Melioidosis: the Vietnamese time bomb

Christopher Brightman, Consultant Microbiologist (retired) and Locum GP
1. Lincoln County Hospital; 2. Lincoln, England

Melioidosis is a rare but potentially fatal infection that is common in parts of the Far East and Australia, as well as India and South America. Cases of infection are rare in the UK, but physicians should be aware of the possibility in travellers from areas where the infection is common.

In 1911, Captain Alfred Whitmore, a British pathologist working in Rangoon, together with his assistant C. S. Krishnaswari, described a ‘glanders-like’ illness among malnourished inhabitants of the city. The condition was particularly common among opiate addicts, and widespread abscesses were found on post-mortem examination of people who had died from this illness. An organism was grown from pus that was similar to (but not identical with) Bacillus mallei, the cause of glanders: Whitmore suggested it should be called Bacillus pseudomallei. He did no further work on the organism.

William Fletcher and Ambrose Stanton, both of whom were working in the Institute for Medical Research at Kuala Lumpur, were the next doctors to study the organism. In 1913, a lethal infection spread through the animal house at the Institute. Fletcher isolated a bacterium from the dead animals that he was unable to identify, and this organism remained unidentified until 1917 when Stanton isolated a similar organism from Tamil workers who fell ill on a rubber estate.

Fletcher showed that the organism was identical to Whitmore’s bacillus. During the next decade this organism was isolated from 39 human cases, as well as from wild and domestic animals. Stanton and Fletcher suggested that the condition be called melioidosis.

Subsequently, cases were described among French colonists in Indochina. They contracted the infection after a car crash in which wounds were contaminated with mud or water. Over a hundred cases were described in French troops between 1948 and 1954, and cases were also reported among American troops during the Vietnam war. This stimulated research into the infection.

A number of soldiers who were exposed to B. pseudomallei in Vietnam suffered no ill effects at the time of the exposure but developed a severe and often fatal illness many years later. This phenomenon gave rise to the expression ‘The Vietnamese time bomb’ for a melioidosis infection. It is estimated that about 225 000 Americans were exposed to B. pseudomallei in Vietnam, but it is not known how many of these will develop melioidosis in later life. In the mid-1970s it became apparent that a large number of people living in north-east Thailand had melioidosis, though the infection was often subclinical. Cases were reported in northern Australia between 1990–1991, in particular during the rainy season.

**Bacteriology**
The generic name of Bacillus pseudomallei has been changed several times since the organism was isolated by Whitmore. It is now called Burkholderia pseudomallei.

Figure 1. Burkholderia pseudomallei colonies on Ashdown’s agar showing characteristic cornflower head morphology
**B. pseudomallei** is a Gram-negative, motile, non-sporulating oxidase-positive bacillus. It can be isolated from soil and water in areas in which melioidosis is endemic. It grows well on simple media and forms characteristic purple, rugose, opaque colonies on Ashdown’s medium, a selective medium used for its isolation (see Figure 1).

**Prevalence**
The incidence of melioidosis in north-east Thailand was about 1:5000 between 1997 and 2006. It is now the most common cause of death in that area after tuberculosis and infection with HIV. The majority of cases occur during the rainy season. It is also found in northern Australia, where in some places it is the most common cause of community-acquired pneumonia. The disease is also endemic in parts of India and South America.

As a result of increased travel by UK residents to the Far East and Australia, more people will be exposed to infection. Unless it is treated in the early stages, acute melioidosis is a very serious infection with a high mortality, so UK doctors should be aware of it as a potential diagnosis – especially in patients on steroids, or with diabetes mellitus or chronic renal failure who return from an endemic area with a febrile illness.

**Epidemiology**
*B. pseudomallei* can be isolated from soil and water in endemic areas. Melioidosis is therefore most common among people working in paddy fields. Though the mode of transmission is uncertain, it is assumed that infection is contracted when the organism is inoculated through abrasions in the skin. However, there is increasing evidence for transmission by aerosols, in particular during the rainy season. Man-to-man transmission and transplacental transmission have been reported, but they are both rare.

**Predisposing factors for infection by B. pseudomallei**
The incubation period is about nine days, but infection can remain latent up to 62 years. Although melioidosis can occur in apparently healthy people, most patients have some underlying disease that affects the immune system. Diabetes mellitus and chronic renal failure are the two most common conditions that predispose to melioidosis. Other conditions that increase susceptibility to infection include liver disease, chronic lung disease and treatment with steroids. Pregnant women are also more susceptible to infection. However, people with HIV infection do not appear to be especially prone to melioidosis.

**Pathogenesis**
Various virulence factors have been described, including substances released from the organism. However, the relative importance of each virulence factor has yet to be properly understood. The ability of *B. pseudomallei* to grow intracellularly, and to remain inactive within granulomata, is undoubtedly important in explaining the ability of this infection to remain dormant for so many years.

**Clinical features**
Infection is most common in people aged 40–60 years, though all ages can be affected. Infection is slightly more common in men than women. This may be because men are more exposed to the organism than are women, rather than being a genuine difference between the sexes.

In endemic areas, 60–70% of the population will have serological evidence of infection with *B. pseudomallei*, though only a small proportion will have evidence of clinical disease. Most patients present with a septicaemic illness. About 50% of patients will have a focus of infection, either in the lungs or the skin. If a patient is not treated, their condition will rapidly deteriorate with the development of metastatic abscesses, particularly in the lungs, liver, spleen, parotid glands and the prostate. Mycotic abscesses are also relatively common, and patients often have a metabolic acidosis. Localised infection can occur, especially in the lungs where cavitation is common, particularly in the upper lobes.

However, abscesses can occur in any organ, including the brain. There are geographical variations in the clinical presentation of melioidosis. As a result, parotitis is common in Thailand, but not in Australia, whereas neurological complications are more common in Australia than in Thailand. This may reflect strain differences in *B. pseudomallei*.

**Diagnosis**
Very few physicians in temperate climates will have seen a case of melioidosis. However, they should have a ‘high index of suspicion’ when examining a patient who has returned from the Far East or Australia with a septicaemic illness, especially if a patient has an underlying illness such as diabetes mellitus.

If a clinician suspects that a patient may have melioidosis, they should speak to a specialist in infectious diseases. If the specialist considers that to be likely, the patient should be sent to an infectious disease unit and a consultant microbiologist should also be informed. Specimens of body fluids, such as blood cultures and pus must not be sent to a bacteriology laboratory before the consultant microbiologist has been told. The patient should be kept in isolation and ‘barrier nursed’ until a decision has been made as to whether or not they have melioidosis.

However, there are a large number of differential diagnoses, depending on the site of infection. In particular, melioidosis should be distinguished from tuberculosis as *Staphylococcus aureus* can cause some of the clinical features of melioidosis.
Infections

**Laboratory diagnosis**

*B. pseudomallei* grows readily on media in common use in a bacteriological laboratory (see Figure 1). The organism can be isolated from blood, sputum and pus and can be identified using routine diagnostic methods such as the Analytical Profile Index strip. Isolates should be sent to a reference laboratory, such as the one at Porton Down, for identification.

A consultant microbiologist must be informed when a specimen is sent from a patient suspected of having melioidosis. *B. pseudomallei* is a category 3 organism and should only be handled in a laboratory in which there are adequate facilities for dealing with this type of organism.

There are no reliable serological diagnostic tests. Those that are available lack specificity and sensitivity.

**Radiography**

About 80% of patients with melioidosis will have an abnormal chest radiograph. Widespread nodular shadowing is the most common abnormality to be seen. A cavitating pneumonia, resembling chronic pulmonary tuberculosis, may be seen in chronic forms of melioidosis. An ultrasonic examination of the abdomen should be done in all patients with melioidosis in order to look for splenic and hepatic abscesses.

**Treatment**

**General measures**

Patients with a confirmed case of melioidosis should be managed in an intensive care unit where they can receive appropriate support.

**Antibiotic treatment**

Current recommendations for antibiotic treatment are based on the results of clinical trials that have been conducted over the last 20 years. Two weeks of intravenous ceftazidime or meropenem should be followed by 10 to 20 weeks of co-amoxiclav or cotrimazole in order to prevent a relapse. About 10% of patients will have a relapse, especially if they have disseminated disease and have received antibiotics for less than three months. Mortality rates can reach 40% in patients with severe disease, even when given appropriate treatment.

**Conclusion**

There is no vaccine available to prevent melioidosis. Though it is most unlikely that a doctor in this country will see a case of melioidosis, they should consider the diagnosis in a patient returning from an endemic area with a febrile illness, especially if the patient has diabetes mellitus.

Doctors who run travel clinics should warn patients travelling to the Far East or Australia about the danger of contracting melioidosis, and the measures that can be taken to reduce that risk. Such advice is particularly important in people who intend to undertake outdoor activities.

Another reason for knowing about melioidosis is that experts consider that *B. pseudomallei* could be used by bioterrorists.

**Key points**

- With increased travel to the Far East and Australia, more people will be exposed to infection;
- Acute melioidosis is a very serious infection with a high mortality, unless the illness is treated in the early stages;
- It should always be considered in patients on steroids, or with diabetes mellitus or chronic renal failure who return from an endemic area with a febrile illness;
- Like Strongyloides, melioidosis can remain dormant for decades, only presenting as a clinical illness when the patient becomes elderly and their immune response less efficient. As a result, it should enter into the differential diagnosis of a febrile illness in an elderly patient who has worked or lived in the Far East;
- Experts consider that *B. pseudomallei* could be used as a weapon by terrorists. All doctors should be aware of this possibility, remote as it may be. The author was involved in an incident in which a white powder was thought to be spores of the anthrax bacillus. Fortunately, that was not the case; however, there would have been less panic had doctors known more about anthrax.

**References**


**Further reading**


**Declaration of interests:** none declared