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Glanders: Historical military use and potential bioterrorism concern

Mohammad Sukmanadi¹ , Aswin Rafif Khairullah² , Bantari Wisynu Kusuma Wardhani³ , Imam Mustofa^{4*} , Siti Hamidatul Aliyah⁵ , Ikechukwu Benjamin Moses⁶ , Riza Zainuddin Ahmad² , Andi Thafida Khalisa⁷ , Bima Putra Pratama⁸ , Muhammad Khaliim Jati Kusala² , Dea Anita Ariani Kurniasih⁹ , Adeyinka Oye Akintunde¹⁰ , Ima Fauziah² , Syahputra Wibowo¹¹ , Abdul Hadi Furqoni⁵ , Kartika Afrida Fauzia¹² , Irma Melati¹³ , and Muhammad 'Ahdi Kurniawan¹⁴ 

¹Division of Basic Veterinary Medicine, Faculty of Veterinary Medicine, Universitas Airlangga, Surabaya, Indonesia

²Research Center for Veterinary Science, National Research and Innovation Agency (BRIN), Bogor, Indonesia

³Research Center for Pharmaceutical Ingredients and Traditional Medicine, National Research and Innovation Agency (BRIN), Bogor, Indonesia

⁴Division of Veterinary Reproduction, Faculty of Veterinary Medicine, Universitas Airlangga, Surabaya, Indonesia

⁵Center for Biomedical Research, National Research and Innovation Agency (BRIN), Bogor, Indonesia

⁶Department of Applied Microbiology, Faculty of Science, Ebonyi State University, Abakaliki, Nigeria

⁷Faculty of Military Pharmacy, Universitas Pertahanan, Bogor, Indonesia

⁸Research Center for Agroindustry, National Research and Innovation Agency (BRIN), South Tangerang, Indonesia

⁹Research Center for Public Health and Nutrition, National Research and Innovation Agency (BRIN), Bogor, Indonesia

¹⁰Department of Agriculture and Industrial Technology, Babcock University, Ikenne, Nigeria

¹¹Eijkman Research Center for Molecular Biology, National Research and Innovation Agency (BRIN), Bogor, Indonesia

¹²Research Center for Preclinical and Clinical Medicine, National Research and Innovation Agency (BRIN), Bogor, Indonesia

¹³Research Center for Limnology and Water Resources, National Research and Innovation Agency (BRIN), Bogor, Indonesia

¹⁴Medical Biotechnology Research Group, Virtual Research Center for Bioinformatics and Biotechnology, Surabaya, Indonesia

ABSTRACT

Burkholderia mallei, the etiological agent of glanders, is a zoonotic bacterium primarily affecting equines and occasionally humans. Although rare today, it remains endemic in certain regions and poses a potential threat to both animal and public health. Historically, *B. mallei* was among the earliest biological agents used in warfare, and its classification as a Category B bioterrorism agent underscores the need for ongoing vigilance. This review is warranted due to several factors: the limited availability of effective treatments or vaccines, the pathogen's ability to cause severe systemic infections, its diagnostic challenges, and its re-emerging status in some parts of the world. Moreover, growing concern over its potential misuse in bioterrorism highlights the urgency for a comprehensive understanding of the bacterium. The aim of this review is to provide a consolidated overview of *B. mallei* and glanders, emphasizing pathogenesis, clinical manifestations in animals and humans, diagnostic methods, differential diagnoses, and current prevention strategies. It also discusses the historical use of *B. mallei* as a biological weapon and its implications for modern biosecurity. By synthesizing existing knowledge, this review contributes to a more structured understanding of glanders and highlights knowledge gaps that require further research. Raising awareness of this neglected zoonosis is essential to strengthen surveillance, improve diagnostic capabilities, and inform policies aimed at mitigating future outbreaks or misuse.

Keywords: *B. mallei*, Bioterrorist, Glanders, Public health, Zoonosis.

Introduction

Glanders is a neglected but highly consequential zoonotic disease caused by *Burkholderia mallei*, primarily affecting equines such as donkeys, horses,

and mules, and occasionally humans (Gaspar *et al.*, 2023; Alikhanov *et al.*, 2024). While the pathogen was first isolated in 1882, and glanders has been eradicated from many industrialized countries, sporadic

*Corresponding Author: Imam Mustofa. Division of Veterinary Reproduction, Faculty of Veterinary Medicine, Universitas Airlangga, Surabaya, Indonesia. Email: imam.mustofa@fkh.unair.ac.id

outbreaks continue to occur in Asia, Africa, and parts of Latin America, underscoring its persistence as a transboundary threat (Kettle and Wernery, 2016; Pal and Paulos Gutama, 2022). This persistence contrasts with the global decline of many other equine diseases, suggesting that glanders is not only an epidemiological relic but also a re-emerging infection that thrives in under-resourced veterinary systems. Unlike strictly historical diseases, its recurrence highlights the need for sustained scientific and policy attention.

Beyond its natural epidemiological burden, *B. mallei* has unique historical and contemporary relevance. It was among the earliest pathogens used as a biological warfare agent during World Wars I and II, and it remains classified as a Tier 1 Select Agent by the Centers for Disease Control and Prevention due to its aerosol transmissibility, high lethality, and diagnostic challenges (Varga et al., 2012; Cote et al., 2020). *Burkholderia mallei* remains classified as a Tier 1 Select Agent due to its transmissibility and lethality (CDC, 2000; CDC, 2024). This dual identity—as both a neglected zoonosis and a biothreat agent—distinguishes glanders from many other infectious diseases, placing it at the intersection of veterinary medicine, public health, and international security. The implications extend well beyond equine health, raising concerns about biodefense preparedness, laboratory safety, and global surveillance.

Historically, several reviews have summarized the general clinical and epidemiological features of glanders (e.g., Al-Ani and Roberson, 2007; Van Zandt et al., 2013). However, most existing reviews remain descriptive, focusing heavily on history, case reports, and classical pathology, while providing limited synthesis of recent scientific advancements. Over the past decade, important new findings have reshaped our understanding of *B. mallei*. For example, genomic studies have revealed an unusually high rate of genetic variation in this bacterium, comparable to RNA viruses, which may underlie its capacity to evade host immune defenses and complicate vaccine development (Memisević et al., 2013; Charron et al., 2023). This discovery challenges the long-standing assumption that bacterial pathogens are genetically stable and highlights why glanders research can inform broader questions of microbial evolution.

Epidemiologically, glanders has often been considered rare or declining, yet recent serological surveys and outbreak reports from South Asia, the Middle East, and South America reveal patterns of underdiagnosis and underreporting (Singha et al., 2020; Resende et al., 2022). In some cases, countries that declared themselves glanders-free experienced reintroductions, linked to uncontrolled horse movement across borders and insufficient veterinary capacity. This suggests that the official absence of glanders may reflect diagnostic blind spots rather than true eradication, creating a false sense of security in trade and animal health policy.

Such analytical insights are largely missing in prior reviews, which tend to present prevalence data without interrogating their reliability or implications.

Another critical gap lies in clinical and pathological interpretation. While glanders in animals and humans presents with fever, respiratory distress, nodules, and septicemia, the overlap with other infectious diseases complicates early recognition. Prior reviews list these differential diagnoses, but few provide a comparative analysis that could guide clinicians toward a more accurate distinction in endemic settings. In practice, this diagnostic ambiguity increases both animal and human mortality, especially where laboratory confirmation is limited.

Treatment and prevention remain equally challenging. Horses testing positive are typically culled to prevent further spread, and no vaccine is available. For humans, long-term antibiotic therapy has been attempted, often by extrapolating from melioidosis treatment protocols (Wiersinga et al., 2018). Yet systematic evaluation of these regimens is sparse, and recent experimental studies on novel antibiotics and immunological interventions have not been comprehensively reviewed. By integrating these scattered data, this article aims to provide a more evidence-based assessment of therapeutic prospects.

The biosecurity dimension further elevates the importance of glanders research. The deliberate weaponization of *B. mallei* by Germany and Japan during the World Wars, and its continued classification as a potential bioterrorism agent, underscore enduring security concerns (Koenig and Schultz, 2016). However, existing literature often recounts this history without linking it to current biodefense strategies. A more critical discussion is needed, particularly regarding gaps in preparedness, laboratory containment policies, and the integration of glanders surveillance into broader frameworks for high-risk pathogens.

Therefore, this review does not merely reiterate the clinical and historical aspects of glanders. Its novelty lies in synthesizing recent molecular insights, critically reassessing epidemiological patterns in the light of underreporting, and analyzing the biosecurity implications in the context of modern biodefense. By highlighting these elements, the review contributes to a more forward-looking understanding of glanders, framing it as both a neglected zoonotic disease and a pathogen of global security significance. In doing so, it underscores the urgent need for interdisciplinary collaboration across veterinary medicine, microbiology, public health, and policy to close the current knowledge and preparedness gaps.

Etiology

B. mallei is a facultative intracellular rod-shaped bacterium that is straight or slightly curved, measuring 2–5 μ in length and 0.3–0.8 μ in width (Whitlock et al., 2009). It does not generate spores. These bacteria are required to be aerobes, with the exception of media

that include nitrate (Mangalea *et al.*, 2017). Glycerol-containing media are preferred by aerobic-growing bacteria as an enrichment agent. On Glycerol Dextrose Agar, there was a smooth, moist, and thick, cream-colored, unified growth after 24 hours of incubation (Kinoshita *et al.*, 2019). Continued incubation causes the growth to thicken, darken, and harden. Electron microscopy has shown a capsule-like layer. The neutral carbohydrate capsule shields cells from adverse environmental conditions (Llobet *et al.*, 2008). *Burkholderia pseudomallei* is closely related to this bacterium, but *B. mallei* is not motile and does not have flagella (Gilad *et al.*, 2007). This organism has a beaded appearance and is challenging to show in tissue slices. The age of the culture and the kind of media influence how they look in cultural media. Older cultures exhibit a great deal of pleomorphism in the organism (Jilani *et al.*, 2023). *B. mallei* is sensitive to the environment and is killed by the majority of conventional disinfectants, including formalin, chlorine, copper sulfate, potassium permanganate, and phenol, within 24 hours of being exposed to direct sunlight (Shams *et al.*, 2011). The organism can live for up to 4 weeks in clean water, around 6 weeks in contaminated cages, and 3–5 weeks in moist media and decomposing matter (Gaspar *et al.*, 2023).

History

Hippocrates identified the earliest indications of glanders disease when he documented its clinical manifestations between 450 and 425 BC (Júnior *et al.*, 2020). One hundred years later, Aristotle used the broad term for epizootics to describe the sickness and called it “melis.” He also mentioned that humans were unintentional hosts and that horses were the disease’s natural reservoir (Neubauer *et al.*, 2005). Glanders’ relationship with battle was expanded during the fourth century AD, when Apsyrtus worked as a veterinarian in Constantine the Great’s army (Torres, 2025). Furthermore, Vegetius was named by Roman military historians in the fifth century AD, who also referred to the illness as “malleus” Historical laboratory-acquired infections have been documented during World War II (Howe and Miller, 1947; Herr *et al.*, 1985).

The French King, Louis XV, commissioned the first veterinary school in Lyons, led by Claude Bourgelat, in 1761 to study Glanders in an attempt to safeguard the French Army’s horses because the region was well-known during the Crusades and other military conflicts (Wilkinson, 1981). Glanders was recognized as an infectious disease in 1876 after Viborg proved its contagiousness in 1797 (Torres, 2025). In 1882, he isolated the bacterium, also known as *Burkholderia mallei*, from the liver and spleen of afflicted horses in Germany (Lauman and Dennis, 2021). In 1956, Henning named *Pfeifferella mallei* (Al-Ani and Roberson, 2007). The authors gave it the name *Pseudomonas mallei* that same year (Wetmore and Gochenour, 1956). Furthermore, Evans named *Actinobacillus mallei*

in 1966 (Evans, 1966). Following that, Merchant & Packer gave it the name *Malleomyces mallei* (Merchant and Packer, 1967). *B. mallei* is the common name used today (Yabuvchi *et al.*, 1992).

Host range

Solipeds, or mammals with a single hoof on each foot, are the natural reservoir of *B. mallei* (Wiersinga *et al.*, 2018). In horses, this condition is typically chronic; in donkeys and mules, it manifests as an acute form that frequently results in death (Van Zandt *et al.*, 2013). Although the majority of other domesticated mammals can contract the disease experimentally, pigs, cattle, and chickens have shown resistance to it (Pal *et al.*, 2022). There have also been reports of the disease developing spontaneously in a number of species, such as cats, dogs, and goats (Khan *et al.*, 2013). Occupational groups at high risk for glanders include laboratory workers, stable keepers, blacksmiths, veterinarians, horse groomers, and horse slaughterers (Kettle and Wernery, 2016).

Epidemiology

Glanders is reported to be endemic in horses in the Middle East and in Asian nations like Bangladesh, Iran, and Mongolia (Khaki *et al.*, 2012; Rahman *et al.*, 2018; Erdemsurakh *et al.*, 2020b). According to Office International des Epizooties (OIE) data, Glanders is prevalent in China (Zheng *et al.*, 2019) and Russia (Zakharova *et al.*, 2018), and it has also been documented in Vietnam (Brightman and Locum, 2020), Korea (Lee *et al.*, 2010), and Pakistan (Khan *et al.*, 2012). Rose Bengal Test (RBT) and Complement Fixation Test (CFT) results indicate that the prevalence of the disease among Mongolian horses ranges from 7.7% to 8.3%. They discovered that compared to endemic native Mongolian horses, there was a greater correlation between seropositive horses produced by crossing native Mongolian horses and thoroughbred horses (Erdemsurakh *et al.*, 2020b). Additionally, researchers in Pakistan’s Punjab province used CFT to detect antibodies against *B. mallei*, followed by western blot analysis (Khan *et al.*, 2012). Table 1 describes the incidence of Glanders by country, endemic status, diagnostic method, and Seroprevalence of glanders in Mongolian horses was reported at 7.7%–8.3% (Erdemsurakh *et al.*, 2020a).

Glanders is also endemic in India, and reports of seroprevalence by indirect Enzyme-linked Immunosorbent Assay (ELISA) and CFT of 0.62% and 1.145% have been made in some areas. Scientists have observed that cases have returned to Maharashtra, Haryana, and Punjab after a 10-year period in which these states were free of Glanders. It is believed that glanders may not have been truly eradicated but instead remained undiagnosed and underreported due to low disease awareness, inadequate veterinary services, and uncontrolled movement of horses across state borders (Singha *et al.*, 2020). Furthermore, two strains of *B. mallei* seemed to have come from the same region by

Table 1. Glanders incidents in several countries that have been reported.

Country	Status	Diagnostic method(s)	Prevalence/Key findings	Reference
Bangladesh	Endemic	Not specified	Reported cases	Rahman <i>et al.</i> (2018)
Iran	Endemic	Not specified	Reported cases	Khaki <i>et al.</i> (2012)
Mongolia	Endemic	RBT, CFT	7.7%–8.3%; higher in crossbred versus native Mongolian horses	Erdemsurakh <i>et al.</i> (2020b)
China	Prevalent	Not specified	Reported cases	Zheng <i>et al.</i> (2019)
Russia	Prevalent	Not specified	Reported cases	Zakharova <i>et al.</i> (2018)
Vietnam	Reported	Not specified	Reported cases	Brightman and Locum (2020)
South Korea	Reported	Not specified	Reported cases	Lee <i>et al.</i> (2010)
Pakistan	Endemic	CFT, Western Blot	Antibody detection against <i>B. mallei</i>	Khan <i>et al.</i> (2012)
India	Endemic, re-emerging	iELISA, CFT	Seroprevalence: 0.62%–1.145%; resurgence in multiple states	Singha <i>et al.</i> (2020)
Bahrain	Outbreak	Not specified	Two strains traced to imported infected animals	Scholz <i>et al.</i> (2014)
Brazil	Endemic, increasing trend	Not specified	Yearly cases impact trade and cause economic losses	Resende <i>et al.</i> (2022)
United Arab Emirates	Regional research hub	OIE surveillance & diagnostics	CVRL Dubai is the OIE reference laboratory for glanders	Hmood and Al-Amery (2022)
Australia	Eradicated	Not specified	Glanders-free since early 20th century	Cárdenas <i>et al.</i> (2019)
Japan	Eradicated	Not specified	Declared glanders-free	Cárdenas <i>et al.</i> (2019)
North America	Eradicated	Not specified	Declared glanders-free	Cárdenas <i>et al.</i> (2019)
Western Europe	Eradicated	Not specified	Declared glanders-free	Cárdenas <i>et al.</i> (2019)

way of the importation of sick animals, as was shown in the Glanders outbreak in Bahrain (Scholz *et al.*, 2014). Glanders remains a major issue in Brazil, where many new cases are reported each year, impacting the animal trade and resulting in significant financial losses (Resende *et al.*, 2022). Given the numerous recent outbreaks reported across multiple countries, glanders is regaining attention as a re-emerging infectious disease of concern (Khan *et al.*, 2013). Asia and certain regions of Africa and South America are thought to be endemic for the new disease (Torres, 2025). Horses and camels carrying glanders serve as a reservoir for the return of glanders into nations that were previously designated as glanders-free (Kettle and Wernery, 2016). The Central Veterinary Laboratory (CVRL) in Dubai is the official organization in charge of glanders research, surveillance, and eradication in the Arab world. It is also the official OIE reference laboratory for glanders (Hmood and Al-Amery, 2022). All animal-related procedures were performed using established protocols and in compliance with OIE’s animal welfare guidelines. By the early 20th century, glanders had been exterminated in the majority of developed nations, which was a significant indication of advancements in veterinary medicine, diagnostic capabilities, and

disease control measures. Glanders was exterminated in Australia, Japan, North America, and Western Europe (Cárdenas *et al.*, 2019).

Pathogenesis

B. mallei enters the body naturally through the gastrointestinal system, integument, and mucous membranes of the eyes and nose (Syed and Wooten, 2021). Bacteria enter the circulation and internal organs, especially the lungs, by penetrating the mucosa of the colon or oropharynx and traveling via lymphatic vessels to the regional lymph nodes (Whitlock *et al.*, 2009). It then travels via the bloodstream to produce sores on the nose, skin, and nodes. The organism enters the body through the skin and travels into the lymphatic passages, causing lymphangitis (Siggins and Sriskandan, 2021). Terminal signs, including bronchopneumonia and death, are primarily caused by anoxia resulting from progressive respiratory failure. Genomic studies highlight the pathogen’s adaptability and virulence (Kyle *et al.*, 2015).

Lesions in humans can be found in the skin, skeletal muscle, bones, joints, lymph nodes, spleen, liver, and, less commonly, the brain, meninges, nose, and eyes (Verma *et al.*, 2014). It was once believed that glanders had no effect on human or animal bones,

but later research has shown that mules, humans, and experimental hamsters can all develop bone lesions (Fritz *et al.*, 1999). *B. mallei*'s primary defenses against phagocytosis include intracellular localization and the existence of a capsule and capsular lipopolysaccharide (LPS) (Bzdyl *et al.*, 2022). The two main virulence factors that glanders bacilli produce *in vivo* during infection are overexpression of type VI secretion protein (T6S) and a functioning type III secretion system (Schell *et al.*, 2007). According to recent *in vitro* research, *B. mallei* significantly influences murine macrophages by inducing the expression of inducible nitric oxide synthase (iNOS), which is essential for the elimination of bacteria by activated macrophages (Brett *et al.*, 2008).

Once *B. mallei* has briefly passed through a number of mammalian hosts, including humans, its genome changes at a very high rate (Romero *et al.*, 2006). Since only RNA viruses have the ability to rapidly alter their genomes as a key part of their strategy to elude the host immune response, it is the first and only bacterial pathogen to possess this ability (Memisević *et al.*, 2013). *B. mallei* may express more virulence genes during *in vivo* infection as a result of this substantial and quick genomic variation. They also found that *B. mallei* uses a mutant gene that codes for a penicillin-binding protein (PBP-1c) involved in cell wall production and β -lactam resistance to avoid immunological detection and phagocytic clearance *in vivo* (Charron *et al.*, 2023). The organism *B. mallei* is not kept as a clonal population like other organisms, but rather as a population of variant or mutant organisms within the host (Whitlock *et al.*, 2009). The development of vaccines and treatments for glanders disease may be impacted by this genetic instability during transmission.

Immune response

Although Burkholderia species may utilize different pathogenic mechanisms, invasion and adherence to host epithelial cells are essential stages of infection and appear to play a major role in overall virulence (David *et al.*, 2015). *B. mallei* depends on the deliberate application of numerous virulence factors and mechanisms to control various host processes and pathways in order to successfully infect host cells recent molecular analyses provide novel insights into virulence pathways (Nikolakakis *et al.*, 2024). Nine *B. mallei* virulence factors and their interactions with host proteins were recently extensively evaluated using a combination of computational and experimental methods in an effort to clarify the mechanisms behind *B. mallei* pathogenicity (Memisević *et al.*, 2013). According to topological research of *B. mallei*-host protein-protein interactions, the parasite targets intracellular multifunctional host proteins, host proteins that engage in mutual contact, and proteins with several interacting partners. The focal adhesion pathway and the ubiquitination degradation system are

two host mechanisms that are significantly impacted by these protein-protein interactions (Memisević *et al.*, 2015). These findings are in line with earlier research that documented connections between the TssN protein and the proteins cullin-1a and polyubiquitin-B. This host protein interacts with two elements necessary for Toll-like receptor (TLR) signaling: inhibitor of I κ B- α and tumor necrosis factor (TNF) receptor-related factor 6 (Duan *et al.*, 2022). This study sheds some light on *B. mallei*'s pathophysiology and supports the theory that the pathogen alters the innate immune response by either directly or in concert with other harmful proteins interfering with host ubiquitination.

A thorough analysis of murine macrophages infected with a variety of Burkholderia species reveals the production of the cytokines TNF α , interleukin 1 β (IL-1 β), and the chemokine murine keratinocyte-derived protein, which is the murine counterpart of human IL-8 (Chiang *et al.*, 2015). The fact that *B. mallei*-infected macrophages release noticeably more IL-6 and IL-10 than *B. pseudomallei*-infected macrophages suggests that these two pathogens alter host signaling cascades in different ways (Lu *et al.*, 2012). Furthermore, compared to other Burkholderia species, macrophages infected with *B. mallei* exhibited considerably greater levels of expression of IL-1 β , IL-10, TNF receptor superfamily member 1B, and IL-36 α mRNA, indicating gene-based variations in the host inflammatory response specific to *B. mallei* (Chin *et al.*, 2010).

Further analysis of the infected macrophages revealed increased phosphorylation of adenosine monophosphate-activated protein kinases, as well as mitogen-activated protein kinases (such as p38, extracellular signal-regulated kinase 1/2, and c-Myc) and regulators of the nuclear factor-kappa B signaling pathway [such as I κ B- α inhibitor, glycogen synthase kinase (GSK) 3 β , Src, and STAT1] (Aiba *et al.*, 2003). The observed variations in pathogenicity among Burkholderia species are correlated with the degree of modulation of target host proteins or processes. *B. mallei* is a stronger inducer of interferon-gamma (IFN γ) production and iNOS expression in infected macrophages than *B. pseudomallei* (Brett *et al.*, 2008). Based on these findings, a representative network of signaling routes and axes was built to explain how signaling cascades are activated in response to Burkholderia spp. infection, in addition to what is currently known about signal transduction. The canonical pathway downstream of TLR4 indicates that the induction of phosphorylated forms of GSK3 β , Src, and adenosine monophosphate-activated protein kinase- α 1 is crucial in controlling the inflammatory response of Burkholderia spp.'s infection (Escobar *et al.*, 2015).

LPS is a powerful inducer of the host's innate immune response and a significant part of the outer membrane of Gram-negative bacteria (Maldonado *et al.*, 2016). Studies of the structure-activity relationship of TLR4

agonists reveal a correlation between the lipid A moiety's composition and LPS's biological activity (Matamoros-Recio *et al.*, 2023). The assessment of *B. mallei* LPS revealed that its biological activity was more influenced by lipid A acylation than by its length (Brett *et al.*, 2007). Therefore, *B. mallei* LPS, which is comparable to *B. pseudomallei* LPS and has penta-acetylated lipid A with 4-amino-4-deoxyarabinose in nearly half of its molecules, may be linked to the overall differential macrophage activation. It also seems to be a weaker macrophage activator than enterobacterial LPS (Korneev *et al.*, 2015). This is supported by the fact that when macrophages were stimulated with isolated *B. mallei* LPS as opposed to those treated with *E. coli* LPS, there was a notable reduction in the mRNA expression or secretion of IL-6, TNF α , and IL-1 β (Duan *et al.*, 2023). The production of IFN-dependent genes and mediators (IFN β and Nitric oxide), as well as cytokines (TNF α , IL-6, IL-10, Granulocyte-macrophage colony stimulating factor, and normal T cells) was similarly lower in *B. mallei*-infected macrophages than in *E. coli*-infected macrophages (Chen *et al.*, 2023).

In order to create a persistent infection, *B. mallei* needs to get past a number of antibacterial processes and products (such as adenosine monophosphate and reactive oxygen and nitrogen species) that are necessary for innate immunity (Saikh and Mott, 2017). The capacity of *B. mallei* isolates obtained from mice spleens at Frederick Memorial Hospital (FMH) to multiply and cause cytotoxicity in macrophage tests was diminished 60 days after infection (Bernhards *et al.*, 2017). Because of the loss of O-specific polysaccharide (OPS) during infection, one isolate of *B. mallei* displayed a change in its LPS phenotype from smooth to rough. It is known that these phenotypic alterations occur when an infection switches from an acute to a chronic or subclinical form, which is less likely to elicit an immunological response from the host. Prior research has indicated that the persistence of *B. pseudomallei* and *B. mallei* may be linked to genetic and phenotypic traits (Massey *et al.*, 2014). The genetic basis for the loss of OPS may be revealed by more research, such as sequencing the OPS biosynthetic gene cluster of this FMH *B. mallei* strain. A key feature of persistent *Pseudomonas aeruginosa* infection is the alteration or loss of OPS (Bernhards *et al.*, 2017).

Pathology

The pathognomonic pathology of Glanders does not provide a conclusive pathological diagnosis. Nodules or ulcers are typically present in a variety of tissues, including the liver, spleen, pleura, lungs, and upper respiratory tract (Mota *et al.*, 2010). Fibrosis, congestion, or nodules may expand the lymph nodes. Infected stallions have also been reported to develop orchitis due to systemic spread of the infection (Spickler, 2018).

Histopathology demonstrating hemorrhage and vasculitis together with skin glanders (Carlson, 2010).

Also common are lymph node foci of pyogranulomatous inflammation (Mota *et al.*, 2010). Nasal glanders are linked to damage to the nasal epithelium and septum, as well as significant widespread purulent inflammation (López and Martinson, 2017). Similar to the skin glands, the nasal glands can also experience hemorrhage, vasculitis, and abscesses that progress into granulomatous lesions (Zachary, 2017).

The lungs of pulmonary glanders have granulomatous or pyogranulomatous lesions (Fritz *et al.*, 1999). Inflammatory cells, such as macrophages, giant cells, lymphocytes, and plasma cells, encircle the lesion, which has a central region of caseous necrosis (Kumar *et al.*, 2013). The lung tissue of horses with pulmonary glanders has also been seen to exhibit intra-alveolar fibrin deposits, localized bleeding, and areas of edema (López and Martinson, 2017).

Clinical symptoms

In animals

Horse glanders can manifest as nasal, pulmonary, or cutaneous, contingent on the location of the initial lesion. The illness could be chronic or acute. Acutely affected horses pass away in a matter of days to weeks (Raj *et al.*, 2024). Critically ill animals frequently experience respiratory symptoms, septicemia, a high temperature, weight loss, and thick mucopurulent nasal discharge after an incubation period of 3–2 weeks (Pal *et al.*, 2016). The nasal form is characterized by a high temperature and lack of appetite, coughing and shortness of breath, eye discharge, sticky yellowish green nasal discharge, nasal nodules and ulcers, and star-shaped crusted ulcers (Pal and Paulos Gutama, 2022). The most prevalent kind, the pulmonary form, develops more slowly than the nasal form but is nonetheless intense. The most prevalent clinical signs of the pulmonary form are as follows: upper respiratory tract infections, pneumonia, pulmonary nodules or abscesses, dry cough, and shortness of breath (Siddique *et al.*, 2023). In contrast to the other two skin types, this one is a chronic infection that begins with minor to undetectable signs before becoming a crippling illness (Torres, 2025). The most typical symptoms include exacerbation episodes, cough, fever, ulcerating and rupturing skin nodules, fluid draining from nodules, sluggish nodule healing, swollen lymph nodes, and joint swelling (Khan *et al.*, 2013).

The clinical manifestations of spontaneous infection in dromedary camels are similar to those observed in horses (Khalafalla, 2016). Cats that have consumed contaminated meat may develop nodules and ulcers in their nasal passages, on the conjunctiva, and deeper in their respiratory tract (Rahman *et al.*, 2020). Infected cats also have a purulent yellowish nasal discharge, which can occasionally be bloody. Dyspnea and enlarged lymph nodes are further symptoms, and infected cats typically pass away in 1–2 weeks (Morrow and Ruggiero, 2025). Glanders were discovered on five dead lions at the Gulhane Zoo in Istanbul, Turkey.

Clinical indicators include nasal mucosal lesions, anorexia, lethargy, ocular discharge, epistaxis, sinusitis, and facial and head edema (Alibasoglu *et al.*, 1986).

In humans

Human glanders may present as bacteremia, acute lung infections, persistent cutaneous infections, or localized skin lesions (Junior *et al.*, 2020). Common symptoms include headache, muscle stiffness, chest pain, fever, and muscle aches. Other symptoms have been recorded, including diarrhea, light sensitivity, and excessive eye tearing (Van Zandt *et al.*, 2013). Localized infections are typically limited to a particular region and are distinguished by suppuration foci. An abscess can drain liquids and ulcerate for a lengthy time (Kianfara *et al.*, 2018). However, localized infections have the potential to spread and result in multitissue infections, septicemia, or pulmonary infections (Virk *et al.*, 2023). The following clinical characteristics were present in eight Fort Detrick laboratory-acquired infections: In order of most frequent occurrence, low-grade fever in the afternoon to evening, malaise, exhaustion, headache, myalgia, including back pain, lymphadenopathy, and chest discomfort (Van Zandt *et al.*, 2013). About 50% of patients have a temporary improvement in their clinical condition following the initial wave of illness symptoms. After this time, which can range from a few days to 2 months, patients exhibit clinical signs of infection (Nasiri *et al.*, 2023).

Diagnosis

Animal glanders can be identified by immunological response (serological testing and mallein test) and antigen detection [bacterial culture/culture and molecular detection/polymerase chain reaction (PCR)] (Abreu *et al.*, 2020). The selection of glanders diagnostic techniques is carried out depending on the intent and purpose, whether for surveillance, disease confirmation, or an eradication program. Table 2 explains the comparison of glanders diagnostic methods summarized from your description, including the type of method, working principle, advantages, and limitations.

The gold standard method for diagnosing the genus *Burkholderia* is culture-based bacterial isolation; however, even with newly obtained, sterile samples, isolating these bacteria is extremely challenging (Li *et al.*, 2022). *B. mallei* isolates can be obtained from blood samples, skin lesions, and exudates from the nasal and upper respiratory tracts (Rocha *et al.*, 2023). *B. mallei* bacteria require specialized media with the addition of enrichment media, like glycerol, because they grow very slowly and can be readily contaminated by other bacteria (Kinoshita *et al.*, 2019).

The *B. mallei* colony on blood agar or Loeffler serum agar is thick, white, semi-translucent, and about 1 mm in diameter. It will turn yellow on the colony. After 3 days, the bacterial growth on glycerin-potato media will resemble a honey coating before turning brown or reddish brown (Abnaroodheleh *et al.*, 2023).

The World Organization for Animal Health does not advise the Mallein test, a hypersensitivity skin test based on water-soluble proteins isolated from microbes, because of concerns about animal welfare (Karimi and Mosavari, 2019). Furthermore, cultural isolation is not a preferred method for glanders diagnosis due to the test's low sensitivity and time-consuming nature, and it is not approved for use in commercial testing (Elschner *et al.*, 2021). Additionally, as supplementary diagnostic techniques like the CFT, malleinized animals may undergo seroconversion and thereafter exhibit positive results (Abreu *et al.*, 2020). However, in isolated endemic locations, the mallein test might be helpful in eliminating glanders. The CFT is recommended by the OIE for glanders surveillance in horses (Elschner *et al.*, 2011).

The PCR test is one molecular detection method for glanders that can lower the risk of environmental and human bacterial contamination (Tikmehdash *et al.*, 2024). The species *B. mallei* and *B. pseudomallei* can be differentiated by PCR techniques (restriction fragment length polymorphism, pulse-field gel electrophoresis, and 16S rRNA sequencing) (Janesomboon *et al.*, 2021). Other commonly used glander detection techniques include immunofluorescence and latex agglutination (Frolov *et al.*, 2020).

The CFT and the ELISA are serological tests that can be used to identify glanders antibodies in horses. Other animals, such as cats and camels, can have glanders detected using the CFT and ELISA tests; however, donkey glanders cannot be detected with CFT (Dehghan Rahimabadi *et al.*, 2023). The OIE recommends the CFT test as a means of checking for glanders in horses that are traded internationally (Elschner *et al.*, 2021). The CFT test's specificity and sensitivity vary based on the antigen and technique (Elschner *et al.*, 2021). False positives and false negatives are issues with CFT and ELISA serological testing for glander diagnosis. They also cannot distinguish between antibodies from *B. mallei* and *B. pseudomallei* (Elschner *et al.*, 2019). Compared to CFT, the Westernblot test is more effective and specific for glander detection using serological means (Elschner *et al.*, 2019). This test can be used in conjunction with other tests and shows great promise in identifying glanders. The western blot test is used to confirm CFT because it is unreliable for testing animal serum with anti-complementary activity or reacting alone with normal antigens; it cannot detect antibodies after 40 days of the disease onset or produce false negatives; and it can cross-react with serum infected with strangles in endemic areas, producing false positives (Elschner *et al.*, 2021).

Differential diagnosis

Clinically, glanders can be mistaken for strangles, sporotrichosis, ulcerative lymphangitis, and epizootic lymphangitis. These diseases are as follows, and due to the stringent control measures mandated by legislation, differential diagnosis must be performed.

Table 2. Diagnostic approaches for glanders.

Method type	Diagnostic technique	Principle/Target	Advantages	Limitations	Additional notes
Serological	Complement Fixation Test (CFT)	Detect antibodies to <i>B. mallei</i>	Recommended by OIE; used for international horse trade	Cannot detect donkey glanders; cross-reactivity with <i>B. pseudomallei</i> ; false positives/negatives possible	Sensitivity/specificity vary depending on antigen and protocol
	Enzyme-linked Immunosorbent Assay (ELISA)	Detect antibodies	Can detect in camels, cats	Similar issues as CFT (specificity & cross-reaction)	Widely used in screening programs
	Western Blot	Confirm presence of specific antibodies	Higher specificity than CFT/ELISA	Not reliable for all serum types; false positives in endemic strangles areas	Used to confirm CFT results
Skin hypersensitivity	Mallein Test	Delayed-type hypersensitivity to <i>B. mallei</i> proteins	May help in isolated endemic regions	Not OIE-recommended; ethical concerns; may lead to seroconversion	Used historically in field testing
Culture-based	Bacterial Isolation	Isolate <i>B. mallei</i> from clinical samples	Gold standard; definitive	Low sensitivity; slow growth; requires enriched media	Colonies have distinct appearance on glycerol-potato and blood agar
Molecular	Polymerase Chain Reaction (PCR)	Detect <i>B. mallei</i> DNA	Fast, sensitive; distinguishes <i>B. mallei</i> from <i>B. pseudomallei</i>	Requires laboratory infrastructure	Lower contamination risk; various PCR-based methods available
Other	Immunofluorescence, Latex Agglutination	Antigen-antibody interaction	Rapid, practical	Less specific than PCR or WB	Often used as supplementary tools

Epizootic lymphangitis

Horses are the main victims of epizootic lymphangitis, a persistent granulomatous and suppurative fungal illness (Rebuma *et al.*, 2024). The fungus *Histoplasma farciminosum* is the cause (Wernery *et al.*, 2025). This condition affects the lymphatic system of the skin, can be minor or asymptomatic, and can appear to resolve yet still be a hidden infection (Seid *et al.*, 2019). Identifying *H. farciminosum* by direct smear and/or culture allows for a quick diagnosis (Abdela *et al.*, 2021).

Sporotrichosis

One type of chronic subcutaneous lymphatic mycosis is sporotrichosis (Mahajan, 2014). This disease differs from glanders in that it occurs sporadically and does not follow the consistent epidemiological trends commonly seen in glanders. The gram-positive fungus *Sporotrichum schenki*, which produces single-walled spores, can be used to positively identify sporotrichosis (Barros *et al.*, 2011).

Ulcerative lymphangitis

The bacterial condition known as ulcerative lymphangitis affects horses and cattle and is brought

on by *Corynebacterium pseudotuberculosis* (El-Karim *et al.*, 2024). The development of nodules in the subcutaneous tissue, particularly in the vicinity of the fetlock joint, is a hallmark of this illness (Abebaw, 2024). The causal organism is isolated in order to confirm the diagnosis.

Strangles

Streptococcus equi is the causative agent of strangles, an acute bacterial disease in horses (Paillot *et al.*, 2010). Abscesses in the surrounding lymph nodes and inflammation of the upper respiratory tract are the hallmarks of this illness (Boyle *et al.*, 2018). Penicillin medication works well for this illness (Pringle *et al.*, 2020).

Melioidosis

Burkholderia pseudomallei is the cause of melioidosis, often known as Whitmore's sickness (Wiersinga *et al.*, 2018). Melioidosis and glanders are related conditions. Their epidemiology differs, but their pathophysiological effects are comparable. The disease is indigenous to Southeast Asia, the Philippines, Indonesia, and other tropical regions, where *B. pseudomallei* flourishes

(San Martin *et al.*, 2018; Anggraini *et al.*, 2024). The condition is particularly common in Thailand, where it was the cause of 40% of community-acquired septicemia deaths and 19% of community-acquired sepsis deaths in one hospital (Jatapai *et al.*, 2018). This disease can infect humans as well as other vulnerable animals (Torres, 2023). Tropical regions have a large distribution of this organism in both soil and water (Swe *et al.*, 2021). Humans can contract the disease via inhaling dust or aerosols or by coming into close contact with infected sources (Hsueh *et al.*, 2018).

Transmission

Animals contract glanders primarily through direct or indirect contact with acutely or chronically infected horses, donkeys, or mules (Khan *et al.*, 2013). The most frequent way that the germs are exposed is by tainted feed or water that contains respiratory secretions (Torres, 2025). The animals most commonly seen to contract *B. mallei* infections from eating meat tainted with the bacteria are carnivores (Libera *et al.*, 2022).

B. mallei is transmitted by contact with contaminated fomites (e.g., horse bridles or grooming tools), inhalation of aerosols, damaged skin, or mucous membranes (Peacock *et al.*, 2008). Animals with the infection will excrete microorganisms in their saliva, urine, tears, and feces (Gaspar *et al.*, 2023). Bacterial shedding can happen intermittently or persistently in horses. The number of animals in the cage, their closeness to diseased animals, and high levels of stress brought on by the surroundings are all risk factors for the spread of glanders in animals (Cárdenas *et al.*, 2019). *B. mallei* can be transferred from sick to healthy animals by the biological vector fly (*Musca domestica*) (Lopez *et al.*, 2003).

Humans can get glanders infections by coming into close touch with diseased animals, fomites, tissue, or bacterial cultures (Van Zandt *et al.*, 2013). Bacteria can enter the body through the mouth, nose, or skin abrasions or sores (Whitlock *et al.*, 2007). The majority of human glander infections occur in lab settings when handling and processing animal materials or *B. mallei* cultures (Virk *et al.*, 2023). These primary transmission routes emphasize the interconnected risk between equids, carnivores, and humans, as visualized in Figure 1.

Military relevance

While the historical weaponization of *B. mallei* is well documented, the contemporary bioterrorism landscape requires a more nuanced analysis. Unlike in the early 20th century, modern bioterrorism threats are shaped by advances in synthetic biology, genetic engineering, and global laboratory accessibility. The possibility of manipulating *B. mallei* strains to enhance antibiotic resistance or alter virulence factors cannot be overlooked (Christopher *et al.*, 1997; Cote *et al.*, 2020). Such modifications could render existing treatment protocols ineffective, complicate diagnosis, and increase the pathogen's persistence in both human

and animal hosts. This underscores the necessity of including *B. mallei* in present-day biodefense surveillance frameworks, even though it has not yet the historical weaponization of *B. mallei* has been well documented (Wheelis, 1998; Regis, 1999; Riedel, 2004).

Preparedness challenges are amplified by the pathogen's clinical ambiguity. As emphasized by Van Zandt *et al.* (2013), glanders presents with non-specific symptoms that mimic pneumonia or tuberculosis, making delayed diagnosis a likely outcome in non-endemic regions. This diagnostic delay is not merely a clinical problem but also a national security vulnerability, since early detection is crucial for containment and effective response. Modern biodefense strategies, therefore, need to invest in point-of-care diagnostic platforms capable of differentiating glanders from other respiratory infections under field conditions.

Another underexplored issue is the gap between international treaties and practical enforcement. The Biological Weapons Convention of 1972 (Smart, 1997) prohibits the development and stockpiling of pathogens such as *B. mallei*, yet history demonstrates that state-level violations occurred decades after ratification (Alibek and Handelman, 1999). This raises questions about verification mechanisms, transparency in research involving select agents, and the dual-use dilemma of scientific advances. For example, work conducted to understand virulence mechanisms or develop medical countermeasures can unintentionally provide knowledge that could be repurposed for hostile use.

The role of veterinary surveillance and animal movement control also deserves critical attention in biodefense planning. As Noor and Ariyanti (2019) noted, equids remain susceptible reservoirs, and clandestine use of infected animals could prolong pathogen circulation after an intentional release. Unlike anthrax, which produces spores with environmental persistence, *B. mallei* relies on living hosts for transmission, making surveillance of equine populations an integral yet often neglected component of biodefense. Thus, international cooperation in animal health monitoring is as important as investment in human clinical preparedness.

Finally, preparedness gaps remain in post-exposure management and public communication. Although glanders is theoretically treatable if identified early (Torres, 2025), the high mortality rate—even under therapy (Barnes *et al.*, 2022)—highlights the need for stockpiling effective antibiotics and developing candidate vaccines. In parallel, public health messaging frameworks must be prepared for scenarios where glanders is deliberately released, as misinformation and panic could exacerbate the impact. Integrating glanders into broader biodefense exercises, alongside pathogens such as anthrax and smallpox, would help policymakers stress-test their response capacity and identify weak points in current systems.

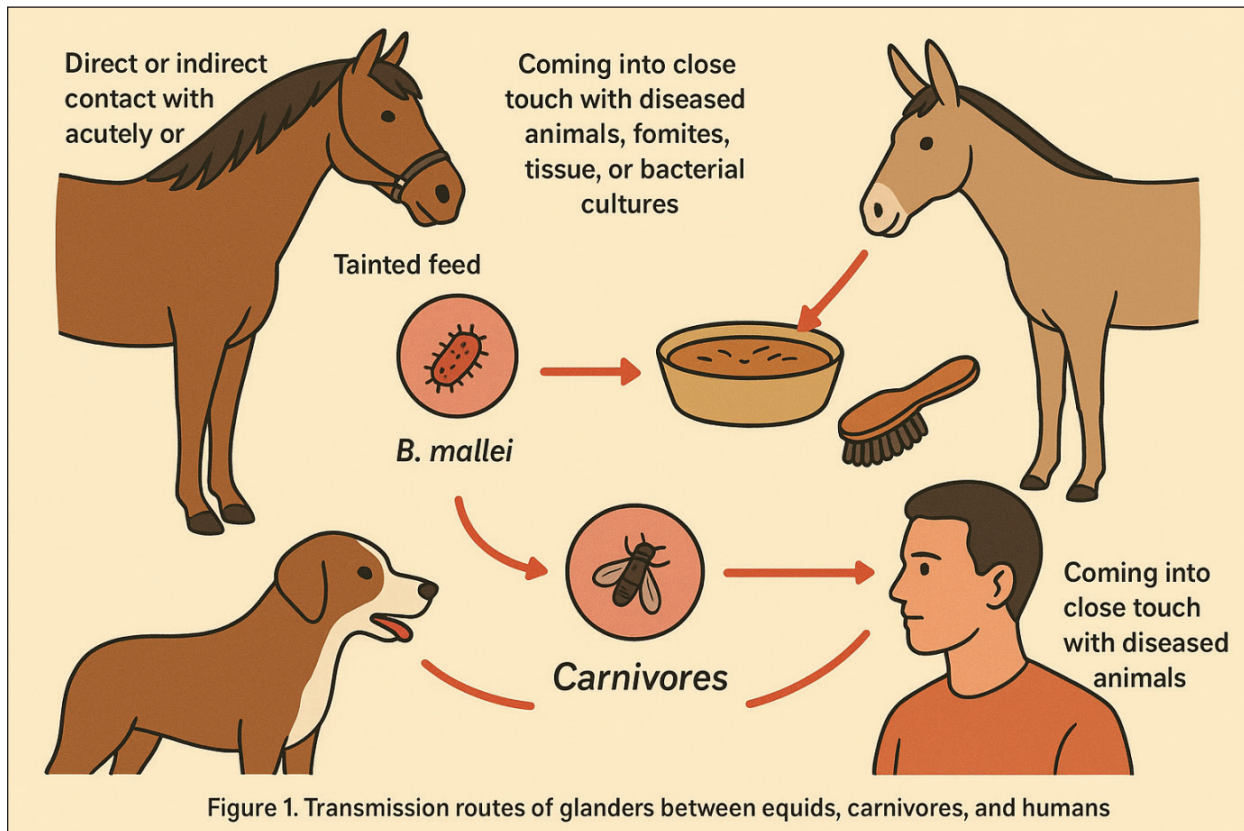


Fig. 1. Transmission routes of glanders between equids, carnivores, and human.

Public health importance

Building on the epidemiological and pathogenic characteristics described earlier, glanders represents a significant public health concern due to its high zoonotic potential and severe clinical outcomes (Noor and Ariyanti, 2019). Several transboundary zoonotic diseases continue to pose significant global threats (Clemmons *et al.*, 2021). environments where humans and animals interact closely—such as farms, military operations, or research laboratories—are at elevated risk of transmission (Van Zandt *et al.*, 2013). The major challenge lies in the difficulty of early diagnosis, since the symptoms can mimic other diseases like pneumonia or tuberculosis, often leading to delayed treatment and higher mortality (Kettle and Wernery, 2016). This diagnostic challenge underscores the need for enhanced clinical awareness and laboratory capacity.

As there is still no vaccine available, public health management relies solely on rapid case detection, targeted antibiotic therapy, and strict isolation protocols (Torres, 2025). Beyond the clinical sphere, glanders also poses broader biosecurity challenges, as *B. mallei* is recognized as a potential bioterrorism agent (Pal and Paulos Gutama, 2022). Consequently, public health preparedness must go beyond medical treatment, incorporating emergency planning, risk

communication, and surveillance strategies to prevent potential outbreaks or deliberate misuse.

To strengthen resilience, robust monitoring systems, continuous training for healthcare and veterinary personnel, and community education are essential. Such integrated measures are critical not only for controlling natural outbreaks but also for mitigating risks associated with intentional release or laboratory exposure (Van Zandt *et al.*, 2013).

Treatment

Infected mules, donkeys, and horses should not be treated with antibiotics. *B. mallei* is resistant to many antibiotics and requires long-term combination antibiotic therapy (Lim *et al.*, 2022). Chronic or latent infections may also arise as a result of ineffective antibiotic treatment. A localized outbreak of glanders affecting 23 horses in Lahore, Pakistan, prompted the implementation of a 12-week treatment program that included oral doxycycline, parenteral enrofloxacin, and trimethoprim/sulfadiazine (Saqib *et al.*, 2012). The fact that there was no relapse during the 360-day follow-up period after antibiotic treatment suggests that long-term antibiotics might be beneficial. This treatment plan is costly, though, and more research with bigger sample numbers and longer-term monitoring is required to ascertain the efficacy of this antibiotic regimen. It is

Table 3. Historical timeline of *B. mallei* in military and biowarfare use.

Year/Period	Event	Details/Notes
1914	German soldier Anton Dilger sent home	Established a secret lab in Maryland, USA to grow <i>B. mallei</i> and <i>Bacillus anthracis</i> for sabotage efforts
1914–1918 (WWI)	German biological sabotage operations	Use of <i>B. mallei</i> to infect horses, mules, and livestock in Mesopotamia, Russia, Romania, France, and the U.S.
1916	Spy incidents	German agent captured in Russia; French cavalry horses deliberately infected; 4,500 mules poisoned in Mesopotamia
1931–1945	Japan’s biowarfare program (Unit 731)	<i>B. mallei</i> used experimentally on horses, civilians, and POWs in Manchuria. Two lab workers died from accidental exposure (1937)
1942	U.S. initiates bioweapons development	Camp Detrick (now Fort Detrick, MD) begins research on biological agents including <i>B. mallei</i>
1944–1953	Laboratory-acquired human infections	7 documented <i>B. mallei</i> infections among Camp Detrick staff (Howe and Miller, 1947)
1972	U.S. signs Biological Weapons Convention	Prohibits development, stockpiling, and production of bioweapons
1973	Offensive programs terminated	U.S. destroys remaining bioweapons and shifts to defensive research only
1982–1984	Soviet use in Afghanistan (alleged)	<i>B. mallei</i> reportedly deployed against opposition forces
2000	8th lab-acquired infection in U.S.	Occurred during defense-related research; confirms continued biohazard risk
2005 (post)	Public disclosure of 7th infection	Case details including location and clinical course made available
Present day	<i>B. mallei</i> as potential bioterror agent	Considered a Category B select agent; high mortality, difficult diagnosis, and treatment challenges

generally not advised to treat diseased horses outside of endemic areas because of the zoonotic risk (Khan *et al.*, 2012).

Antibiotics are the main treatment used for glanders in humans. Since human cases of this bacteria are uncommon, there aren’t many precise, research-based treatments available. Nonetheless, a similar therapeutic strategy is frequently employed, as for melioidosis, another bacterially induced infectious condition (Wiersinga *et al.*, 2018). Common medicines that must be used for a sufficient amount of time to guarantee that the *B. mallei* bacteria are totally removed from the body include ciprofloxacin, gentamicin, streptomycin, and doxycycline (Kenny *et al.*, 1999). A combination of antibiotics and hospitalization may be required in cases of severe or persistent infection. Delaying treatment might raise the risk of major complications, such as organ failure and death, because glanders’ symptoms frequently mimic those of other illnesses, like pneumonia or tuberculosis. For this reason, early diagnosis is crucial (Torres, 2025). Medical professionals who treat sick patients must wear personal protective equipment (PPE) to reduce the risk of infection, and infected patients must be isolated to stop the disease from spreading (Rahman *et al.*, 2020).

Vaccination

The development of a vaccine against *B. mallei*, the causative agent of glanders, remains one of the most pressing challenges in biodefense research. Despite extensive investigations, no licensed vaccine is currently available (Torres, 2025). This reflects both the biological complexity of the pathogen and the limited translational success of candidate vaccines. A critical evaluation of past and recent strategies provides valuable insights into the barriers that continue to comprehensive overviews of glanders in biodefense contexts are available (Welkos *et al.*, 2018).

Killed and inactivated vaccines

Historically, killed or chemically inactivated *B. mallei* preparations were among the first candidates evaluated. While these formulations were relatively simple to produce, they consistently failed to induce long-lasting or protective immunity in animal models (Avril *et al.*, 2024). Their immunogenicity was limited to humoral responses, with insufficient activation of cell-mediated immunity, which is essential to combat an intracellular pathogen such as *B. mallei* (Saikh and Mott, 2017). Thus, despite their early promise in experimental settings, inactivated vaccines have been deemed inadequate for practical use.

Live-attenuated vaccines

Live-attenuated vaccines have attracted considerable interest due to their ability to mimic natural infection and stimulate both humoral and cellular immunity. Studies using attenuated *B. pseudomallei* (a closely related organism) demonstrated partial protection in murine models (Khakhum *et al.*, 2019). However, the risk of reversion to virulence and potential safety concerns in immunocompromised hosts remain significant barriers (Ghattas *et al.*, 2021). For a pathogen considered a high-priority bioterrorism agent, the safety profile of live-attenuated strains represents an unacceptable risk, limiting their potential for deployment (Johnson and Ainslie, 2017).

Subunit and recombinant protein vaccines

A more targeted approach has involved subunit vaccines based on outer membrane proteins, type VI secretion system components, and LPSs (Swietnicki, 2021). These antigens have shown the capacity to generate measurable humoral immune responses, sometimes combined with partial survival benefit in experimental challenges (Waag *et al.*, 2012). Nevertheless, the protective efficacy remains inconsistent, and immunity tends to wane without booster immunization (Johnson and Ainslie, 2017). Furthermore, reliance on humoral responses alone has been insufficient, as protective immunity against *B. mallei* likely requires a strong T-cell-mediated component (Wang *et al.*, 2020).

DNA and vector-based vaccines

More recent research (2020–2025) has explored DNA vaccines and viral-vector platforms encoding immunodominant *B. mallei* antigens (Wang *et al.*, 2020; Chapartegui-González *et al.*, 2021; Badten and Torres, 2024; Sengyee *et al.*, 2025). These strategies aim to provide durable cellular responses and overcome some limitations of protein-based vaccines. Preclinical data indicate induction of antigen-specific T-cell activity, yet survival outcomes following challenge have varied across different models. Moreover, challenges related to stability, delivery systems, and scale-up for biodefense applications persist (Lafontaine *et al.*, 2018).

Comparative evaluation

When compared systematically, it becomes clear that each vaccine strategy offers distinct strengths and weaknesses: inactivated vaccines provide safety but poor efficacy; live-attenuated strains offer stronger immunity but unacceptable risks; subunit and recombinant approaches are safer but lack durable protection; while DNA/vector-based methods are innovative yet remain in early developmental stages. Importantly, the failures and partial successes across platforms highlight that *B. mallei*'s intracellular lifestyle, immune evasion strategies, and ability to establish chronic infection present formidable barriers to vaccine design.

Critical outlook

From a biodefense and bioterrorism preparedness perspective, the lack of a licensed vaccine against

glanders represents a significant vulnerability. The consensus emerging from recent research suggests that no single antigen or approach will be sufficient. Instead, a multiantigen, multiplatform strategy, potentially combining subunit vaccines with nucleic acid or vector-based systems, may offer the best chance of achieving protective and durable immunity. Furthermore, a stronger emphasis on comparative studies across standardized animal models is urgently needed to identify correlates of protection. Without such critical advances, vaccine development against *B. mallei* will continue to lag behind other priority pathogens, leaving populations at risk in both natural and intentional exposure scenarios (Bondi and Goldberg, 2008).

Control

Since there is currently no vaccine to prevent glanders in humans or animals, all positive instances of the bacteria must be swiftly discovered, killed, and disposed of appropriately to guarantee efficient prevention and control (Torres, 2025). Extreme caution, including the use of the proper PPE, should be used when handling sick animals and contaminated fomites (Pal and Paulos Gutama, 2022). If glanders is suspected to be the cause of death, the animal carcass should be buried or incinerated without post-mortem examination to avoid the risk of environmental contamination and disease transmission (Verma *et al.*, 2014). Strict disinfection procedures must be followed for the grounds, feed and water troughs, and other locations. *B. mallei* should be disinfected because it is extremely sensitive to common disinfectants such benzalkonium chloride, iodine, potassium permanganate, 1% sodium hypochlorite, 70% ethanol, mercuric chloride in alcohol, and 2% glutaraldehyde (EFSA Panel on Animal Health and Welfare (AHAW) *et al.*, 2022). It is less susceptible to phenolic disinfectants. Additionally, these bacteria can be eliminated by subjecting them to UV light or heating them to 55°C for ten minutes (Rito *et al.*, 2024). Isolation, hygiene, and sanitation protocols should be followed. Contaminated materials should be cleaned using a solution of one part household bleach (0.5% sodium hypochlorite solution) to nine parts water (Mohapatra and Mishra, 2022). Targeted awareness campaigns on glanders should be prioritized in endemic regions, especially among equine veterinarians, animal handlers, and regulatory authorities. These efforts are particularly important during trade seasons or outbreaks, and should focus on early detection, biosecurity measures, and mandatory reporting procedures.

Conclusion

In conclusion, glanders disease is still a major zoonotic illness that has a major impact on public safety and horse health, especially in regions where it is still endemic. *B. mallei*'s use as a biological weapon emphasizes the necessity of ongoing monitoring, investigation, and

biosecurity protocols to stop its spread and safeguard populations of humans and animals.

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Conflict of interest

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MS and ARK served as the primary authors of this review, drafting the major sections including epidemiology, pathogenesis, and clinical aspects. BWKW prepared treatment and control strategies, while IM contributed to the introduction and military relevance and helped coordinate the draft. BPP also worked on revising, and editing the draft. SHA, IBM, and RZA revised the pathology, public health, and vaccination sections, respectively. ATK revised the biosecurity and biodefense section. MKJK, DAAK, AOA, IF, and SW critically reviewed key sections, including epidemiology, zoonoses, pathogenesis, and biosecurity. AHF, KAF, IMe, and M'AK managed and edited references. All authors reviewed and approved the final manuscript.

Data availability

No data were generated in this study. All cited information is available in the original open access publications referenced.

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