

GLANDERS

Aetiology Epidemiology Diagnosis Prevention and Control References

AETIOLOGY

Classification of the causative agent

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

Resistance to physical and chemical action

Temperature:	Destroyed through heating to 55°C (131°F) for 10 minutes, or with ultraviolet irradiation.
Chemicals/Disinfectants:	Susceptible to many common disinfectants such as iodine, mercuric chloride in alcohol, potassium permanganate, benzalkonium chloride (1/2000), sodium hypochlorite (500 ppm available chlorine), 70% ethanol, 2% glutaraldehyde; less susceptible to phenolic disinfectants.
Survival:	Sensitive to sunlight with inactivation in 24 hours of direct exposure and heat as above; 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; infections are usually fatal
 - Donkeys are most susceptible, mules somewhat less and horses demonstrate some resistance manifested in chronic forms of the disease, especially in endemic areas
- Susceptibility to glanders has been demonstrated in camels, bears, wolves and dogs
- Carnivores may become infected by eating infected meat; cattle and pigs are resistant
- Small ruminants may also be infected if kept in close contact to glanderous horses

Sources of infection and transmission

- Most common source of infection appears to be ingestion of contaminated food or water likely via discharges from the respiratory tract or ulcerated skin lesions from carrier animals
- Animal density and proximity favour spread as well as stress-related host factors
- Subclinical carries often prove to be more important in transmission of disease than clinical cases

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. Glanders continues to be reported from Brazil, China, India, Iran, Iraq, Mongolia, Pakistan, Turkey, and the United Arab Emirates and is thought to be endemic in various areas of the Middle East, Asia, Africa and South America. Geographic distribution determined through serological surveys for *B. mallei* is complicated due to cross-reactions with *B. pseudomallei*.

It is important to note that this disease is a zoonotic agent and recent cases have been reported in scientists and researchers.

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>] or refer to the latest issues of the World Animal Health and the OIE *Bulletin*.

DIAGNOSIS

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

Clinical diagnosis

Forms of glanders in animals are most commonly described according to the location of the primary lesions thus three forms of the disease are commonly described; nasal, pulmonary and cutaneous. There are also references to the course of disease as acute (usually associated with donkeys) or chronic (associated with horses in endemic areas). 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 manifest few signs other than a nasal discharge and dyspnoea.

Nasal form (nasal glanders)

- Begins clinically with a 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

Pulmonary form (pulmonary glanders)

- Usually requires several months to develop; first manifests itself through fever, dyspnoea, paroxysmal coughing or a persistent dry cough accompanied by laboured breathing
- Diarrhoea and polyuria may also occur; all leading to a progressive loss of condition

Cutaneous form (cutaneous glanders)

- Develops insidiously over an extended period; begins with coughing and dyspnoea usually associated with periods of exacerbation leading to progressive debilitation
- Initial signs may include fever, dyspnoea, coughing and enlargement of the lymph nodes

Lesions

Nasal form (nasal glanders)

- 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 (pulmonary glanders)

- 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 sometimes found in the liver, spleen and kidneys

Cutaneous form (cutaneous glanders)

- Nodules begin to 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 nodules are sometimes found in the liver and spleen
- Orchitis has been associated with glanders
- Latent glanders may only demonstrate minor 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 form of the disease.

- Strangles (*Streptococcus equi*)
- Ulcerative lymphangitis (*Corynebacterium pseudotuberculosis*)
- Botryomycosis
- Sporotrichosis (*Sporotrix schenckii*)
- Pseudotuberculosis (*Yersinia pseudotuberculosis*)
- Epizootic lymphangitis (*Histoplasma farciminosum*)
- Horsepox
- Tuberculosis (*Mycobacterium tuberculosis*)
- Trauma and allergy

Laboratory diagnosis

All manipulations with potentially infected/contaminated material must be performed at an appropriate biosafety and containment level determined by biorisk analysis (see Chapter 1.1.3 *Biosafety and biosecurity in the veterinary microbiology laboratory and animal facilities*).

Samples

Laboratory samples must be securely packaged, kept cool (not frozen) and shipped as outlined in Chapter 1.1.1 of the OIE *Terrestrial Manual*, Collection and shipment of diagnostic specimens.

Identification of the agent

- Whole lesions or sections of lesions, respiratory exudates smears from fresh lesions
 - greater difficulty in isolating agent from older lesions or tissue sections
- Samples should be kept cool (not frozen) and shipped on wet ice as soon as possible
- Sections of lesions in 10% buffered formalin and air dried smears of exudate on glass slides should be submitted for microscopic examination

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
- Cultural characteristics
 - isolation from unopened uncontaminated lesions
 - bacteria grow aerobically and prefer media that contain glycerol
 - *Burkholderia mallei* is non-motile

- Identification of *Burkholderia Mallei* by polymerase chain reaction and real-time PCR - guidelines and precautions outlined in Chapter 1.1.5
- Validation and quality control of polymerase chain reaction methods used for the diagnosis of infectious diseases, should be observed
 - Laboratory animal inoculation
 - not recommended because of welfare concerns
 - male guinea-pig inoculated intraperitoneally and observation for severe localised peritonitis and orchitis (the Strauss reaction); sensitivity of only 20%,
 - hamsters are also susceptible
 - The Strauss reaction is not specific for glanders and can be provoked by other organisms, therefore *B. mallei* must be cultured from the infected testes
- Other methods: only appropriate for use in specialised laboratories
 - PCR-restriction fragment length polymorphism
 - pulsed field gel electrophoresis
 - ribotyping
 - VNTR and MLST

Serological tests

- Complement fixation test in horses, donkeys and mules (a prescribed test for international trade)
 - accurate and reliable serological method for diagnostic use
 - will deliver positive results within 1 week post-infection and will also recognise sera from exacerbated chronic cases
 - specificity of CF testing has been questioned
- Enzyme-linked immunosorbent assays - plate and membrane ELISA
 - neither procedure has been shown to differentiate between *B. mallei* and *B. pseudomallei*.
 - validation pending: C-ELISA and I-ELISA have the potential to be used as alternative tests after completion of their validation
 - 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) - validated in Russia

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 appropriate disease chapter of the latest edition 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 epizootics depends on a program of early detection and the humane elimination of test positive animals in conjunction with strict animal movement controls, effective premise quarantines and thorough cleaning and disinfection outbreak areas
- Affected animal carcasses should be burned and buried
- All disposable materials on positive premises (feed and bedding) should be burned or buried and conveyances and equipment should be carefully disinfected

Medical prophylaxis

- Antibiotic treatments have been used in endemic zones.

- should be noted that this may lead to subclinical carrier animals which can infect humans and other animals
- Experimentally effective treatments include: doxycycline, ceftrazidime, gentamicin, streptomycin, and combinations of sulfazine or sulfamonomethoxine with trimethoprim
- 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*.

REFERENCES AND OTHER INFORMATION

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<p>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 April 2013.</p>
