nitrate) (Kinoshita *et al.*, 2019) [11]. *B. mallei* can survive for 3 to 5 weeks in wet, humid, or dark environments, and it can survive in water at room temperature for a month (Dvorack and Spickler, 2008) [8]. Numerous common disinfectants can kill *B. mallei*, although have lower susceptibility to phenolic disinfectants. The organism is killed under the heat and sunlight (CFSPH, 2018) [7].

## Epidemiology

### Geographic distribution

In earlier times, Glanders was more wide spread worldwide, but now has been eradicated from most of the areas like Western Europe, Australia and Northern America (Van Zandt *et al.*, 2013) [25], but the disease does remain endemic in the Middle East, Asia, Africa, and South America (UPMC, 2014) [24]. From 1998 to 2007, cases of glanders were reported from Latin America countries like Brazil, African countries like Eritrea and Ethiopia, Asian countries like Iran, Iraq and United Arab Emirates (Pal and Gutama, 2022) [18]. With increasing out breaks in some locations over the last decade, now it is considered as an important re-emerging bacterial zoonotic disease (Khan *et al.*, 2013; Pal, 2016) [10, 21].

### Susceptible host

The natural reservoirs of *B. mallei* are the solipeds. Usually the disease is chronic in horses, while it occurs in acute form and often fatal in donkeys and mules (Van Zandt *et al.*, 2013) [25]. Pigs, cattle and chicken were shown to be resistant to the disease, but the majority of other domesticated mammals can be experimentally infected. Some species, including goats, dogs, and cats, have also been observed to spontaneously contract the disease (CDC, 2012; CFSPH, 2018; Malik *et al.*, 2012) [5, 7, 14]. The equine keepers, veterinarians, farriers, and animal workers are occupational groups that are at high risk to glanders (Pal, 2016) [21].

### Mode of transmission

Glanders is mainly transmitted by contact with infected horses, mules and donkeys, most often via their respiratory secretions and exudates from skin lesions. This bacterium can enter the body through skin abrasions and mucous membrane contamination, or inhalation of aerosols. There have been reports of vertical transmission from the dam and venereal transmission from stallions to mares (CFSPH, 2018) [7]. It may become food borne disease when ingestion of *B. mallei* contaminated food and water but it is not an important route of human infections (Van Zandt *et al.*, 2013) [25]. Rarely, human-to-human transmission is observed. However, it might happen as a result of occupational exposure in the medical practices or at autopsies (CDC, 2000; Gregory and Waag, 2007) [6, 9].

## Clinical signs

### In humans

The incubation period can range from 1 to 14 days-shorter incubation periods (1 to 2 days) are possible with inhalation,

while longer intervals are conceivable with skin exposure. A shorter incubation period of 1 to 2 days is achievable with inhalation, while longer intervals are conceivable with skin exposure. When exposed by inhalation, one experiences respiratory symptoms with fever that can develop into airway necrosis and ulceration. Following may be lobar or bronchopneumonia, swollen lymph nodes in the neck and mediastinum, pustular skin lesions, and spread to internal organs. Skin nodules may grow and develop pus after skin exposure, and adjacent lymph nodes may expand. This frequently comes with symptoms including exhaustion, fevers, chills, and malaise (UPMC, 2014; Pal, 2007) [24, 19]. Bloodstream infections from glanders typically result in death within 7 to 10 days without treatment (CDC, 2012) [5]. Half of naturally occurring infections are caused by chronic human glanders, which is characterized by many subcutaneous and intramuscular abscesses, lymphadenopathy, and lymphangitis (USAMRIID, 2004) [23].

### In animals

The disease commonly occurs in three forms as pulmonary, cutaneous (farcy) and nasal glanders (Malik *et al.*, 2012) [14]. Farcy more likely occurs through direct inoculation, whereas Glanders occurs through inhalation or, more frequently, ingestion. In glanders, the entire upper and lower respiratory tracts are affected by an acute or chronic lung infection, and numerous abscesses occur due to dissemination. Contrarily, farcy manifests as swelling in subcutaneous tissues that ulcerate. Local lymph nodes and adjacent lymphatic veins harden and expand (USAMRIID, 2004) [23]. Clinical signs in infected dromedary camels were similar to those in equids. A purulent, yellowish nasal discharge that occasionally contained blood was also noticeable in the affected cats. Dyspnea and swelling of the lymph nodes were further symptoms, and infected cats typically die within one to two weeks (CFSPH, 2018) [7].

### Diagnosis

The gold standard way to diagnose glanders is through bacterial isolation (Blue *et al.*, 1998) [2]. *B. mallei* can be successfully isolated from horse specimens using the novel selective agar known as BM agar (Kinoshita *et al.*, 2019) [11]. Historically, glanders were eliminated using melanization which is delayed hypersensitivity testing, that involves administering a subcutaneous, intracutaneous, or ophthalmological application of a crude preparation of *B. mallei* antigens (Marek and Manninger, 1945) [15]. The test result is read at 24 hours and 48 hours after injection. Animals showing edematous swelling of the eyelids, other signs such as purulent discharge from inner canthus or conjunctiva, fever, depression and pain are considered positive for glanders (Malik *et al.*, 2012) [14]. Serological procedures that are used to identify glanders includes the counter immuno electrophoresis (CIE), competitive enzyme-linked immunosorbent assay (cELISA), immunoblot, indirect haemagglutination assay (IHA), agar-gel immuno diffusion, indirect fluorescence assay test (IFAT), and dot ELISA (Khan *et al.*, 2013) [10]. For specific identification of glanders, PCR based tests can be used (Koirala *et al.*, 2022) [12].

### Treatment

Because of the disease was not common and known in many

places, scarcity of information exists regarding the use of antimicrobial for the treatment of diseased humans. However, *B. mallei* infections have responded after severe stages to antibiotic therapy because the treatment was given after delayed diagnosis or occurrence of disease. *B. mallei* was susceptible to many antibiotics in laboratory. The others challenges to treat patients was because *B. mallei* is a facultative intracellular pathogen that many drugs are incapable of penetrating host cells. The other challenges was ability of *B. mallei* strains resistance to several antibiotic. The drugs like sodium sulfadiazine effectively treated acute glanders but penicillin were not effective (Schweizer and Torres, 2010) [22]. It is a disease that must be reported and affected animals must be slaughtered and disposed of safely (Malik *et al.*, 2012) [14]. Drugs like ceftazidime, gentamicin, sulfadiazine, Imipenem, and others are used alone or in combination in horses (Lehavi *et al.*, 2002) [13].

### Prevention and control

No human or veterinary vaccines are available for immunization/prevention of glanders still today (Pal, 2007) [19]. To prevent further transmission, it is very essential that dead bodies due to glanders should not be opened and must be properly buried or incinerated. Contaminated environments like manure, bedding and feed residue should be burned or buried and follow required disinfection programme for houses, feed and water trough. The isolation of suspected animals and humans, properly tested and positive animal should be culled. There should be restriction of the movement of animals to the suspected area. Proper hygiene and sanitation procedures should be adopted (Pal, 2007; Burtneck *et al.*, 2012) [19, 3]. Occupation at risk like veterinarians, animal handlers and persons in contact with infected animals should follow appropriate biological safety measures, wear personal protective equipment. Creating awareness programs about the ways of transmission, prevention and controls of glanders need to be carried out continuously (Khan *et al.*, 2013; Pal *et al.*, 2013) [10, 20].

### Conclusion

Glanders is a zoonotic disease of equines (horses, donkeys, mules) having high fatality rate and is caused by gram negative bacteria called *B. mallei*. The bacterium has the potential to be used as biological weapon in bioterrorism. Because the disease is highly contagious and fatal, active diagnosis and treatment of glanders in animals is essential. Early isolation and identification of bacteria is crucial. Glanders is notifiable disease and therefore, it is highly imperative of informing timely to regulatory measures in order to take necessary action for culling/disposal of diseased animals. Up today there is no effective vaccine for glanders and the treatments needs long courses of various antibiotics treatment, it's important to eliminate diseased animals and *B. mallei* have potential threat to be used as a biological weapon. In areas that are at risk or where the disease is endemic cooperation of equine owners with veterinarians are essential for disease detection and control and awareness creation among society regarding control and prevention of the disease is important.

### Author's contribution

All the authors contributed equally. They read the final version, and approved it for the publication.

### Conflict of interest

The authors declare that they do not have any conflict of interest.

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