

Glanders: A Potential Bioterrorism Weapon Disease

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Abstract Glanders, also known as farcy, is an infectious bacterial zoonotic disease of solipeds caused by *Burkholderia mallei*. The only known natural reservoir of *B. mallei* is horses, donkeys, and mules. It has long been known as an equine and human disease, although it can also afflict felidae, small ruminants, camels, bears, and walrus. Despite the fact glanders that has been eradicated from most of the countries, it has regained its status as re-emerging disease due to recent outbreaks. Glanders is spread mostly by direct or indirect contact with infected horses, donkeys, and mules. Contact with diseased animals, contaminated fomites, tissues, or bacterial cultures can infect humans. Humans are accidental hosts, and disease is mainly caused by occupational exposure. Glanders is divided into three types of disease: nasal, pulmonary, and cutaneous, which can appear alone or in combination. It can be acute in nature, as observed in donkeys, and mules, or chronic in nature, as found in horses. The isolation and identification of *B. mallei* from clinical samples is the gold standard method for diagnosing glanders. The detection rate of glanders is increased when both serological and molecular testing approaches are used together. The mallein test is frequently used for field diagnosis in animals. Currently, no vaccine is available for humans or animals. Glanders could be used as a bioterrorism weapon. The presence of glanders in the absence of animal interaction, occupational exposure, and/or travel to an endemic location, such as Asia, Africa, or the Middle East, is presumed to be a bioterrorism occurrence. The disease's occurrence also results in international trade limitations. Early identification of disease in sensitive animals, strict quarantine measures, testing and safe destruction of contaminated carcasses, disinfection of infected premises, and raising knowledge about glanders and its zoonotic implications are all part of the prevention and management of this zoonosis.

Keywords: *burkholderia mallei*, equine, glanders, re-emerging, zoonoses

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1. Introduction

Glanders is an infectious re-emerging fatal bacterial zoonosis of solipeds caused by *Burkholderia mallei*. The only known natural reservoir of *B. mallei* is horses, donkeys, and mules [1]. Members of the feline family, from domesticated cats to lions, camels, sheep, and goats are susceptible to infection, whereas pigs, cattle, and birds are immune [2,3]. Glanders was a global concern in equids for generations, but by the mid-nineteenth century, it had been eradicated from most countries. Outbreaks are now rare and only occur in certain geographic areas [4]. Glanders is divided into three types of disease that might show alone or in combination: nasal, pulmonary, and cutaneous glanders [5].

Glanders is an occupational concern for individuals who operate in close proximity to equids (e.g., veterinarians, animal caretakers, mounted workers, researchers, etc.), as the majority of previously recorded naturally occurring cases were from close and regular contact with either live equids or tissues [6]. Glanders is a

biological warfare weapon classified as a category B Select Agent that has been deployed in the past. It was used to infect horses and then soldiers in both world wars. Glanders is a transboundary animal infection that must be reported to the World Organization for Animal Health (OIE) due to its economic impact on international animal and by-product trade [7]. The main purpose of this communication is to describe glanders as a serious re-emerging bacterial zoonosis of public health significance.

2. Aetiology

Glanders is an infection caused by the bacterium *Burkholderia mallei*, which was previously known as *Pseudomonas mallei*, but Aristotle called it after the Latin word *malleus*, which means "malignant sickness" [8]. *Burkholderia mallei* belong to the *Burkholderiales* bacterial order, family *Burkholderiaceae*, and genus *Burkholderia* [9]. The bacterium is Gram negative, non-motile, non-encapsulated bacillus and does not generate spores [10,11]. *Burkholderia pseudomallei*, the causative agent of melioidosis, is closely related to it and appears to

have developed from it. The heat and sunlight kill the organism, but the wet or humid surroundings let it survive longer [4].

3. Epidemiology

Glanders has been eradicated in North America, Australia, and Europe through to import controls, testing, and the eradication of affected animals. Glanders, on the other hand, are still found in a variety of Asian, African, Middle Eastern, and South American countries. Recent occurrences in regions where glanders was previously eradicated suggest that the disease's global distribution is no longer as constrained [12]. Cross-reactions with *B. pseudomallei* make serological surveys difficult to conduct, making it difficult to pinpoint the exact geographic distribution of *B. mallei* [4]. Glanders were detected in Brazil, Eritrea, Ethiopia, the former Soviet Union, Iran, Iraq, Mongolia, Turkey, and the United Arab Emirates between 1998 and 2007 [13]. Bahrain reported the first case of the disease in April 2010, while the condition resurfaced in Brazil in 2009 [14]. Glanders is an occupational hazard for those who work in close proximity to equids (e.g., veterinarians, animal caretakers, mounted workers, researchers, etc.), as the majority of previously reported naturally occurring cases were from close and frequent contact with either live equids or tissues [6].

4. Transmission

In glanders, several mechanisms of transmission have been reported [10]. It is carried through direct or indirect contact with horses, donkeys, or mules, and can be acute or chronic in nature [15]. The ingestion of organisms by contact with secretions of infected animals is the most common mechanism of transmission. The organisms are mostly transmitted through the nasal discharges and purulent exudates from draining cutaneous lesions; however, the infection can also be transmitted through urine, saliva, tears, and feces [16,17]. Indirectly through the ingestion of food or water contaminated with discharges from an infected animal. It can also be contracted through sharing feed or water containers, tack, grooming equipment, and other similar items [12]. Mechanical vectors could be flies. Venereal transmission from stallions to mares has been reported, as well as vertical transmission from the dam [4]. After consuming tainted meat, carnivores can become infected [18].

Contact with diseased animals, contaminated fomites, tissues, or bacterial cultures can infect humans [4]. Infectious elements from diseased animals come into touch with mucous membranes or broken skin, which leads to transmission [19,20]. Infected aerosols or dust can also carry *B. mallei* [21]. The skin and inhalational exposures have resulted in laboratory-associated infection [22]. Human-to-human transmission has been recorded in addition to animal exposure. Two cases of sexual transmission were suspected, as were other cases in family members caring for the patients [21].

5. Clinical Findings

5.1. In Animals

Glanders in equines can take numerous forms, including nasal, pulmonary, and cutaneous, depending on where the initial lesion is located. The disease might be acute or chronic in nature. Acutely affected horses die in a matter of days to weeks [12]. After a 3 to 2 week incubation period, critically affected animals frequently develop septicemia, a high temperature, weight loss, and a thick, mucopurulent nasal discharge, as well as respiratory symptoms [10,23]. High fever and loss of appetite, labored breathing with coughing, sticky yellowish-green nasal discharge, ocular discharge, ulcers and nodules in the nasal canal, and scabbed ulcers in star shape are all symptoms of the nasal type. The pulmonary type is the most prevalent and takes longer to develop than the nasal form; but, like the nasal form, it is still acute. The following are the most common clinical symptoms associated with this form: Coughing that is dry, labored breathing, pneumonia, nodules and/or abscesses in the lungs, and infection in the upper respiratory tract are all possibilities. The cutaneous type, unlike the other two, is a persistent infection that begins with minor to unnoticed symptoms and progresses to a debilitating state. Exacerbation episodes, cough, fever, skin nodules that rupture and ulcerate, nodule discharges, slow nodule healing, lymph node enlargement, and joint swelling are the most common symptoms [5,24].

Clinical symptoms in spontaneously infected dromedary camels resembled those seen in equids. Nodules and ulcers were observed in the nasal passages and on the conjunctivae, as well as deeper in the respiratory tract, in cats that ate infected meat. A purulent yellowish nasal discharge was also present in affected cats, which was sometimes bloody. Swelling of the lymph nodes and dyspnea were also symptoms, and infected cats usually died within 1 to 2 weeks [4]. Glanders was discovered in five dead lions at the Istanbul Gulhane Zoo in Turkey. The nasal mucosa lesions, anorexia, apathy, ocular discharge, epistaxis, sinusitis, swelling face and head were among the clinical signs observed [25].

5.2. In Humans

Localized cutaneous lesions, persistent skin infection, acute lung infection, or bacteremia are all possible manifestations of glanders in humans. Fever, muscle aches, chest pain, muscle stiffness, and headache are all common symptoms. Excessive tearing of the eyes, light sensitivity, and diarrhea has all been reported as additional symptoms [26]. Localized infections are usually limited to a specific area and are characterized by suppuration foci. The abscesses might become ulcerated and drain for a long time. Localized infections, on the other hand, can spread and cause pulmonary, septicemic, or multi-tissue infection [19]. The eight laboratory-acquired infections from Fort Detrick had the following clinical features: afternoon to evening low-grade fever, malaise, weariness, headache, myalgias including backache, lymphadenopathy, and chest discomfort (in order of most common occurrence). After

the first wave of disease symptoms, about half of the patients felt better and were clinically better for a length of time. The patients exhibited clinical indications of infection after this interval, which lasted anywhere from a few days to two months [14].

6. Diagnosis

All work with potentially infectious materials must be done in a lab that fulfills the Containment Group 3 pathogens' standards [12]. The isolation and identification of *B. mallei* from clinical samples is the gold standard method for diagnosing glanders [5]. *Burkholderia mallei* can be grown on nutritional, blood, and MacConkey agar, among other media. On these usual culture media, viscid, smooth, and creamy colonies of *B. mallei* can be produced after 48 hours at 37°C (98°F). The organism can grow as both an aerobic and facultative anaerobe in the presence of nitrogen [13]. The mallein test is often used for field diagnostics in animals [1]. Malleinization (delayed hypersensitivity testing, i.e., applying a crude preparation of *B. mallei* antigens subcutaneously, intracutaneously, or ophthalmically and observing the resultant fever, swelling, or outflow of pus from the eye in positive animals) was once employed to eradicate glanders [27]. The complement fixation test (CFT), competitive enzyme-linked immunosorbent assay (cELISA), immunoblot (IB), indirect haemagglutination assay (IHA), agar-gel immuno diffusion (AGID), indirect fluorescent assay test (IFAT), counter immuno electrophoresis (CIE), and dot ELISA are all serological tests used to diagnose glanders [5]. For specific identification, PCR based on 16S and 23S rRNA gene sequences might be utilized [24].

7. Treatment

7.1. In Animals

It is a disease that must be reported and affected animals must be slaughtered and disposed of safely [28]. Treatment can only be utilized in valuable horses due to its high cost, but it should not replace the test and slaughter policy [29]. Even in endemic areas, treatment can be dangerous since the disease can spread to humans and other animals, and treated animals can become asymptomatic carriers [2]. Treatment for glanders usually necessitates a long course of treatment, with most treatments lasting at least 20 days [29, 30]. Sulfazine or sulfamonomethoxine in combination with trimethoprim was found to be effective in preventing and treating experimental glanders [12]. A number of antibiotics, such as ceftazidime, sulfadiazine, trimethoprim-sulfamethoxazole, gentamicin, Iipenem, and others are used alone or in combination in horses [31].

7.2. In Humans

Because human cases of glanders are uncommon, there is little knowledge on how to treat the organism with antibiotics. In both experimental animals and humans, sulfadiazine has been demonstrated to be effective.

Tetracyclines, ciprofloxacin, streptomycin, novobiocin, gentamicin, imipenem, ceftazidime, and sulfonamides are usually ineffective against *Burkholderia mallei*. Chloramphenicol resistance has been reported [12]. In light of the advent of ceftazidime-resistant clinical isolates in Southeast Asia, piperacillin/tazobactam as an alternative to the currently used antibiotic ceftazidime for the treatment of glanders and melioidosis [14,32].

8. Prevention and Control

There is no glanders vaccination available for animals or humans at this time [21]. All positive cases of glanders must be identified, euthanized, and properly disposed of quickly to ensure effective prevention and control [12]. When handling diseased animals and contaminated fomites, extreme caution should be exercised, including the use of proper personal protection equipment (PPE) [4]. The carcass should not be opened if the cause of death is glanders. It has to be buried or burned. Burning or burying manure, bedding, and feed leftovers are recommended. It is necessary to maintain a rigorous disinfection program for the premises, feed and water troughs, and other areas. *Burkholderia mallei* is particularly susceptible to conventional disinfectants, such as benzalkonium chloride, iodine, mercuric chloride in alcohol, potassium permanganate, 1% sodium hypochlorite, 70% ethanol, and 2% glutaraldehyde, and should be disinfected. Phenolic disinfectants are less effective on it. It can also be destroyed by heating it to 55°C for 10 minutes or by exposing it to UV light. The isolation, hygiene, and sanitation protocols should all be followed. One part of home bleach (0.5 percent sodium hypochlorite solution) to 9 parts of water should be used to clean contaminated material. It is imperative that glanders awareness programs must be conducted periodically [5].

9. Conclusion

Glanders is a highly contagious disease caused by *B. mallei* that causes nodular and ulcerative skin lesions, as well as mucous membrane in the nasal and respiratory mucosa. The disease is endemic in many regions, such as Africa, Asia, the Middle East, and Central and South America. Outbreaks of glanders have increased significantly in several parts of the world, and are now designated re-emerging disease. Although it is largely a disease of solipeds, it can also affect other species, including humans. Glanders can be transmitted through direct or indirect contact with horses, donkeys, or mules, and can be acute or chronic in nature. Those who operate in close proximity to horses are at risk of developing glanders. Ulcers, nodules, and satellite scars on the respiratory tract, skin, and subcutaneous tissues are visible on the surface, while pyogranulomatous lesions are visible under the microscope. Mallein and CFT tests are prescribed for disease diagnosis, with mallein being the primary test for field diagnosis. Presently, no vaccine is available to prevent the infection with *B. mallei* either in animals or humans. *Burkholderia mallei* is considered a potential agent for biological warfare and poses a

significant threat to human health. Occupational groups are advised to take necessary precautions to prevent the infection from this pathogen.

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Competing Interests

Conflicts of interest are not declared by the authors.

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