Buruli ulcer

Synonyms: Bairnsdale ulcer, Daintree ulcer, Mossman ulcer, Searl ulcer, Kakerifu ulcer, Toro ulcer

What is a Buruli ulcer?[1]

Buruli ulcer is a chronic debilitating disease that mainly affects the skin and sometimes bone. The name Buruli comes from an area of Uganda where many cases were reported in the 1960s.

Buruli ulcer is caused by *Mycobacterium ulcerans* and belongs to the family of bacteria that causes tuberculosis and leprosy. Although the causative organism of Buruli ulcer is an environmental bacterium, the mode of transmission to humans remains unknown. The organism produces a unique toxin – mycolactone – that causes the damage to the skin. Early diagnosis and treatment are crucial to minimising morbidity, costs and prevent long-term disability.

How common are Buruli ulcers? (Epidemiology)[1]

The largest number of endemic cases occurs in central and western Africa. Other affected areas include Australia, South-East Asia, and sporadic cases in Central America and South America.

The annual number of suspected Buruli ulcer cases reported globally was around 5000 cases up until 2010, when it started to decrease until 2016, reaching its minimum with 1961 cases reported. The number of cases then started to rise again every year, up to 2713 cases in 2018. Since then, the numbers of cases have been declining in 2019 (2271); 2020 (1458) and 2021 (1370). The reductions seen in 2020 and 2021 could be linked to the impact of COVID-19 on active detection activities.

In Africa, about half of the patients are children under 15 years. In Australia, the average age is around 60 years.

The exact mode of transmission of *M. ulcerans* is still unknown.

Risk factors

- For many years the mode of transmission has been unknown, however use of polymerase chain reaction (PCR) has revealed that water bugs and small fish carry *M. ulcerans* in their salivary glands. [2]
- Many victims are agricultural workers or children who live near slow-flowing or stagnant water.
- Direct skin inoculation is believed to be the route of transmission by a bite.

Buruli ulcer symptoms (presentation) [1]

The incubation period varies from 2 months to several years. The initial injury often goes unnoticed.

Buruli ulcer often starts as a painless swelling (nodule), a large painless area of induration (plaque) or a diffuse painless swelling of the legs, arms or face (oedema). The disease may progress with no pain and fever.

Without treatment or sometimes during antibiotics treatment, the nodule, plaque or oedema will ulcerate within 4 weeks. Bone is occasionally affected, causing deformities.

The disease has been classified into three categories of severity:

- Category I, single small lesion (32%) less than 5 cm on diameter.
- Category II, non-ulcerative and ulcerative plaque and oedematous forms between 5-15 cm (35%).
- Category III lesions more than 15 cm in diameter including, disseminated and mixed forms such as, osteomyelitis and joint involvement (33%).

Lesions frequently occur in the limbs: 35% on the upper limbs, 55% on the lower limbs, and 10% on the other parts of the body.

Differential diagnosis[1]

These include:

- Filariasis.
- Leprosy
- Yaws
- Deep fungal infection such as blastomycosis or coccidioidomycosis
- Mycetoma.
- Cutaneous leishmaniasis.
- Ulcerative squamous cell carcinoma
- Other causes of ulceration such as diabetes, arterial and venous insufficiency lesion.

Investigations[1] [3]

In most cases, experienced health professionals in endemic areas can make a reliable clinical diagnosis.

Four standard laboratory methods can be used to confirm Buruli ulcer:

- Polymerase chain reaction (PCR).
- Direct microscopy.
- Histopathology.
- Culture: the bacterium grows best at temperatures between 29–33 °C and needs a low (2.5%) oxygen concentration.

X-rays and ultrasound may be required for deep lesions.

Buruli ulcer treatment and management[1]

Treatment consists of a combination of antibiotics and interventions such as wound and lymphoedema management and surgery.

- Daily oral rifampin and intramuscular streptomycin for 8 weeks was introduced in the early 2000s and is recommended by the WHO:[4]
    - A review of treatment studies performed in 8 African countries and one in Australia showed that this regimen achieved on average a 50% cure rate.
    - This antibiotic regimen is very effective for lesions that are less than 10 cm in diameter, as these patients may not require surgery.
- A recent study suggests the combination of rifampicin (10 mg/kg once daily) and clarithromycin (7.5 mg/kg twice daily) is now the recommended treatment.
- In Australia, a combination of rifampicin (10 mg/kg once daily) and moxifloxacin (400 mg once daily) is routinely used with good results, but its effectiveness has not been proven in a randomised trial.
- Priority research for treatment is to shorten the duration of treatment from 8 weeks.
- Interventions such as wound and lymphoedema management and surgery (mainly debridement and skin grafting) are used to speed up healing, thereby shortening the duration of hospitalisation.
- Physiotherapy is needed in severe cases to prevent disability. Those left with disability require long-term rehabilitation.

Complications

- Buruli ulcer has been associated with osteomyelitis during the ulcerative stage.
- Scarring, contractures, and lymphoedema may cause severe deformity and psychosocial difficulties.
- Untreated advanced disease can cause death by sepsis.

Prognosis[3]

- Early case detection and rapid initiation of treatment are key elements to prevent the development of large, disfiguring ulcers often associated with permanent physical disability and stigma.

- Early aggressive surgical treatment appears to provide the best chance of cure.
- Ulcers have been reported to heal spontaneously, but can result in a depressed scar with contractures and consequent severe deformities.
- Circumferential involvement of extremities can require amputation.

Prevention[1]

- There are currently no primary preventive measures for Buruli ulcer. The mode of transmission is not known.
- Bacillus Calmette–Guérin (BCG) vaccination appears to provide limited protection.
- The objective of Buruli ulcer control is to minimise the suffering, disabilities and socioeconomic burden. Early detection and antibiotic treatment are the cornerstones of the control strategy.

Further reading

- Buruli ulcer; DermNet.

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Originally Published: 20/11/2023	Next review date: 22/09/2023	Document ID: doc_1897