

From soil to sepsis

Melioidosis, an emerging tropical infectious disease

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Melioidosis is an infectious disease caused by the environmental bacterium *Burkholderia pseudomallei*, and it is endemic to tropical regions of Australia. Even with optimal supportive care, about 10% of Australians with melioidosis will die from their infection.

KEY POINTS

- Melioidosis, a disease caused by the environmental bacterium *Burkholderia pseudomallei*, has a case fatality rate in Australia of about 10%.
- Melioidosis primarily affects individuals with comorbidities that include diabetes, hazardous alcohol consumption, chronic lung disease, chronic kidney disease, immunosuppression and malignancy.
- The disease is endemic in tropical Australia and Southeast Asia; however, cases are increasingly being reported in the Pacific, South Asia, Africa and the Americas.
- Melioidosis most commonly presents as pneumonia, but can also affect the skin, musculoskeletal system, abdominal viscera and the CNS.
- Diagnosis is confirmed by culturing *B. pseudomallei* from clinical specimens. Routine imaging of the chest, abdomen and pelvis is used to assess disease extent.
- Treatment involves an intensive intravenous antibiotic phase followed by a prolonged oral eradication phase. Side effects of this therapy can make adherence to treatment challenging.
- Prevention relies on minimising environmental exposure and optimising the management of predisposing comorbidities, as there is no approved vaccine and chemoprophylaxis has limited utility.



The organism that causes melioidosis, *Burkholderia pseudomallei*, is an environmental bacterium that lives in soil and surface water in tropical and subtropical regions. Most cases in endemic tropical regions occur during the monsoonal wet season when moist soil provides optimal conditions for the organism's growth.¹

Exposure to *B. pseudomallei* occurs via percutaneous inoculation, inhalation or ingestion, and many individuals with melioidosis have a history of occupational or recreational exposure to soil or surface water. However, most people who encounter the organism do not develop melioidosis.² Indeed, about 90% of individuals who are diagnosed with melioidosis have a comorbidity that predisposes them to developing the disease.³ This is most commonly diabetes mellitus, but melioidosis also occurs more frequently in individuals with hazardous alcohol consumption, chronic lung disease, chronic kidney disease, immunosuppression and malignancy.³⁻⁵ Many of these comorbidities are seen more often in individuals who are socioeconomically disadvantaged, which is one of the reasons why the incidence of melioidosis is higher in Australia's Aboriginal and Torres Strait Islander people.⁶

Global distribution

B. pseudomallei is endemic in tropical Australia and Southeast Asia, but the area of endemicity is expanding, with cases being reported increasingly in the Pacific, South Asia, Africa and the Americas, and in individuals who have travelled to these regions.^{7,8} The incidence of melioidosis is increasing in Australia and is highest in the Top End of the Northern Territory and tropical North Queensland. Almost 300 cases were reported in Australia in the

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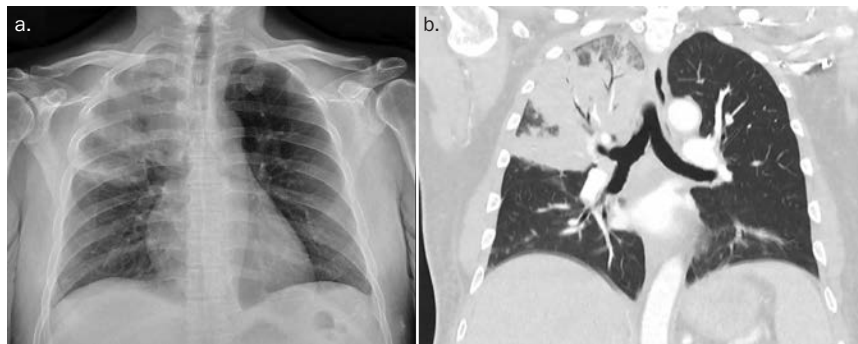
first five months of 2025. The increase in cases in Australia has been linked to urban expansion, and clustering after severe weather events has also been documented.⁹⁻¹² The recent appearance of cases in Southeast Queensland has been linked to two climate change-associated La Niña events.¹³ However, despite the recent increase in disease incidence, most individuals at risk of melioidosis – even those living in endemic regions – have never heard of this life-threatening condition.¹⁴

Clinical presentation

About 85% of cases of melioidosis will present acutely and these patients will usually have had symptoms for less than a week, but more subacute presentations (with symptoms present for several months) are also seen. Reactivation from latent infection occurs, and may be precipitated by immunosuppression or concurrent illness, but it is far less frequent than previously believed and represents only about 3% of all cases.¹⁵

The clinical manifestations of melioidosis are protean and multiple organs are often involved concurrently, but pneumonia is present in most cases (Figure 1 and Figure 2).^{4,16} Patients with pneumonia usually present with a short history of fever, cough and dyspnoea. However, they may also present with weeks of respiratory symptoms that have not responded to the usual empirical therapies. Bacteraemia is present in up to 70% of cases of melioidosis and about 25% of Australian patients present with septic shock.^{17,18}

Other typical presentations of melioidosis include skin and soft tissue infections (~15% of cases), infections of the bones and joints (~10% of cases) and abscesses of the liver, spleen or both (~5% of cases). Prostatic involvement, which occurs in about 20% of affected men, is a characteristic manifestation and all men with melioidosis should be screened for this complication (Figure 2).¹⁹ CNS involvement occurs in only 4% of cases, but it is one of the most feared manifestations and may present as encephalomyelitis, brain abscess, meningitis or as



Figures 1a and b. (a, left) A chest x-ray and (b, right) a computed tomography scan demonstrating right upper lobe pneumonia in a patient with diabetes who presented with seven days of fever and cough. Figures courtesy of the authors.

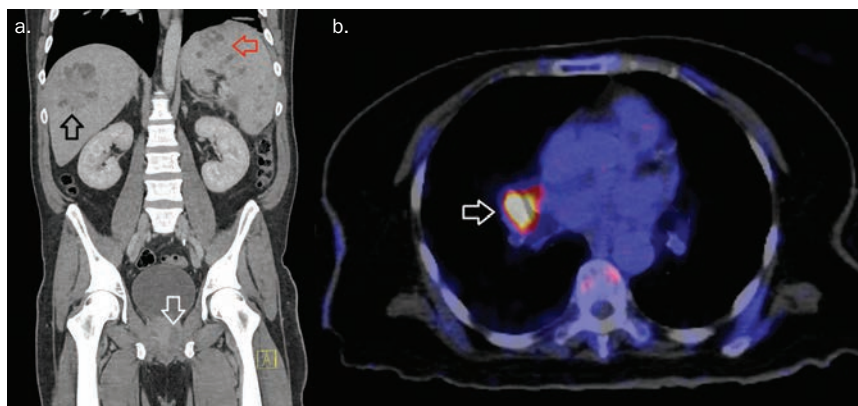
an extradural collection.²⁰ *B. pseudomallei* may also cause lymphadenopathy, nodules or masses that may be mistaken for cancer, emphasising the importance of sending biopsies for culture in the appropriate clinical context (Figure 2).²¹

Less than 5% of cases of melioidosis occur in children, which may be explained by the fact that children are less likely to have predisposing comorbidities. Children with melioidosis usually have milder disease, with the most common manifestation being localised skin infection (Figure 3).²² However, disseminated disease can also be seen and fatalities have been reported in previously well children despite optimal supportive care.²³ These fatal paediatric cases, and cases in adults without risk

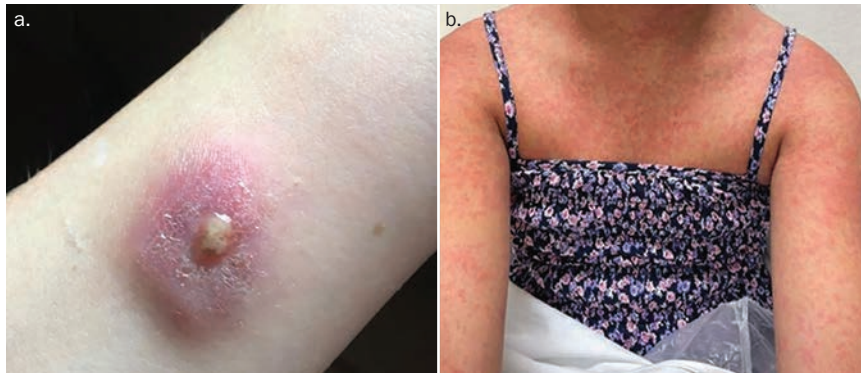
factors for melioidosis, may be due to the presence of virulence factors in the organism, a larger inoculum at the time of infection or undiagnosed immune dysfunction in the patient.^{20,24}

Diagnosis

In endemic regions, the diagnosis of melioidosis is often suspected in patients with predisposing comorbidities who present with typical symptoms during the wet season. The diagnosis is confirmed by culturing *B. pseudomallei*, a Gram-negative rod, from blood, sputum, urine, pus or other clinical specimens; the organism grows well on traditional culture media (Figure 4).²⁵ As multi-organ involvement is common and many patients are bacteraemic, the



Figures 2a and b. (a, left) Multi-organ involvement of the liver (black arrow), spleen (red arrow) and prostate (white arrow) in a patient with disseminated melioidosis. (b, right) A positron emission tomography scan demonstrating mediastinal lymphadenopathy in another patient who was believed to have a lung malignancy until *Burkholderia pseudomallei* was cultured from a biopsy. Figures courtesy of the authors.



Figures 3a and b. (a, left) Isolated melioidosis of the skin. The patient presented with a three-week history of a 2 cm abscess on his left forearm. The abscess was lanced and a swab isolated *Burkholderia pseudomallei*. (b, right) A maculopapular rash, which developed after initiation of trimethoprim-sulfamethoxazole as eradication therapy and resolved after its cessation.

Figures courtesy of the authors.

concurrent collection of multiple clinical specimens will facilitate diagnosis. True colonisation is extremely uncommon, therefore isolation of *B. pseudomallei* almost always warrants further investigation and treatment. In endemic regions, laboratories are adept at identifying *B. pseudomallei*; however, laboratories that are unfamiliar with the organism may disregard it inappropriately as an environmental contaminant.²⁶

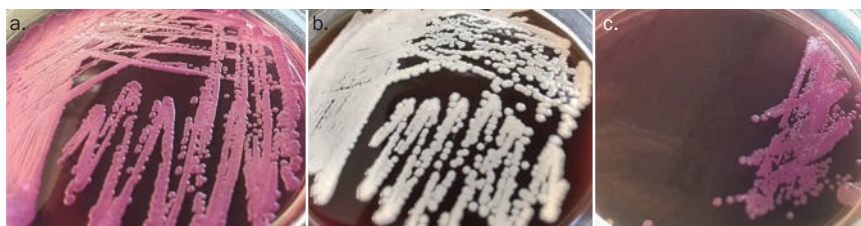
There is interest in the use of newer diagnostic strategies, including molecular testing, to expedite the diagnosis of melioidosis, but these assays are not yet widely available.²⁷ Serology has limited utility in the diagnosis of the disease as it has poor sensitivity early in the disease course and may be positive in healthy individuals in endemic areas.²⁷

Further diagnostic evaluation

Melioidosis can be rapidly fatal, but person-to-person transmission is extremely unusual,

and no special precautions are required for health workers caring for patients with melioidosis. It is essential for clinicians who are unfamiliar with the infection to seek prompt specialist advice.

Almost all cases will require hospitalisation where patients will usually have CT imaging of the chest, abdomen and pelvis to identify the extent of disease.²⁸ This will help define deep tissue collections that may require drainage and determine the duration of antibiotic therapy.²⁹ In patients with CNS involvement or bone and joint involvement, CT imaging results may be normal and MRI is preferred. Computed tomography-positron emission tomography (CT-PET) may also help identify unrecognised foci of disease.^{30,31} For pregnant women and children, imaging strategies that minimise radiation exposure, including ultrasound, are a reasonable alternative, although these individuals require close follow-up.



Figures 4a to c. Colonies of *Burkholderia pseudomallei* after 48 hours of incubation on (a, left) Ashdown's medium, (b, middle) horse blood agar and (c, right) MacConkey agar with crystal violet.

Figures courtesy of the authors. Prepared with the assistance of Ms Shannon Clarke.

Antibiotic treatment

There are two phases of antimicrobial therapy for melioidosis: an initial intravenous intensive phase and a subsequent oral eradication phase, which is prescribed to help prevent relapse. *B. pseudomallei* is intrinsically resistant to many commonly prescribed antibiotics, so during the initial intensive phase patients receive ceftazidime or meropenem. The duration of intensive therapy varies with the clinical phenotype, although a minimum of two weeks is recommended and source control is essential.²⁹ After initial stabilisation and management in hospital, many patients are treated with outpatient parental antibiotic therapy. This therapy is given via a peripherally inserted central catheter with an elastomeric infuser device.³² This approach is safe, effective and is preferred by many patients.³³

Relapse, which occurs in up to 4% of people, is more common in patients who are unable to adhere to prescribed antibiotic therapy and can be fatal.⁵ Adherence to currently recommended treatment regimens can be challenging: Australian treatment guidelines recommend a minimum of three months of high-dose trimethoprim-sulfamethoxazole (TMP-SMX) during the eradication phase, a phase of care that will frequently be co-managed by the GP.²⁹ Over 50% of patients receiving high-dose TMP-SMX have side effects that necessitate cessation, dose reduction or a switch to alternative agents such as doxycycline or amoxicillin-clavulanate, which are less effective.³⁴ The most common serious side effect from TMP-SMX is acute kidney injury, but fatal cutaneous reactions, including drug reaction with eosinophilia and systemic symptoms or toxic epidermal necrolysis, have also been seen.³⁴

Outcomes and follow-up

Although the case fatality rate of melioidosis has declined significantly in Australia's well-resourced health system over recent decades, it is still about 10%.^{4,5} Most individuals with melioidosis

PRACTICE POINTS TO HELP GPs RECOGNISE AND MANAGE MELIOIDOSIS IN AFFECTED INDIVIDUALS

- The causative organism of melioidosis, *Burkholderia pseudomallei*, lives in the soil and surface water in tropical and subtropical regions. About 75% of cases in endemic regions occur in the monsoonal wet season (December to April in Australia).
- About 85% of cases of melioidosis occur in individuals with the predisposing comorbidities of diabetes mellitus, hazardous alcohol consumption, chronic lung disease, chronic kidney disease, immunosuppression and malignancy.
- Although pneumonia is the most common clinical manifestation in melioidosis, almost any organ can be affected. Up to 70% of patients are bacteraemic and the disease can evolve rapidly to septic shock. Melioidosis is diagnosed by culturing *B. pseudomallei*, a Gram-negative bacillus, from blood, sputum, urine, pus or other clinical specimens on traditional laboratory culture media.
- All individuals with a diagnosis of melioidosis should be managed with the assistance of a specialist clinician. Initial workup and management almost always requires hospitalisation and often involves multidisciplinary care. Patients require a minimum of two weeks of targeted intravenous antibiotics and a minimum of three months of oral eradication to reduce the risk of relapse, which is otherwise common. These long courses of antibiotics are commonly complicated by adverse drug reactions and close monitoring is essential.
- There is no vaccine and no strategy that has yet been proven to reduce the incidence of the disease in the general population. Nevertheless, it remains prudent for GPs to advise their patients with predisposing comorbidities to minimise exposure to soil and surface water during the wet season and to stay indoors during heavy rain.

will have a comorbidity that has predisposed them to developing the disease. Their diagnosis of melioidosis is therefore an opportunity to identify this comorbidity and optimise its management to improve the individual's long-term health outcomes.³⁵

Prevention

Strategies to prevent melioidosis largely revolve around advising individuals with predisposing comorbidities to minimise exposure to soil and surface water during the wet season and to stay indoors during heavy rain. However, it is recognised that adherence to these recommendations is challenging, and they have not been shown to be effective in clinical trials.³⁶

There are data to support chemoprophylaxis in selected populations, but the relatively low incidence of melioidosis in even high-risk populations – and the potential side effects of TMP-SMX – means that chemoprophylaxis has a very limited role in combating the disease.³⁷⁻³⁹

There is presently no approved vaccine for melioidosis, although public health

strategies to reduce the incidence of predisposing risk factors – or at least optimise their management – might reduce the risk of melioidosis and the other complications of these comorbidities.^{16,35}

Conclusions

The global incidence of melioidosis is rising but the disease remains under-recognised. This brief overview provides some insights to assist clinicians in identifying and managing patients with this life-threatening condition. The emergence of melioidosis is a further reminder of the complex interplay between host, pathogen and the environment that drives the incidence of many infectious diseases, and the resulting implications for the general population and the health systems that care for them. Some practice points for GPs are listed in the Box. MT

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A list of references is included in the online version of this article (www.medicinetoday.com.au).

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