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Glanders

Farcy
Equinia
Malleus
Droes




Common names for glanders include, equinia, malleus and droes. There are two forms of the disease. It is called “glanders” when the principal lesions are seen in the nostrils, submaxillary glands and lungs and it is called “farcy” when lesions are on the surface of limbs or body.

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Overview

- Organism
- History
- Epidemiology
- Transmission
- Disease in Humans
- Disease in Animals
- Prevention and Control



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In today’s presentation we will cover information regarding the organism that causes glanders and its epidemiology. We will also talk about the history of the disease, how it is transmitted, species that it affects, clinical and necropsy signs observed. Finally, we will address prevention and control measures for glanders.

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The Organism



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The Organism

- *Burkholderia mallei*
 - Gram negative bacillus
 - Exists primarily in infected host
 - Withstands drying for 2-3 weeks
 - Killed by sunlight and high temp
- Related to *Burkholderia pseudomallei*
 - Cause of melioidosis



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Glanders is caused by the bacteria *Burkholderia mallei*. This bacteria has gone through several name changes including, *Pseudomonas mallei*, *Malleomyces mallei* and *Actinomyces mallei*. It is a gram negative bacillus and predominately exists in infected hosts but may remain viable for several months in warm moist environments. It tends to form slender rods in cultures and can appear bipolar or safety pin shaped after staining because of terminal granules. It can withstand drying for 2-3 weeks, but is killed by sunlight and high temperatures. The organism is closely related to *Burkholderia pseudomallei*, the cause of melioidosis and is serologically indistinguishable in some cases. The genetic homology between the two is great and because of this many consider them to be biotypes or isotypes. Photo: www.mbl.edu/animals/Limulus/blood/bacilli.jpg.

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History



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History

- 3rd Century BC
 - Described by Aristotle
- 1664: Contagious nature recognized
- 1830: Zoonotic nature suspected
- 1891: Mallein test developed
- 1900: Control programs implemented

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The first recorded description of glanders is from the third century from Aristotle. In 1664 glanders was recognized as a contagious organism and in 1830 it's zoonotic potential was suspected. In the late 1800's the Mallein test was developed for diagnosis of glanders. At the turn of the century the U.S., Canada and Great Britain all implemented glanders-control programs.

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History

- World War I
 - Suspected use as biological agent to infect Russian horses and mules
 - Affected troops and supply convoys
 - Large number of human cases in Russia during and after WWI




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During World War I, glanders was believed to have been spread deliberately to infect large numbers of Russian horses and mules on the Eastern Front. This effected the troops and supply convoys as well as artillery movement because of their dependence on horses and mules. Human cases of glanders also increased in Russia during and after WWI. Photo courtesy of http://www.pbs.org/wgbh/nova/bioterror/agen_glanders.html and www.firstworldwar.com/diaries/graphics/horsesdrinking.jpg

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History

- World War II
 - Japanese infected horses, civilians and POW's
 - U.S. and Russia investigated use as biological weapon





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It is widely held that the Japanese deliberately infected horses, civilians, and prisoners of war with glanders during World War II. The United States studied glanders as a possible biological weapon in 1943-44 but did not weaponize it. The former Soviet Union is also believed to have been interested in *B. Mallei* as a potential biological weapon agent after World War II. www.civilwarhome.com/images/cavalry.jpg www.continet.com/ppsh/cavalry.jpg; www.firstworldwar.com/diaries/graphics/horsesdrinking.jpg .

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History

- 1934
 - Eliminated from animals the U.S.
- 1945
 - Six lab acquired cases at Camp Detrick
- 2000
 - Human case in laboratory worker at USAMRIID




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Glanders was eliminated from U.S. domesticated animals in the 1930's. Six unrelated cases of Glanders occurred in 1945 among laboratory workers on a biologic-weapons program at Camp Detrick, Maryland. One recent human case of glanders in a laboratory worker occurred in 2000. A microbiologist at USAMRIID (U.S. Army Medical Research Institute of Infectious Disease) contracted glanders in March 2000. He became febrile and presented with a mass in his left axilla. Despite the fact he received aggressive antibiotic therapy, he developed multiple splenic and hepatic masses and eventually respiratory distress. With continued antibiotic treatment he eventually recovered. A diagnosis of glanders was not confirmed until 2 months later though a tentative diagnosis was suspected due to his work history. This was the first human case reported in the US since 1945. Despite the efficiency of spread in a laboratory setting, glanders has only been a sporadic disease in humans. No epidemics of human disease have been reported.

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Transmission

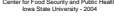


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Transmission: Humans

- Direct contact with infected animals
 - Abraded skin
 - Mucous membranes
- Inhalation
- Person-to-person (rare)
- Ingestion has never been recorded in humans





Glanders is transmitted to humans by direct contact with infected animals. The bacteria enter the body through abraded or lacerated skin and through mucosal surfaces of the eyes, nose and mouth. The bacteria can also be acquired through inhalation of infectious material. Cases of human-to-human transmission have also been reported. No known cases of human intestinal glanders are recorded.


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Transmission: Animals

- Ingestion: Major route
- Inhalation: Less likely
- Direct contact: Minor route
 - Enhanced by shared food and water facilities




Glanders is introduced into horse populations by diseased or latently infected animals. Ingestion of the organism is the major route of infection. Experimental evidence suggests that inhalation of the organism is less likely to result in typical cases of the disease. Acquiring the disease through skin or mucous membranes is possible but regarded as of minor importance in the natural spread of the disease. Close contact between animals alone does not usually result in transmission, but is transmission is facilitated if animals share feeding or watering facilities.
[www.kancorind.com/images_copy\(1\)/Drinking_Horses.jpg](http://www.kancorind.com/images_copy(1)/Drinking_Horses.jpg)

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Epidemiology




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Epidemiology

- Endemic
 - Parts of Africa, the Middle East, and Asia
- Sporadic cases
 - South and Central America
- Possible occurrence
 - Balkan states and former Soviet republics
- Once widespread, has been eradicated in many countries



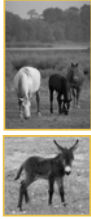
Glanders is endemic in parts of Asia, Africa, the Middle East, and Asia and possibly the Balkan states, former Soviet republics, Mexico, and South America. Sporadic cases occur in South and Central America. Cross reactions with serological tests for melioidosis (*Burkholderia pseudomallei*) most likely confounds the true estimates of worldwide distribution. Although glanders was once widespread throughout the world, it has been eradicated from many countries by test and slaughter programs.

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Host Range

- Affects solipeds
 - Donkeys and mules
 - Acute form
 - Horses
 - Chronic form
- Carnivores, humans and goats susceptible
- Swine and cattle resistant



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Glanders is primarily a disease of solipeds – particularly horses, donkeys and mules. Donkeys and mules have been regarded as most likely to experience the acute form of the disease, horses a more chronic form of the disease. Carnivores are susceptible if they consume infected meat, felids appear to be more susceptible than canids. Several laboratory animals are susceptible to infection including hamsters and guinea pigs. Humans also are susceptible to infection. Swine and cattle are resistant but goats can be infected.
www.foxtrottersusa.com/donkey41501.jpg

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Who Is At Risk?

- Veterinarians
- Groomers
- Horsemen
- Butchers
- Lab workers



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Humans that have occupational exposure are at the highest risk for infection. This includes: veterinarians, groomers, horsemen, butchers, workers in laboratory settings, and people who work closely with horses. Photos:
www.fritzantiques3.homestead.com/383horsevet.html
www.hhs.gov/of/reports/account/acct99/images/image70.gif
www.greecefoods.com/agora/butchers.JPG

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Disease in Humans



Four forms of glanders are seen in humans: the local cutaneous form, pulmonary form, septicemic form and the chronic form. Generalized symptoms of glanders include fever, muscle aches, chest pain, muscle tightness and headache. Occasionally tearing of the eyes, photophobia and diarrhea are seen. Without treatment there is a 95% fatality rate with all forms of glanders.

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Disease in Humans

- Four forms of infection
 - Localized cutaneous
 - Pulmonary
 - Septicemia
 - Chronic form
- Generalized symptoms
 - Fever, malaise, muscle aches, chest pain
- Case-fatality rate: 95% (untreated)

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With the cutaneous form of glanders, a localized infection with erythema and ulceration will develop within 1 to 5 days at the site where the bacteria entered the body. Swollen lymph nodes and inflammatory nodules may also occur. Infections involving the mucous membranes in the eyes, nose, and respiratory tract will cause increased mucus production from the affected sites and ulceration at the site of contact. Nodules are a hallmark lesion of infection. They generally appear along the course of lymph vessel, form ulcers and exude a highly infectious exudate.

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Clinical Signs: Cutaneous

- Incubation period: 1-5 days
 - Erythema and ulceration of skin
 - Lymphadenopathy
 - Nodules
 - Along lymph vessels
 - Highly infectious exudate
- Case fatality rate: 20% treated

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Clinical Signs: Pulmonary

- Incubation period: 10-14 days
 - Inhalation of aerosolized bacteria
 - Hematogenous spread to lungs
 - Pneumonia, pulmonary abscesses, pleural effusion

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The pulmonary form occurs from inhalation of aerosolized bacteria or through hematogenous spread. The period of incubation is from 10 to 14 days. Pneumonia, pulmonary abscesses and pleural effusions can occur. Chest x-rays will show localized infection in the lobes of the lungs.

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Clinical Signs: Septicemia

- Incubation period: 7-10 days
 - Any site of infection can lead to sepsis
 - Fever, chills, myalgia, chest pain, rash
 - Tachycardia, jaundice, photophobia, lacrimation
- Case-fatality rate: 60% treated
- Rapidly fatal

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The incubation period of the septic form is 7 to 10 days. This form occurs when the bacteria enter the blood stream in large enough numbers. The septicemic form can occur independently, or as a result of the pulmonary or cutaneous forms. It can also cause the pulmonary and/or cutaneous forms. Symptoms include a high fever, chills, myalgia, chest pain, rash. Tachycardia, jaundice, photophobia, lacrimation and diarrhea can also occur. There is a 60% case fatality rate even with antibiotic treatment and death can occur within just a few days.

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Clinical Signs: Chronic

- "Farcy"
 - Multiple abscesses
 - Muscles, joints, spleen, liver
- Case-fatality rate: 60% (treated)
- Relapses common

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The chronic form of glanders is known as "farcy". This form produces multiple abscesses with the muscles of the arms and legs, or in the spleen, liver and joints. There is a 60% case fatality rate even with treatment and relapses are common.

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Differential Diagnosis

- Typhoid fever
- Tuberculosis
- Syphilis
- Erysipelas
- Lymphangitis
- Pyemia
- Yaws
- Melioidosis

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Human glanders may be confused with a variety of other diseases, including typhoid fever, tuberculosis, syphilis, erysipelas, lymphangitis, pyemia, yaws, and melioidosis.

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Diagnosis: Humans

- Culture and gram stain
 - Sputum, urine, skin lesions, blood
 - Gram negative bacilli
 - Safety pin appearance
- Agglutination tests
 - May be positive after 7-10 days
 - High background titer in normal sera makes interpretation difficult

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Glanders is diagnosed in the laboratory by isolating the bacteria. Culture and gram stain of blood, sputum, urine, or skin lesions can be performed. Blood cultures, however, are generally not useful as they tend to remain negative until the patient is near death. Gram stain may reveal small gram-negative bacilli, which stain irregularly with methylene blue and may have a safety pin appearance. Meat nutrient agar with the addition of a 1-5% glucose may accelerate growth of bacteria. Agglutination tests may be positive after 7-10 days but a high background titer found in normal sera makes interpretation difficult.

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Diagnosis: Humans

- Complement fixation
 - More specific
 - Positive if titer is equal to or greater than 1:20
- Chest radiograph

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Compliment fixation tests are more specific and are considered positive for glanders if the titer is equal to or greater than 1:20. A chest radiograph may demonstrate bilateral bronchopneumonia, miliary nodules, segmental or lobar infiltrates and cavitating lesions.

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Treatment

- Limited information on treatment
- Long term antibiotic treatment necessary (1-12 months)
- No proven pre- or post-exposure prophylaxis
- No vaccine


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Limited information exists regarding antibiotic treatment of glanders since the disease had largely disappeared by the time antibiotics became available. Long term treatment may be necessary, up to 12 months for extrapulmonary suppurative disease. Currently no proven pre-exposure or post-exposure prophylaxis is available. No vaccine is available for human glanders.

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Animals and Glanders




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Disease in Animals

- Forms of disease not clearly distinct
 - May occur simultaneously
 - Chronic form in horses
 - Acute form in donkeys and mules
- Acute form
 - Fever, cough, dyspnea, thick nasal discharge, ulcers
 - Lymph node and vessel involvement
 - Death



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The forms of disease in animals are not as clearly distinctas in humans and may occur simultaneously. Chronic infections with slow progression are more common than the acute form of glanders. The acute form (more common in donkeys and mules than in horses) typically progressed to death with about a week. Acute, chronic and latent forms of glanders are seen in horses, mules and donkeys. The clinical signs in the acute form (also called nasal form) may include a high fever, cough, inspiratory dyspnea, a thick nasal discharge and deep, rapidly spreading ulcers on the nasal mucosa. Healed ulcers become star-shaped scars. The submaxillary lymph nodes are usually swollen and painful and the lymphatic vessels on the face may be thickened. Secondary skin infections, with nodules, ulcers and abscesses may be seen. Affected animals usually die within 1 to 2 weeks.

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Disease in Animals

- Chronic form
 - Coughing, malaise, fever, weight loss
 - Nasal discharge and ulcers, skin nodules
 - Lymph node and vessel involvement
 - Swelling of joints and leg edema
- Latent form
 - May be few symptoms
 - Nasal discharge
 - Glanderosus orchitis common

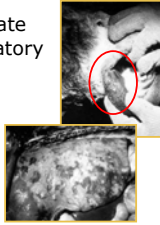
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The chronic form which may include cutaneous and pulmonary involvement, develops insidiously. The symptoms may include coughing, malaise, unthriftiness, weight loss and an intermittent fever. A chronic purulent nasal discharge may be seen, often only from one nostril. Other symptoms may include ulcers and nodules on the nasal mucosa, enlarged submaxillary lymph nodes, chronic enlargement and induration of lymphatics and lymph nodes, swelling of the joints and painful edema of the legs. The skin may contain nodules, particularly on the legs, that rupture and ulcerate. This form is slowly progressive and may be fatal. In the latent form, there may be few symptoms other than a nasal discharge and occasional labored breathing. Lesions may be found only in the lungs. Lesions may also occur in the liver or spleen and in male animals, glanderosus orchitis is a common lesion.

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Gross Lesions-Necropsy

- Ulcers, nodules, stellate scars in upper respiratory
- Pneumonia
- Firm rounded miliary nodules
- Swollen lymph nodes and vessels



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At necropsy there may be ulcers, nodules and stellate scars in the nasal cavity, trachea, pharynx, larynx, skin and subcutaneous tissues. Catarrhal bronchopneumonia with enlarged bronchial lymph nodes may be present. The lungs, liver, spleen and kidneys may contain firm, rounded, encapsulated miliary gray nodules similar to tubercles. The lymphatic vessels may be swollen, the lymph nodes are typically enlarged and fibrotic and contain focal abscesses. In addition, necrosis may be noted in the internal organs and testes. The upper photo shows a granulomatous lesion in the lip of a donkey. Lower photo is an extensive pyogenic granulomatous pneumonia in a donkey. Photos from: http://www.vet.uga.edu/vpp/gray_book/photos/pages/057.htm

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Differential Diagnosis

- Melioidosis
- Strangles
- Lymphangitis
- Other forms of pneumonia
- Gutter pouch empyema
- Dermatophilosis
- Dermatomyces

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Signs of glanders must be distinguished from melioidosis, strangles, lymphangitis, ulcerative lymphangitis, and other forms of pneumonia. Purulent sinusitis, guttural pouch empyema, and other causes of nasal catarrh should also be considered. Skin lesions may be similar to those of dermatophilosis or dermatomyces such as sporotrichosis.

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Diagnosis: Animals

- Isolation of *Burkholderia mallei*
 - Blood, sputum, urine or skin lesions
- Mallein test
 - Intrapalpebral or conjunctival injection
 - Swelling 1-2 days later
- Serology
- Complement fixation and ELISA
 - Most reliable in horses
 - Cannot be used in donkey or mule

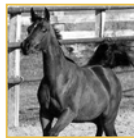
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Glanders can be diagnosed by bacteriologic isolation of *B. mallei* from skin lesions or blood sample. Inoculation into guinea pigs, the mallein test and serology can also be used. In the mallein test, a positive reaction is indicated by eyelid swelling 1 to 2 days after intrapalpebral injection of a protein fraction of *B. mallei*, or by conjunctivitis after administration in eyedrops. This is similar to tuberculin testing. A variety of serologic tests are available, including complement fixation, ELISA, indirect hemagglutination, counter-immunoelectrophoresis and immunofluorescence. The most accurate and reliable tests in horses are complement fixation and ELISA. Agglutination tests are unreliable for horses with chronic glanders and animals in poor condition. Complement fixation tests cannot be used with donkey or mule serum.

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Treatment

- Antibiotics effective
- Treatment controversial
 - Asymptomatic carriers may result




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Antibiotics may be effective but treatment is not generally recommended, as infections can be spread to humans and other animals, and treated animals may become asymptomatic carriers.

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Prevention and Control

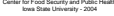


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Prevention: Humans

- Elimination of disease in animals
- Biosafety level 3 required in labs
- Protective clothing during exams and necropsy
 - Gloves and mask



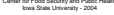
In countries where glanders is endemic in animals, prevention of the disease in humans involves identification and elimination of the infection in animal populations. Within the health care setting, transmission can be prevented by using common blood and body fluid precautions. Biosafety level 3 containment practices are required for laboratory staff when working with glanders. Field veterinarians and veterinary pathologists must take strict precautions to prevent human infections by the cutaneous or respiratory route during clinical or post-mortem exams of suspected cases. Adequate protective clothing, including gloves, and face masks should be worn.

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Prevention

- Horses
 - Early detection and quarantine with disinfection
- Reportable to state veterinarian
- Vaccine not available for humans or animals




Prevention in animal settings include early detection and quarantine procedures. Glanders is reportable to state veterinary offices. A vaccine is not available for humans or animals.

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Glanders as a Biological Weapon

- History
- Very few organisms required to cause disease
- Easily produced
- Pulmonary form has high mortality
- Limited experience with disease can slow diagnosis and treatment




Glanders has several characteristics that make it a potential agent for biological warfare and terrorism. Very few *Burkholderia mallei* organisms are required to cause disease and the organism is easily produced. In a single year in the 1980s, the Soviet Union produced more than 2,000 tons of dry agent of glanders. When the bacteria is inhaled as an aerosol, the disease can have a very high mortality rate. Additionally, diagnosis and treatment of glanders may be complicated by the lack of knowledge of its infection. Patients who recover do not develop a protective immunity, thus the agent could be reused.

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Acknowledgments

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Acknowledgments

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