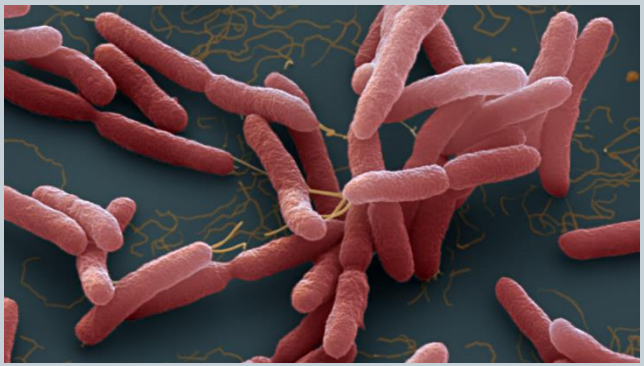
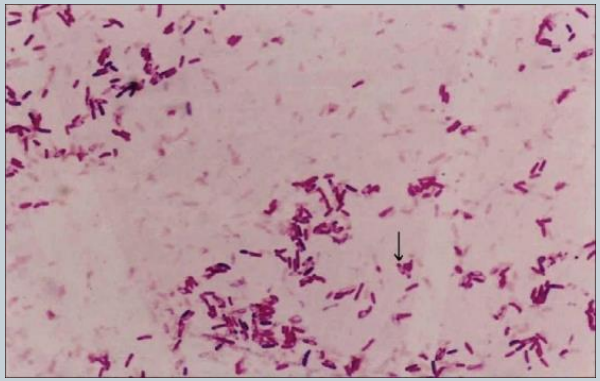
Melioidosis

EXT. THIPPAYAPORN LOPAISANKRIT

Overview

- *Burkholderia pseudomallei*
- Gram negative bacilli, safety pin appearance
- Important cause of community-acquired sepsis in Southeast Asia and northern Australia
- Mortality rate up to 40%
- Increasing number of incidence





Epidemiology

- Geographic distribution

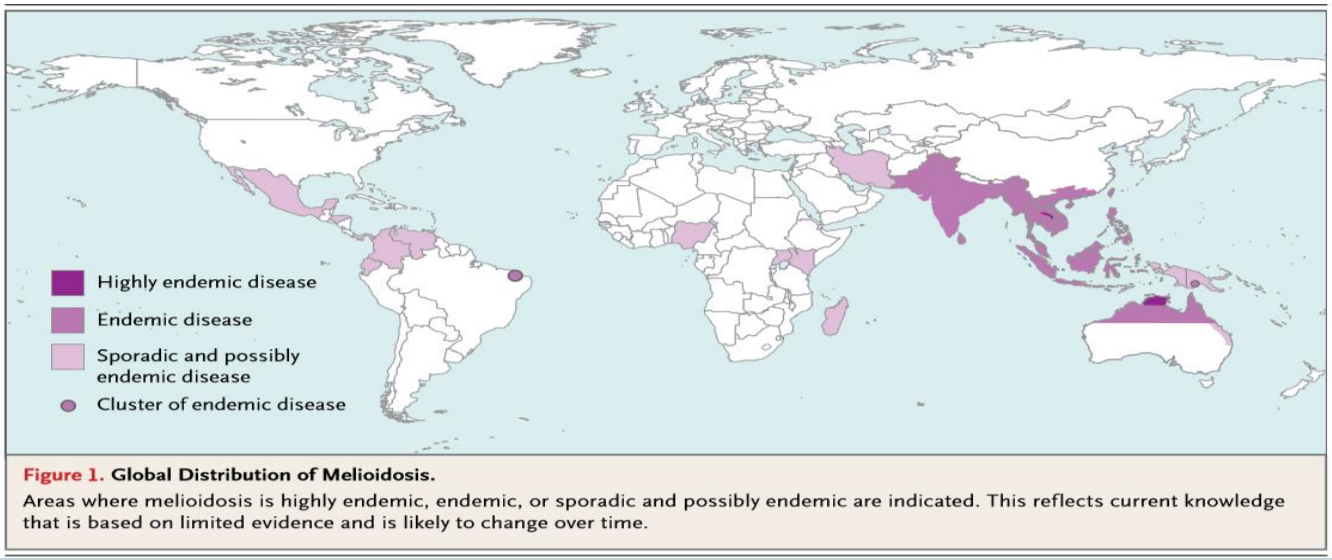


Figure 1. Global Distribution of Melioidosis.
Areas where melioidosis is highly endemic, endemic, or sporadic and possibly endemic are indicated. This reflects current knowledge that is based on limited evidence and is likely to change over time.

- Thailand is one of endemic countries with incidence up to 50 per 100,000 cases and up to 40% mortality

Epidemiology

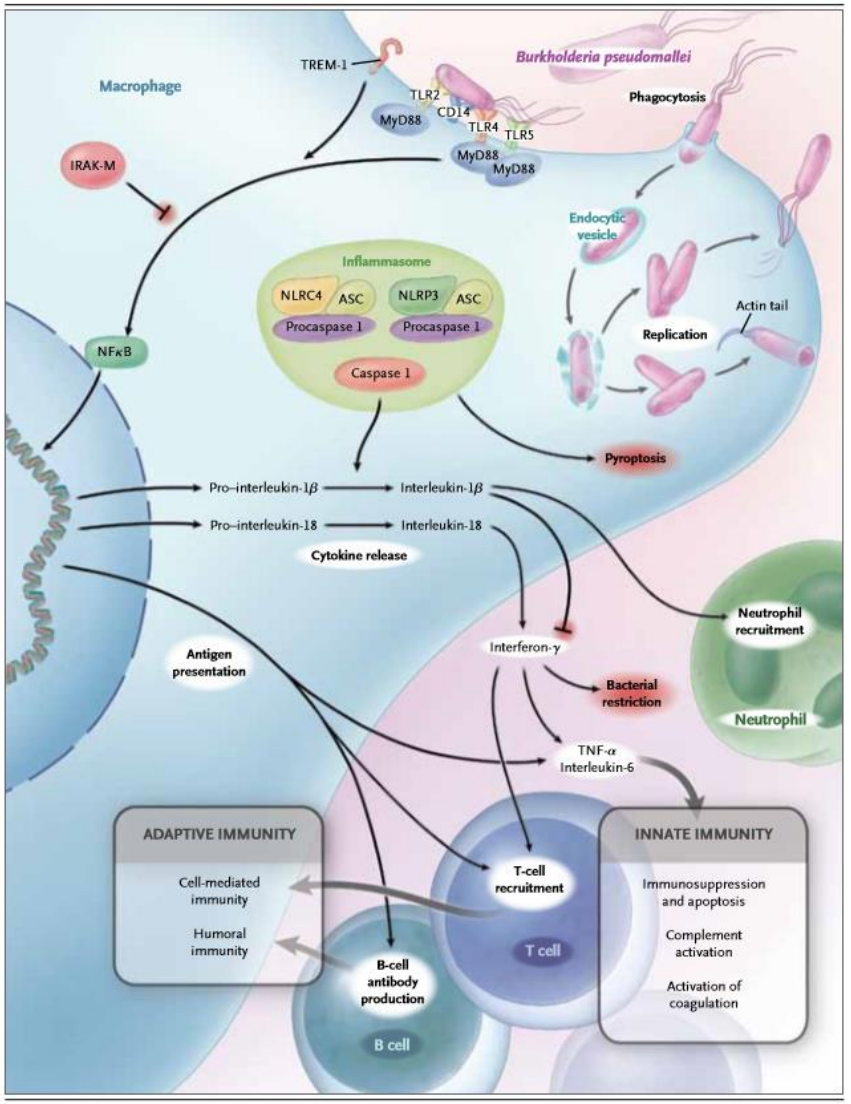
- Affects persons who are in regular contact with soil and water. 81% of cases are farmer.
- Up to 80% of cases have one or more risk factors
  - Diabetes
  - Heavy alcohol use
  - COPD
  - CKD
  - thalassemia
  - Glucocorticoid therapy
  - cancer
- Seasonal : rainy season
- Age : 40-60 yrs

Transmission

- Route:
  - Percutaneous inoculation (penetrating injury or open wound)
  - Inhalation
  - Ingestion (contaminated food or water)
- Incubation period 1-21 days
  - 1-21 days (Mean = 9 days)
  - Depends on strain, virulence, mode of infection, risk factors

Pathogenesis

- Escape from endocytic vacuole and replicate
- Cell-to-cell spread (cell membrane protrusion by actin tails)
- Caspase-1 induced macrophage apoptosis
- Neutrophil recruitment -> tissue damage



Clinical manifestations

- Can be asymptomatic infection
- Disease can be caused by primary infection or reactivation of latent focus
- Various clinical manifestations, ranging from acute fulminant septic illness to chronic infection (11%)
- Can relapses months or years later

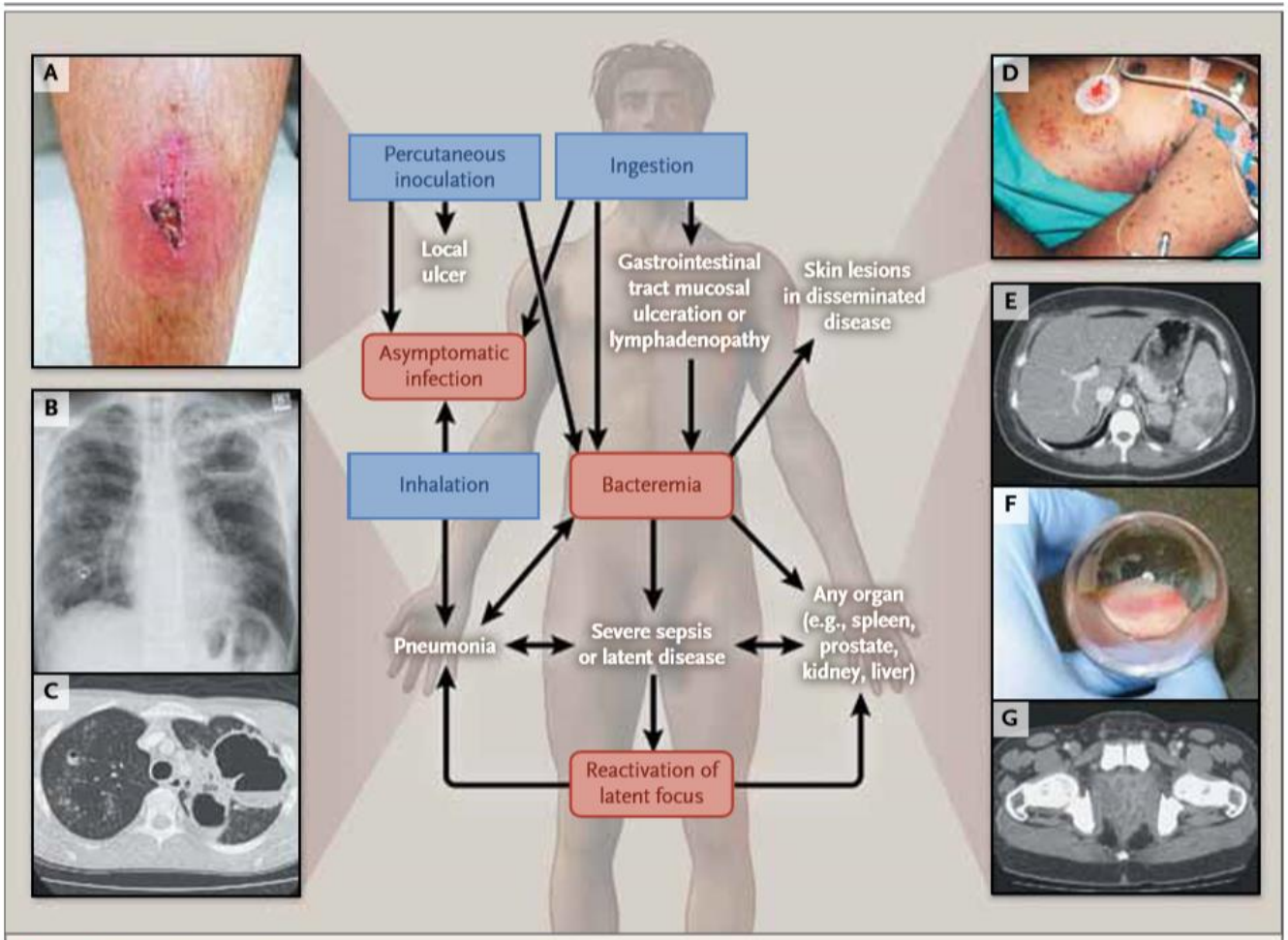


Figure 3. Clinical Events after Infection with *B. pseudomallei*.

Melioidosis may have a wide range of clinical manifestations, and severity varies from an acute fulminant septic illness to a chronic infection. Shown are the routes of infection (blue boxes: percutaneous inoculation, inhalation, and ingestion), the natural history of infection (red boxes: asymptomatic infection, bacteremia, or reactivation of latent focus), and the diverse disease manifestations (white text). Panel A shows cutaneous melioidosis in a healthy host. Panel B shows lung abscesses on the chest radiograph of a patient with acute melioidosis pneumonia, and Panel C shows the corresponding computed tomographic (CT) scan. Panel D shows the skin manifestations in a fatal case of disseminated melioidosis. Panel E shows splenic abscesses on an abdominal CT scan. Panel F shows aspirated pus in a patient with prostatic and periprostatic abscesses, and Panel G shows the abscesses on a CT scan from the patient.

Clinical manifestations

- Primary presenting features
  - Pneumonia
  - Genitourinary tract infection
  - Skin infection
  - Bacteremia without evidence focus
  - Septic arthritis or osteomyelitis
  - Encephalitis or myelitis
  - parotitis
- Chronic form mostly presents with Internal organ abscesses (liver, spleen,kidney)
  - usually afebrile with better prognosis

TABLE 4.

Variation in clinical pattern of melioidosis worldwide

Clinical presentation	% of patients in:				
	Royal Darwin Hospital series (1989-1999; *n* = 252) (111)	Singapore series (1989-1996; *n* = 331)[a] (191)	Kuala Lumpur series (1976-1991; *n* = 50)[b] (346)	Infectious Diseases Association of Thailand series (*n* = 686)[c] (344)	Sapprasithiprasong Hospital series (1986-1987; *n* = 63)[b] (74)
Pneumonia or pleural effusion	58	NR[d]	58	45	23
Genitourinary infection	19	NR	10	7	8
Skin or soft tissue infection	17	NR	24	13	13
Neurological melioidosis or brain abscess	4	NR	6	3	NR
Splenic abscess	4	NR	2	2	NR
Liver abscess	2	NR	4	7	NR
Other intra-abdominal	3	NR	4	5	NR
Prostatic abscess	18 (of males)	NR	NR	0.3	NR
Parotid abscess	0	NR	NR	2	NR
Bone or joint	4	NR	12	5	4
Pericardial effusion	1	NR	2	3	NR
No clinical focus	10	NR	NR	NR	51
Septic shock	20	NR	16	NR	30
Bacteremia	46	43	100[b]	58	100[b]
Mortality	19	39	65	38-61	68

[a]Culture-confirmed cases only.
[b]Bacteremic cases only.
[c]Summary of reported cases presented in 1985 from Khon Kaen Hospital (1982 to 1985), Ubon Ratchathani (1982 to 1985), Srinagarind Hospital (1978 to 1985), Nakorn Ratchsima (1983 to 1985), Chulalongkorn Hospital Bangkok (1980 to 1985), and Nontaburi (1983 to 1985).
[d]NR, not recorded.

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Melioidosis: Epidemiology, Pathophysiology, and Management

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Pulmonary melioidosis

- Clinical
  - Fever
  - Cough, often with purulent sputum and rarely hemoptysis
- CXR

Acute :

  - Localized or diffuse patchy infiltration typically starting in the upper lobes
  - multiple small pulmonary nodules
  - may rapidly progress resulting in cavitation or pulmonary abscess formation

Chronic

  - Same but slower progress
  - May mimic tuberculosis

Pulmonary melioidosis

Chest x-ray.

Initial chest x-rays n (%)	Acute N = 90	Subacute/ chronic N = 72
Localized patchy alveolar infiltration	27 (30.0)	27 (37.5)
Upper lobe	8 (8.9)	14 (19.4)
Other location	19 (21.1)	13 (18.1)
Cavitary lesion	7 (7.8)	5 (6.9)
Atelectasis	0 (0)	4 (5.5)
Calcified node	0 (0)	1 (1.4)
Hilar adenopathy	0 (0)	4 (5.6)
Lobar infiltration	3 (3.3)	1 (1.4)
Multilobar infiltration	8 (8.9)	5 (6.9)
Fibroreticular infiltration	5 (5.6)	11 (15.3)
Localized	3 (3.3)	3 (4.2)
Both upper lobes	1 (1.1)	3 (4.2)
Diffuse	1 (1.1)	5 (6.9)
Bilateral diffuse patchy alveolar infiltration	15 (16.7)	5 (6.9)
Bilateral multiple nodular lesions	10 (11.1)	3 (4.2)
Other		
Lung abscess	2 (2.2)	5 (6.9)
Mass-like lesion or pulmonary nodule	1 (1.1)	6 (8.3)
Interstitial infiltration	4 (4.4)	3 (4.2)
Miliary pattern	1 (1.1)	1 (1.4)
Pleural effusion	11 (12.2)	11 (15.3)
Hydropneumothorax	1 (1.1)	2 (2.8)
Pneumothorax	0 (0)	1 (1.4)
Pericardial effusion	0 (0)	2 (2.8)

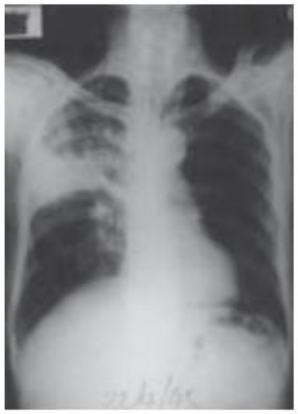

Fig 1–Localized patchy alveolar infiltration in the right upper lobe.

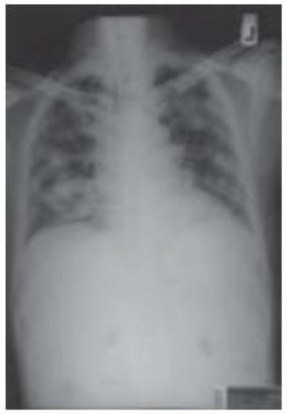

Fig 2–Bilateral diffuse patchy alveolar infiltration.

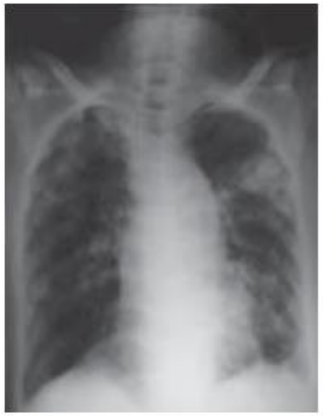

Fig 3–Bilateral multiple nodular lesions.

CLINICAL MANIFESTATION OF PULMONARY MELIOIDOSIS IN ADULTS

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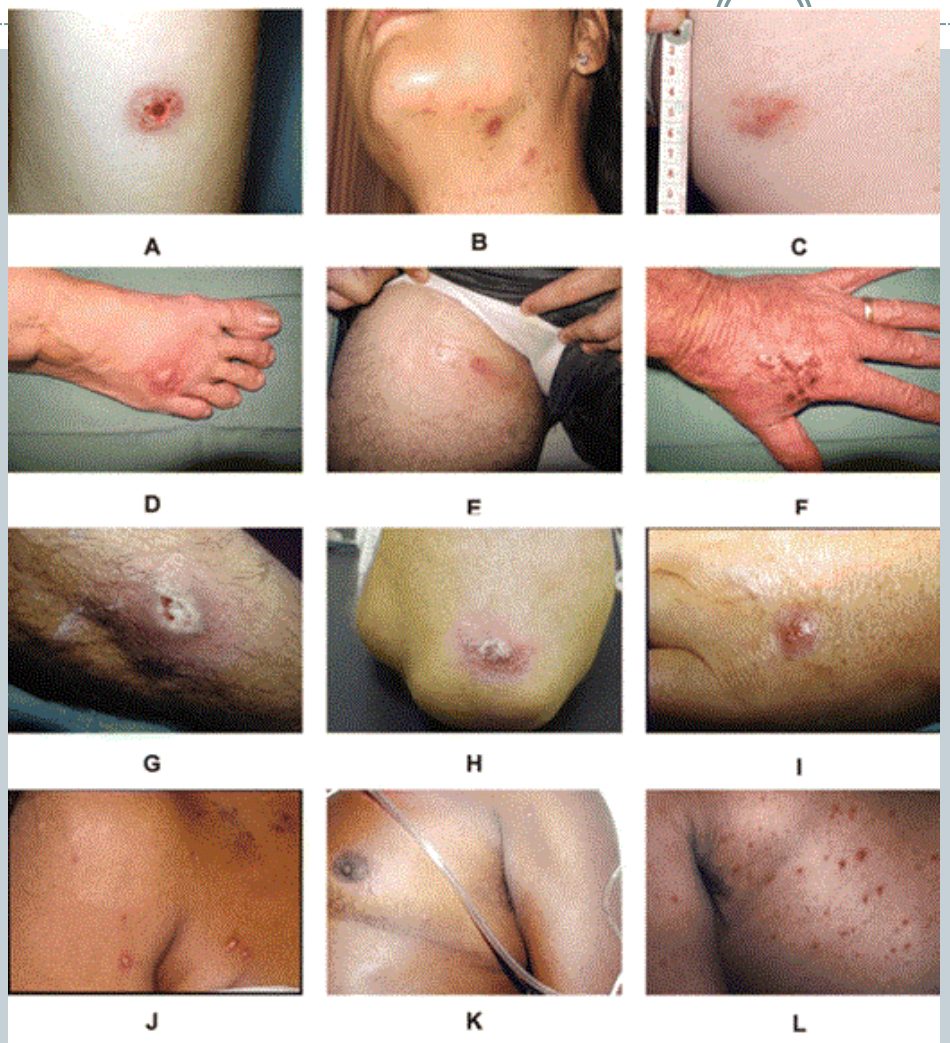
Cutaneous melioidosis

- Most common presentation was with an ulcer, with or without a purulent exudate.
- Other appearances included single pustules, boils, crusted erythematous lesions, and dry asymmetric erythematous flat lesions. Cellulitis was rare.
- Secondary skin melioidosis in the form of multiple pustules

Cutaneous melioidosis



Cutaneous Melioidosis in the Tropical Top End of Australia: A Prospective Study and Review of the Literature

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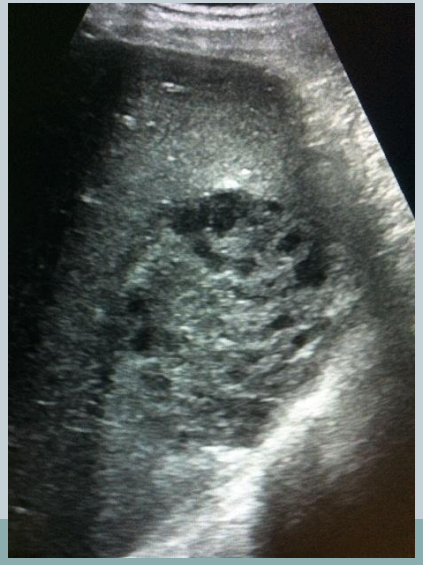
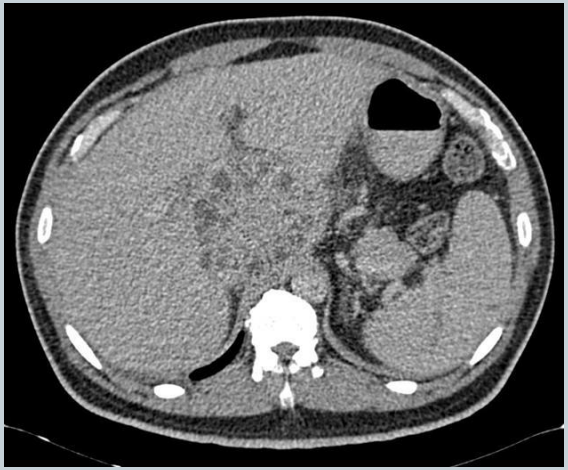
Internal organ abscesses

- Most commonly in the liver and spleen.
  - Appearances can range from a large 'honeycomb' type abscess to a multitude of microabscesses.
  - It can also occur, albeit far less commonly, in the pancreas, kidneys and even prostate gland (higher incidence in Australia than elsewhere)





Diagnosis

- Gram stain
  - Inconclusive diagnosis
- Culture
  - Gold standard
  - Ashdown medium
- Antigen detection
  - PCR
- Antibody detection
  - IHA
  - Inadequate for confirming the diagnosis, especially in endemic regions
  - In Thailand, background seropositive rate can be as high as 50%
  - Cut-off titer are varied
- Additional imaging : CXR, USG or CT scan depends on clinical suspicious

Diagnosis

- Melioid titer
- Cut-off at 1:160
  - Sens = 49-47%, Spec= 67-97%
- Cut-off at 1:320
  - Sens = 30-63%, Spec= 79-99%
- Useful in
  - Children
  - Non-endemic area
  - 4-fold rising at 1-2 wk

Treatment

BOX. Treatment recommendations for diagnosed melioidosis

Initial intensive therapy (lasting ≥14 days)		
Ceftazidime	50 mg/kg up to 2 g	Every 6 hours (IV*)
	or	
Meropenem	25 mg/kg up to 1 g	Every 8 hours (IV)
	or	
Imipenem	25 mg/kg up to 1 g	Every 6 hours (IV)
	and (optional)	
Trimethoprim-sulfamethoxazole	8 + 40 mg/kg up to 320 + 1,600 mg	Every 12 hours (PO†)
Eradication therapy (lasting ≥3 months)		
Trimethoprim-sulfamethoxazole	8 + 40 mg/kg up to 320 + 1,600 mg	Every 12 hours (PO)
	and (optional)	
Doxycycline	2 mg/kg up to 100 mg	Every 12 hours (PO)

* Intravenously.
† Orally.
SOURCE: Adapted from Currie BJ. Melioidosis: an important cause of pneumonia in residents of and travelers returned from endemic regions. Eur Respir J 2003;22:542–50.

Treatment

- The only treatment to demonstrate a mortality benefit is ceftazidime in a sequential open-label randomized trial of ceftazidime against chloramphenicol-doxycycline-TMP-SMX (known as conventional therapy) in severe disease.
- In Thai adults, the use of ceftazidime was associated with a 50% reduction in mortality, from 74 to 37%.
- Current studies include a trial of ceftazidime alone compared with ceftazidime with TMP-SMX, where no significant differences in mortality were demonstrated.
- A trial comparing the four-drug regimen(TMP-SMX, doxycyline, and chloramphenicol) with TMP-SMX and doxycycline has recently been completed in Thailand and suggests that TMP-SMX with doxycycline is associated with relapse rates equivalent to those with the four-drug regimen
- A future trial comparing TMP-SMX alone with TMP-SMX and doxycycline is planned.

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