MELIOIDOSIS GUIDELINE SUMMARY

What is melioidosis?

- Melioidosis is an infection caused by a soil and water bacterium called *Burkholderia pseudomallei*. Infection occurs through skin inoculation, ingestion or inhalation.

- Melioidosis is common and considered endemic to South East Asia.

- **Medical risk factors** include diabetes, chronic renal, lung or liver disease, hazardous alcohol use, immunosuppressive therapy, malignancies and thalassemia. Presence of medical risk factors increases risk of severe, potentially life threatening, disease.

- **Occupational and lifestyle risk factors** include those in contact with soil or water such as farmers, (rice, vegetable, rubber, orchards), fishing, construction workers, playing sport, drinking untreated water.

- Mortality following infection is high, with over 50% of patients dying within 48 hours of positive blood cultures

CLINICAL PRESENTATIONS

- Acute presentations accounts for the majority of infections (85% of cases). Chronic infection (those with symptoms for more than 2 months) accounts for 11% of infections. Reactivation of latent (hidden infection after prior exposure many months to years before) infection can occur (<4%).

- Pneumonia is the most common clinical presentation (>50%).

- Clinical presentation is varied and includes acute life-threatening pneumonia and/or sepsis, deep visceral abscesses (liver, spleen, kidney, prostate), head and neck abscesses, skin infections (ulcers, abscesses, cellulitis), joint and bone infections and bacteremia with no focus of infection.

- Melioidosis can affect any organ of the body and is a great mimicker of other diseases particularly TB.

- Children are less likely to have medical risk factors than adults; they account for 5-15% of all cases and often have head and neck abscesses with or without other sites of infection.

- Chronic infection can present with chronic respiratory symptoms, cervical lymphadenopathy, chronic skin ulcers/abscesses or deep visceral abscesses. These presentations can often be confused with TB or other infections.

DIAGNOSIS

- Diagnosis can be confirmed by culture of *Burkholderia pseudomallei* from any specimen type (blood, urine, sputum, pus, bodily fluids, bone, throat or rectal swabs).

- More than half of all patients presenting with sepsis are blood culture positive on admission to hospital, so **blood cultures are important to collect** on all patients suspected to have melioidosis.

- **To increase diagnostic yield, all** patients suspected to have an infection should have **blood, throat swabs** and urine collected.

Blood culture collection recommendations:

Adult	**2 adult bottles x 10 ml each**, separate venipuncture	Specimen should be collected prior to commencement of antibiotic therapy Be prepared to repeat if initial diagnosis remains negative and melioidosis remains a likely diagnosis
Children	1 pediatric bottle 2-5ml	

- **Additional specimens should also be collected** when present e.g. sputum, pus.

- As melioidosis and tuberculosis can present in a similar manner, sputum specimens should be sent for **both bacteriological culture and mycobacterial testing**. Two specimens may be required.

- It is recommended that laboratories use selective media (Ashdown's) for non-sterile specimens (e.g. throat swabs and sputum) to increase the chance of isolation and identification.

- Doctors should always include clinical presentation, risk factors and the suspicion of melioidosis on the microbiology request form so laboratory staff can process specimens appropriately.

- All suspect and culture confirmed cases should have chest x-ray and abdominal ultrasound performed to rule out additional sites of infection

DIFFERENTIAL DIAGNOSIS

Acute lung symptoms **-** other causes of community acquired pneumonia - *Streptococcus pneumoniae*
Chronic lung symptoms – TB (especially those with AFB smear negative sputum or those with previously treated TB), other infections, malignancy including metastases
Sepsis – other common causes of sepsis (E. coli, Staphylococcal infection, Salmonella Typhi/Paratyphi etc)
Deep abscesses – *Staphylococcus aureus, Klebsiella pneumoniae*, TB, amoebic abscess
Lymphadenopathy – TB (especially those who may have previously been unsuccessfully treated with anti-tuberculous treatment)
Skin abscesses – *Staphylococcu. aureus*, other infections
Chronic skin ulcers/wounds unresponsive to commonly prescribed antibiotics – mycobacteria, fungus
Septic arthritis/osteomyelitis – *Staphylococcus aureus*, TB

TREATMENT

- Start empirical treatment **only after collecting all essential clinical specimens** (**blood cultures**, **throat swab**, urine at a minimum)

- **Repeat blood cultures** weekly until negative. Duration of intensive phase treatment is taken from the **last** date of culture-positive blood or drainage specimen.

- There are 2 phases of treatment – intensive and eradication phases.

Intensive phase:

IV ceftazidime 2g IV every 6-8 hours (q6-8h) for at least 14 days
(children 50mg/kg per dose) (maximum 8 g per day for both children and adults)

Don't change treatment if patient's fever continues (median time to fever clearance is 9 days)

Consider adding **co-trimoxazole** (TMP-SMX) to intensive phase **if**
- deep tissue infection or
- patient's condition worsening despite drainage of pus or
- wanting to ensure tolerance (no side effects) to co-trimoxazole prior to discharge on oral medications.

Eradication Phase: After at least 14 days IV therapy and clinical improvement, change to oral **co-trimoxazole** for at least 3 months (12 weeks). Prolonged therapy is required to minimize risk of relapse. Osteomyelitis and CNS infection require 6 months treatment. Folic acid is also recommended when prescribing co-trimoxazole.

Table 1: Dosing of co-trimoxazole and folic acid by weight

Tablet and strength	Children	Adults		
		<40 kg	40-60 kg	>60 kg
80 mg TMP-400mg SMX (single strength) tablets	6/30mg/kg (Max. 3 po q12)	6/30mg/kg (Max. 3 po q12)	3 po q12	4 po q12
160mg TMP-800mg SMX (double strength tablets)	6/30mg/kg (Max. 1.5 po q12)	6/30mg/kg (Max.1.5 po q12)	1.5 po q12	2po q12
Folic acid	0.1 mg/kg (Max. 5mg)	0.1 mg/kg (Max. 5mg)	5mg	5mg

- Alternative treatments include co-amoxiclav (ratio 4:1) or doxycycline (100 mg bd). They are less effective than co-trimoxazole (TMP-SMX) with higher treatment failure rates

Table 2: Dosing of co-amoxiclav by weight

Tablet and strength	<60 kg	≥60kg
Co-amoxiclav (amoxicillin/clavulanate) 500 mg/125 mg tablet 8 hourly (must have **ratio 4:1** of **amox:clav**)	20/5mg/kg (Max. 2 tabs po q8h)	3 tabs po q8h

- Both phases should be extended beyond pre-specified duration if clinical response is slow or secondary foci develop whilst on treatment
- **Drain all abscesses where possible**
- Check for **secondary foci** (infections developing in other sites) particularly when patient's fever continues beyond expected time (median time to clearance is 9 days)
- Manage medical risk factors as well as possible to improve outcomes e.g. ensure good blood glucose control in diabetics
- **Regular clinical follow up** is required during admission and then **monthly** when discharged to ensure compliance and clinical improvement
- Mortality rate is high if patient is untreated or receives incorrect treatment
- Relapse is common if choice, duration or dosing of antibiotic therapy is inappropriate/incorrect.
- **Adherence to antibiotic therapy is crucial** in preventing relapse. Patient and caregivers should be counselled on a regular basis regarding the need to complete therapy**.**

PREVENTION

- Prevention should be targeted at the most common methods of transmission including:

    - Ingestion
        - Only drink treated or boiled water
        - Clean all vegetables with boiled or treated water only
        - Drink only pasteurized milk
        - Eat only cooked meat; infected carcasses should be destroyed

    - Skin inoculation
        - When in contact with soil or water during occupational or lifestyle activities (farming, construction, fishing, gardening), take precautions such as appropriate skin cover (boots or waterproof shoes, gloves)
        - If broken skin is exposed to water or soil e.g. during floods, wash well with soap and water
        - Avoid walking through floods with bare feet or uncovered skin
        - All skin abrasions and burns should be cleaned thoroughly

    - Inhalation
        - During rain and windstorms, stay indoors where possible
        - If going outside during rain or windstorms, wear protective mask to reduce the risk of inhalational exposure

- Person to person transmission in hospitals is very unlikely; ward staff do not need to take special precautions and patients do not have to be isolated.

- Microbiology laboratory staff should refrain from sniffing culture plates and all work should be carried out in a biosafety cabinet