

Burkholderia mallei (Glanders) and Burkholderia pseudomallei (Melioidosis)

Unless otherwise noted, all information presented in this article is derived from the following sources:

- 1. *Textbook of Military Medicine: Medical Aspects of Chemical and Biological Warfare*. Chapters 6-7. Washington, DC: Office of the Surgeon General at TMM Publications; 2007. Available at: http://www.bordeninstitute.army.mil//published_volumes/ biological_warfare/biological.html.
- 2. Currie B. Burkholderia pseudomallei and Burkholderia mallei: Melioidosis and glanders. Chapter 218 in: Principles and Practice of Infectious Diseases. Churchill Livingston, 2004.

Background

Glanders and melioidosis are infectious diseases caused by species of the bacterial genus *Burkholderia*. Glanders is caused by infection with the bacterium *Burkholderia mallei*, and melioidosis is caused by *Burkholderia pseudomallei*. Both have the potential to produce fatal disease and have been identified by the Centers for Disease Control and Prevention (CDC) as Category B biological agents. The Department of Health and Human Services (HHS) has identified these diseases as top priorities for development of medical countermeasures.

Glanders

Glanders, which was described by both Hippocrates and Aristotle, is largely a disease of historical significance, but the disease does remain endemic in the Middle East, Asia, Africa, and South America. Horses, mules, and donkeys are animals most often afflicted by glanders, but the disease can spread to other animals. In humans, the main route of transmission has been occupational exposure among workers who handle infected animals; however, infection may also occur if contaminated meat is ingested or if respiratory secretions are inhaled.

Glanders as a Biological Weapon

B. mallei was one of the first agents to be used for biowarfare in the modern era. During World War I, German agents targeted horses and livestock in the United States, Romania, Spain, Norway, and Argentina through inoculation and feed contamination. Several countries experimented with glanders bioweapons in the second half of the 20th century.

Of note, the *B. mallei* cannot persist in the environment outside its host (unlike *B. pseudomallei*—the agent of melioidosis). This potentially limits its usefulness as a bioweapon.

Transmission

Human-to-human transmission can occur with this agent via highly infectious respiratory droplets and cutaneous secretions.

Infection Control Measures

Airborne and standard contact precautions should be employed in the care of all infected individuals given glanders' potential for transmission. Laboratory workers should utilize BSL-3 lab precautions, as laboratory acquired cases have occurred.

Signs and Symptoms

The incubation period for glanders varies depending on the site of infection and the characteristics of transmission. The incubation period can range from 1 to 14 days—shorter incubation periods (1 to 2 days) are possible with inhalation, and longer periods are possible with skin exposure.

Constitutional symptoms—which include malaise, fever, chills, and fatigue—are common at the onset, and then, depending on the method of infection, more specific symptoms may follow.

Inhalational exposure results in respiratory symptoms with fever, which can progress to ulceration and necrosis of the airways. Lobar or bronchopneumonia, neck and mediastinal lymph node swelling, pustular skin lesions, and spread to internal organs may follow. Without antibiotics, death may occur within 10 days.

After skin exposure, skin nodules may form and become pusfilled; swelling of nearby lymph nodes may occur. This is often accompanied by symptoms such as fatigue, fevers, chills, and malaise. Systemic dissemination at 1 to 4 weeks can result in infection in almost any organ, and in the central nervous system.

Diagnosis and Countermeasures

Diagnosis is based on growing the organism in culture media; no rapid test is available.

Antibiotics including carbapenems, cephalosporins (ceftazidime and cefepime), macrolides (azithromycin, clarithromycin), doxycycline, TMP/SMX, and gentamicin are active against

Presentation Types	Characteristics	
Acute	Localized	Acute local infection with ulceration of oral, nasal, and/or eye tissues
	Pulmonary	• Infection of the lungs following inhalation of aerosolized <i>B.mallei</i> or by spread via the blood
		• May result in pneumonia, pulmonary abscesses, and pleural effusions
	Septicemic	Systemic infection in the bloodstream
		• Following sudden onset of symptoms, death occurs within 7-10 days
Chronic	Asymptomatic	• Characterized by flare-ups and remissions of infection over the course of years; some patients may be asymptomatic
		• The most common symptom is abscesses that may occur on the skin or intramuscular abscesses in the limbs
		• Liver, spleen, or skin may also be affected

glanders. An intensive regimen of intravenous antibiotics for 10 to 14 days is required, followed by 3 months of oral eradication therapy. Postexposure prophylaxis with doxycycline, as well as potential vaccine candidates, are being studied.

Melioidosis

Like glanders, melioidosis is a disease that afflicts both humans and animals. It has varied clinical presentations, including asymptomatic infection, localized skin ulcers/abscesses, chronic pneumonia, and fulminant septic shock with abscesses in multiple internal organs. Most cases originate in Southeast Asia—where it is a common cause of pneumonia—and northern Australia. And most cases are the result of exposure to the bacteria in muddy soils or surface water. The disease was first identified in 1912 in morphine addicts in Burma. Unlike *B. mallei, B. pseudomallei* is found in the environment, where it resides in water and soil.

Melioidosis as a Biological Weapon

Several countries have studied *B. pseudomallei* for use as a bioweapon. Melioidosis is considered a potential biological weapon because of the ease with which strains may be obtained from the environment, the ability to engineer strains that are resistant to multiple antibiotics, and the lack of a vaccine.

Transmission

Human-to-human transmission is rare, but it has been documented.

Infection Control Measures

Airborne and standard contact precautions should be employed in the care of patients when severe pneumonia with productive sputum is present. Laboratory workers should utilize BSL-3 lab precautions.

Presentation Types	Characteristics	
Acute	Localized	Acute, local infection (with ulceration) of subcutaneous tissue, lymph nodes, and occasionally salivary glands
	Pulmonary	• Infection of the lungs following inhalation of aerosol is the most common form of infection
		• May result in pneumonia, pulmonary abscesses, and pleural effusions
		• Cutaneous abscesses may develop and take months to appear
	Septicemic	Systemic infection in the bloodstream
		• Death occurs within 7 to 10 days of onset of symptoms
Chronic	Asymptomatic	• Flare-ups and remissions occur over the course of years
		• The most common symptom is abscesses that may occur on the skin or intramuscular abscesses in the limbs
		• Liver, spleen, or skin may also be affected

Signs and Symptoms

The inoculating dose, mode of infection, and host risk factors (eg, presence of diabetes or alcoholism) influence the incubation period of melioidosis, which can range from 1 to 21 days. Clinical presentation can range from localized skin abscesses to disseminated infection with septic shock and pneumonia, which carries a mortality rate of 90%. A chronic form of melioidosis that mimics tuberculosis was once known as the "Vietnamese Time Bomb" due to the potential for reactivation of the infection in U.S. soldiers who had returned home after serving in the Vietnam War.

Diagnosis and Countermeasures

As with glanders, diagnosis is made through culture detection of the organism, and no rapid test is available. Initial treatment consists of a course of intravenous antibiotics for 14 days followed by oral therapy for 3 months. Antibiotics including carbapenems, cephalosporins (ceftazidime and cefepime), doxycycline, and TMP/SMX are active against melioidosis. Notably, macrolides and gentamicin are not active against *B. pseudomallei*.

Secondary prophylaxis with TMP/SMX, doxycycline, or amoxicillin-clavulanate may be considered, but only in certain scenarios (since the agent is not easily transmitted from person to person, in the lab, or zoonotically), and particularly if the exposed person has diabetes or alcoholism.

See Also

Textbook of Military Medicine: Medical Aspects of Chemical and Biological Warfare. Chapters 6-7. Washington, DC: Office of the Surgeon General at TMM Publications; 2007. Available at: http://www.bordeninstitute.army.mil//published_volumes/ biological_warfare/biological.html.Accessed October 13, 2011. Currie B. Burkholderia pseudomallei and Burkholderia mallei: Melioidosis and glanders. Chapter 218 in *Principles and Practice* of Infectious Diseases. Churchill Livingston, 2004.