GLANDERS

AETIOLOGY

Classification of the causative agent

Glanders is a zoonotic bacterial infection caused by *Burkholderia mallei*, a Gram negative, non-motile, non-encapsulated and non-spore-forming bacillus of the family *Burkholderiaceae*. This bacterium was previously known as *Pseudomonas mallei* and is closely related to the agent of melioidosis, *Burkholderia pseudomallei*.

Resistance to physical and chemical action

Temperature:	Destroyed through heating to 55°C for 10 minutes
Chemicals/Disinfectants:	Susceptible to many common disinfectants such as iodine, benzalkonium chloride (1/2000), sodium hypochlorite (500 ppm available chlorine), 70% ethanol, 2% glutaraldehyde
Survival:	Sensitive to sunlight with inactivation in 24 hours of direct exposure and heat; possible survival for over 6 weeks to various months in contaminated areas; can remain viable in tap water for at least 1 month; agent is susceptible to desiccation as humid/wet conditions favour survival. Polysaccharide capsule of bacterium is considered an important virulence factor and enhances survival

EPIDEMIOLOGY

Hosts

- *Equidae,* humans, occasionally *Felidae*, and other species are susceptible; untreated infections are usually fatal
    - Donkeys are most susceptible, mules somewhat less and horses demonstrate some resistance, i.e. chronic forms of the disease
    - *Felidae* seem to be particularly susceptible, with cases documented in domestic cats, tigers, lions, leopards and other felids
- Susceptibility to glanders has been reported for camels, bears, wolves, jackals and hyenas and dogs
- Carnivores may become infected by eating infected so-called glanderous meat
- Small ruminants may also be infected and clinical cases were described in dromedary camels if kept in close contact to glanderous horses
- Many other domesticated mammals can be infected experimentally (pigs and cattle were reported to be resistant). Hamsters and guinea-pigs are susceptible to glanders after experimental inoculation, mice do not become ill unless the dose of organisms is high, and laboratory rats are resistant to infection. Wild rodents (e.g. field mice and voles) can also be infected experimentally. Birds are highly resistant
- Glanders is a zoonotic disease and one recent case has been reported in a scientist

Sources of infection and transmission

- Most common source of infection appears to be ingestion of food or water contaminated via discharges from the respiratory tract or ulcerated skin lesions from carrier animals
- Animal density and proximity favour spread as well as stress
- Subclinical carriers often prove to be more important in transmission of disease than clinical cases: Chronically or subclinically infected equids can shed *B. mallei* intermittently or constantly into food and water troughs
- Contamination of skin abrasions and mucous membranes, or inhalation of contaminated aerosols
- There are reports of venereal transmission from stallions to mares, and vertical transmission from the mare
- *B. mallei* is readily spread with fomites
- Use of contaminated harnesses and grooming tools

- Flies might act as mechanical vectors
- In non-endemic regions, cases may be seen in people who work with the causative organism, *Burkholderia mallei* in laboratories

Occurrence

Glanders has been recognised as an important disease of equids since its early documentation by Hippocrates. Through veterinary intervention and national control programmes the worldwide disease prevalence has been significantly reduced.

The disease has been eradicated in North America, Australia and Europe through testing and then eliminating any positive animal, coupled with import control measures.

However, glanders remains sporadically reported in a number of Asian, African, Middle Eastern, and South American countries. In April 2010, Bahrain notified the first occurrence of the disease; in Brazil, the disease reappeared in 2009. Germany notified the occurrence of the disease in a limited area in 2014/2015

For more recent, detailed information on the occurrence of this disease worldwide, see the OIE World Animal Health Information Database (WAHID) interface [http://www.oie.int/wahis/public.php?page=home].

DIAGNOSIS

The incubation period varies according to the route and intensity of exposure and intrinsic factors of the host and so can range from a few days to many months; many cases become apparent in 2–6 weeks.

For the purposes of the OIE *Terrestrial Animal Health Code*, the incubation period for glanders is 6 months.

Clinical diagnosis

The disease is most commonly named according to the location of the primary lesions: nasal, pulmonary and cutaneous (farcy) glanders.

Clinical cases are often a combination of the three forms, and may be acute (or subacute), chronic or latent. Nasal and pulmonary forms tend to be more acute in nature, while the cutaneous form of the disease is a chronic process. Acute cases of glanders die from a few days to within few weeks (1–4). A latent form of glanders has also been described but may provoke few signs, e.g. nasal discharge and dyspnoea.

Donkeys and mules often develop acute glanders after exposure, although mules appear to be somewhat more resistant and the course of the illness may be slower. Horses usually develop chronic glanders.

Nasal form

- Begins clinically with high fever, loss of appetite and laboured breathing with coughing
- A highly infectious, viscous, yellowish-green, mucopurulent discharge is present and this may crust around the nares
- A purulent ocular discharge has also been described
- Nodules in the nasal mucosa may produce ulcers
- The regional (submaxillary) lymph nodes become enlarged bilaterally or unilaterally. They are usually indurated in acute illness, and may occasionally suppurate and drain
- Nasal infections can spread and involve the lower respiratory tract

Pulmonary form

- Pulmonary involvement occurs in most clinical cases. signs are fever, dyspnoea, paroxysmal coughing or a persistent dry cough accompanied by laboured breathing

- Affected animals develop nodules and abscesses in the lungs, or bronchopneumonia in some cases
- Some infections are inapparent; others are characterized by mild to severe respiratory signs, with fever or febrile episodes and progressive debilitation. Diarrhoea and polyuria may also occur; all leading to a progressive loss of condition

Cutaneous form ("farcy")

- Develops insidiously over an extended period; usually associated with periods of exacerbation leading to progressive debilitation
- Initial signs may include fever, dyspnoea, coughing and enlargement of the lymph nodes
- Multiple nodules develop in the skin, often along the course of lymphatic vessels. These often rupture and ulcerate, discharging an oily, thick yellow exudate
- The ulcers heal very slowly, often continuing to discharge fluid, although dry ulcers may also be seen
- Some animals also have swelling of the joints, painful edema of the legs or glanderous orchitis. While skin lesions may appear anywhere, they are reported to be most common on the inner thighs, limbs and abdomen

Animals with cutaneous glanders can remain in good condition for a time, but they eventually become debilitated and die

Lesions

Nasal form

- Ulceration in nasal glanders may spread within upper respiratory passages; perforation of the nasal septum has been observed
- Ulcers of the nasal area, trachea, pharynx and larynx may resolve in the form of star-shaped cicatrices ("stellate scars")
- Regional lymph nodes (e.g. submaxillary) are enlarged and indurated and may rupture and suppurate; these often will adhere within deeper tissues

Pulmonary form

- Lung lesions in pulmonary glanders commence as small light-coloured nodules surrounded by a haemorrhagic zone or as a consolidation of pulmonary tissue and a diffuse pneumonia
- Pulmonary nodules progress to caseous or calcified state; these eventually discharge their contents thus spreading disease to the upper respiratory tract
- Pyogranulomatous nodules are found in the liver, spleen and kidneys

Cutaneous form

- Nodules appear in subcutaneous tissue along the course of lymphatics of the legs, costal areas and ventral abdomen and upon rupturing excrete an infectious purulent, yellow exudate
- Ulcers result from rupturing of these nodules and these may heal or extend to surrounding tissue
- Infected lymphatics may result in swollen, thickened, cord-like lesions
    - coalescence of lymphatic lesions resemble a string of beads and are sometimes referred to as "farcy pipes''
- Pyogranulomatous nodulars are found in the liver and spleen
- Orchitis has been associated with glanders
- Latent glanders may only demonstrate lesions of the lung

Differential diagnosis

As with all transboundary diseases of animals, clinical signs alone do not allow a definitive diagnosis especially in early stages or the latent from of the disease.

- Strangles (*Streptococcus equi*)
- Ulcerative lymphangitis (*Corynebacterium pseudotuberculosis*)
- Botryomycosis

- Sporotrichosis (*Sprortrix schenkii*)
- Epizootic lymphangitis (*Histoplasma farciminosum*)
- Tuberculosis (*Mycobacterium tuberculosis*)
- Trauma and allergy

Laboratory diagnosis

Laboratory manipulations should be performed with appropriate biosafety and containment procedures as determined by biological risk analysis (see Chapter 1.1.9 *Tests for sterility and freedom from contamination of biological materials intended for veterinary use*)

Samples

Laboratory samples must be securely packaged, kept cool and shipped as outlined in Chapter 1.1.3 *Transport of biological materials* of the OIE *Terrestrial Manual*

Identification of the agent

- Whole lesions or sections of lesions, respiratory exudates, smears from fresh lesions
    - more difficult to isolate the agent from older lesions or tissue sections
- Samples should be kept cool and shipped on wet ice as soon as possible

Serological tests

- Serum sample should be collected aseptically

Procedures

Identification of the agent

- Morphology of *Burkholderia mallei*
    - Identification of methylene blue or Gram-stained organisms from fresh lesions
    - Gram negative non-sporulating, non-encapsulated rods
    - Presence of a capsule-like cover has been demonstrated by electron microscopy *Burkholderia mallei* is non-motile
- Cultural characteristics
    - The bacteria are fairly numerous in smears from fresh lesions, but scarce in older lesions. It is preferable to attempt isolation from unopened, uncontaminated lesions
    - Bacteria grow aerobically and prefer media that contain glycerol
    - Confirmation of the identity of suspected isolates is by polymerase chain reaction (PCR)
- PCR and real time PCR
    - Several PCR and real-time PCR assays for the identification of *B. mallei* have been developed, but only one conventional PCR and one real-time PCR assay were evaluated using samples from a recent outbreak of glanders in horses. Thus, inter-laboratory studies are needed to confirm the robustness of these assays

Serological tests

- Complement fixation test in horses, donkeys and mules
    - accurate and reliable serological method for diagnostic use
    - will usually deliver positive results within 1 week post-infection and will also recognise sera from exacerbated chronic cases
- Enzyme-linked immunosorbent assays - plate and membrane ELISA
    - avidin–biotin dot ELISA - not validated
- Immunoblot assays
    - best evaluated serological test available - sensitive and specific
    - not able to differentiate glanders from melioidosis infection; not yet been evaluated for use in donkeys

- Other serological tests
    - Rose Bengal plate agglutination test (RBT)

Test for cellular immunity

- The mallein test
    - not generally recommended because of animal welfare concerns
    - useful in remote endemic areas where sample transport or proper cooling is not possible

For more detailed information regarding laboratory diagnostic methodologies, please refer to the Chapter 3.5.11 of the OIE *Manual of Diagnostic Tests and Vaccines for Terrestrial Animals* under the headings "Diagnostic Techniques" and "Requirements for Vaccines".

PREVENTION AND CONTROL

Sanitary prophylaxis

- Prevention and control of glanders requires a programme for early detection, testing of suspect clinical cases, screening of apparently healthy equids, and humane elimination of reactors.
- As *B. mallei* can be transmitted to humans, all infected or contaminated (or potentially infected or contaminated) material must be handled in a laboratory with appropriate biosafety and biosecurity controls following a biorisk analysis.
- Prevention and control of glanders epizootics depends on a programme of early detection and the humane elimination of test positive animals in conjunction with strict animal movement controls, effective quarantine of the facilities and thorough cleaning and disinfection of the contaminated area where the outbreak occurred
- All disposable materials (feed and bedding) should be destroyed and conveyances and equipment should be carefully disinfected

Medical prophylaxis

- Antibiotic treatments have been used in endemic zones
    - this may lead to subclinical carrier animals that can infect humans and other animals
- Case fatality rates can reach 95% if no treatment is administered

For more detailed information regarding safe international trade in terrestrial animals and their products, please refer to the latest edition of the OIE *Terrestrial Animal Health Code*.

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The OIE will periodically update the OIE Technical Disease Cards. Please send relevant new references and proposed modifications to the OIE Scientific and Technical Department (scientific.dept@oie.int). Last updated January 2020