

Buruli ulcer and Australian wildlife

Fact Sheet

January 2024

Key points

- *Mycobacterium ulcerans* causes slow-growing, destructive skin ulcers in humans and some Australian mammals.
- Infection is endemic in certain areas of Vic and Far North Qld, and has been reported in the NT and Batemans Bay area of NSW.
- The bacterium is an environmental pathogen, with evidence of both vector-borne (bite from infected mosquitoes) and zoonotic transmission (via faecal contamination from the environment, or rarely, bite from infected possum) occurring in Vic.
- People who work with wildlife in endemic areas of Australia should be alert to the possibility of this disease, especially if they encounter native mammals with skin ulcers.

Introductory statement

Mycobacterium ulcerans disease (referred to globally as Buruli ulcer (BU), also as ‘Bairnsdale ulcer’ in Vic and ‘Daintree ulcer’ in Qld) is recognised as one of the world’s neglected tropical diseases. It is primarily considered a human disease and infection in humans is characterised by progressive, painless destruction and necrosis of the skin, leading to the formation of ulcers. Australia is the only developed country with significant local transmission of *M. ulcerans* disease in humans. The mode of transmission and environmental reservoirs are not completely understood, but research in Australia increasingly suggests a role for mosquitoes as vectors, with small mammals, particularly ringtail and brushtail possums, as reservoirs.

Aetiology

Mycobacterium ulcerans [MU] (Family *Mycobacteriaceae*) is a slow growing mycobacterium, closely related to *M. marinum*, and to the mycobacteria that cause tuberculosis and leprosy. *Mycobacterium ulcerans* produces a destructive toxin, mycolactone, which causes tissue damage and inhibits the local immune response.

One Health implications

Wildlife and the environment: *M. ulcerans* can cause disease in a range of native mammal species, however there is no evidence of population-level impacts. Small mammals, particularly ringtail and brushtail possums, may be reservoirs for the bacterium.

Domestic animals: *M. ulcerans* can cause disease in a range of domestic animals in endemic areas (see below), but cases occur infrequently.

Humans: disease occurs in humans in endemic areas and is notifiable in the state of Victoria ^[1]. All age groups of humans are at risk, however severe disease is more common in older patients in Australia ^[2].

Natural hosts

The bacterium has been reported a range of both domestic and wildlife mammalian species in endemic areas of Australia. Laboratory-confirmed disease has been diagnosed in humans, koalas (*Phascolarctos cinereus*) ^[3], common ringtail possums (*Pseudocheirus peregrinus*), a common brushtail possum (*Trichosurus vulpecula*), a mountain brushtail possum (*T. cunninghami*), a long-footed potoroo (*Potorous longipes*), a black rat (*Rattus rattus*)¹ as well as horses, dogs, a cat and an alpaca. The organism has been found in the faeces of ringtail and brushtail possums, northern brown bandicoots (*Isodon macrourus*) and feral red foxes in endemic areas of Australia ^[4-9].

World distribution

Human disease occurs in over 30 countries worldwide. Foci of infection have been reported in Australia (see below), Africa (e.g. Benin, Cote d'Ivoire and Ghana), Asia and the Western Pacific (e.g. Japan and Papua New Guinea), and the Americas (e.g. French Guiana).

Occurrences in Australia

There are several recognised endemic areas for BU in humans in Australia: Far North Qld (FNQ) between Mossman and the Daintree River, the Capricorn Coast of Qld, East Gippsland near Bairnsdale, Vic; and the Mornington and Bellarine Peninsulas of Vic, not far from Melbourne. In 2019, two new transmission areas were identified in Victoria, Airey's Inlet (Surf Coast) and the Geelong suburb of Belmont ^[10]. Buruli ulcer has been reported in the NT ^[11]. In 2023, three cases (two retrospective) were identified in humans in the Batemans Bay area of NSW, with all cases believed to have been infected locally since 2021 ^[12].

Since 2020, cases have been reported in ringtail possums, and humans, in Essendon, Moonee Ponds and Brunswick West, inner northern suburbs of Melbourne ^[13]. These are the first non-coastal locations in Vic recognised as potential risk areas for MU infection ^[14]. In April 2022, this was extended to include the neighbouring suburbs of Pascoe Vale South and Strathmore ^[10]. In Vic, case numbers in humans have increased significantly over the past decade [340 reported human cases in Vic in 2018; 285 in 2021 ^[15]], as have the number of human cases associated with severe disease ^[2].

Laboratory-confirmed cases of MU disease in wildlife have only been reported in Vic. All reported cases in wildlife have been identified in locations where human cases have also occurred. There have been no confirmed cases of MU disease in wildlife in Qld, NT or other states. In NSW, in reptiles, there have been confirmed infections with a different subspecies of MU, not associated with human disease (J Fyfe pers. comm. September 2018).

¹ National wildlife health information system (eWHIS) data.

A study found 9 of 42 ringtail and 1 of 21 brushtail possums examined at an endemic Victorian site had clinical BU lesions. Of these cases, 82% (9/11) of ringtail possums also had MU positive faeces, compared to 16% (5/31) of ringtail possums without BU lesions, at the same location ^[4].

Epidemiology

Globally, the geographic distribution of human BU case clusters is always highly focal ^[6].

The epidemiology of MU disease in Australia is not well understood and appears to be changing in south-east Australia, with increasing numbers of human cases and expansion into new geographic areas ^[2]. The reasons for the change in epidemiology are not known. Most recent Australian studies have focused on endemic and emerging-endemic areas in Victoria. More information is available at www.health.vic.gov.au/infectious-diseases/beating-buruli-in-victoria.

The **incubation period** is unknown in animals, but in humans it may be as long as several months (median 4.5 months) ^[16]. Humans come into contact with the pathogen only in specific geographic areas, which are frequently near water bodies – either along coastal areas or inland near slow flowing rivers, swamps and lakes. In Vic, the presence of environmental water does not appear to be as clear a risk factor as in West Africa ^[9].

The **mode of transmission** is unconfirmed, but MU is considered an environmental pathogen and is very rarely transmitted from person-to-person (only one case of human-to-human transmission has been documented, in a West African child bitten by a playmate) ^[17]. Exposure to the pathogen is thought to occur primarily via contaminated water, soil or vegetation in specific geographic areas, or by the puncture of a biting insect ^[9, 18], or by the bite wound from an infected small mammal such as a possum. Skin injuries are considered a potential route of infection from an environmental reservoir of *M. ulcerans* ^[19]. There is increasing evidence that terrestrial mammals and mosquitos are likely to play an epidemiological role ^[20]. *Aedes notoscriptus* mosquitoes are likely vectors in Vic, where they have been shown to carry *M. ulcerans*, and to sequentially feed from ringtail possums and humans ^[18].

Clinical cases have been reported in a range of **marsupial species** from endemic areas of Vic ^[4, 7]. There appears to be a significant disease burden in ringtail possums in some areas and adult animals appear to be most commonly affected. Ringtail possums appear more likely to have persistent lesions and to suffer from systemic disease associated with BU than other infected marsupials ^[7].

Research has investigated a potential role for a **mammalian reservoir or amplifying host**. In Vic, common ringtail and common brushtail possums from endemic areas, both with and without clinical disease, have been shown to shed MU in their faeces ^[4, 6, 7, 9, 18, 21]. Focal areas of high prevalence of MU in possum faeces corresponded to focal areas of human cases ^[4, 6, 21]. Studies in Vic have found an association between cases in humans and the presence of ringtail possums with MU positive faeces in the same area ^[9, 21]. MU was also found in the faeces of feral red foxes and it is hypothesized that they may play a role in geographic spread of the disease ^[9].

These findings suggest a common environmental source of infection and an epidemiologically important role for possums, and possibly foxes. One hypothesis is that possums or other terrestrial

mammals act as an environmental reservoir of MU in SE Australia; they may ingest the organism from the environment, amplify it and shed it in the faeces. There is only one report identifying direct transmission of MU from a ringtail possum to a human in Australia [20].

Research increasingly suggests a role for **mosquitoes or other biting vectors** in the transmission of *M. ulcerans* from the environment to humans in Vic [22-26], however it is likely that there are several routes of infection, including possibly other puncturing injuries [25].

The epidemiological model in **FNQ** appears to be different to SE Australia, with outbreaks occurring sporadically, possibly associated with heavy rainfall and associated environmental changes. Research in these areas found MU in northern brown bandicoot faeces, indicating a possible role for this wildlife species in the ecology of MU disease [5].

It is possible that there are different modes of transmission for different geographic and epidemiological scenarios [27] and that there are differences in virulence across geographically separate strains. Evidence suggests transmission may occur after exposure times of less than two hours [16]. The long incubation period in humans and frequently, an extended period to diagnosis have hindered an understanding of the epidemiology.

Clinical signs and diagnosis

In wildlife, the most common clinical presentation is an ulcer or lesion, usually on the animal's nose, ear, paw or tail (Fig. 1). Behavioural signs may include lethargy, limited movement and, in the case of koalas, resting on the ground. Slow-growing destructive skin ulcers are also typical in humans and other domestic animals.

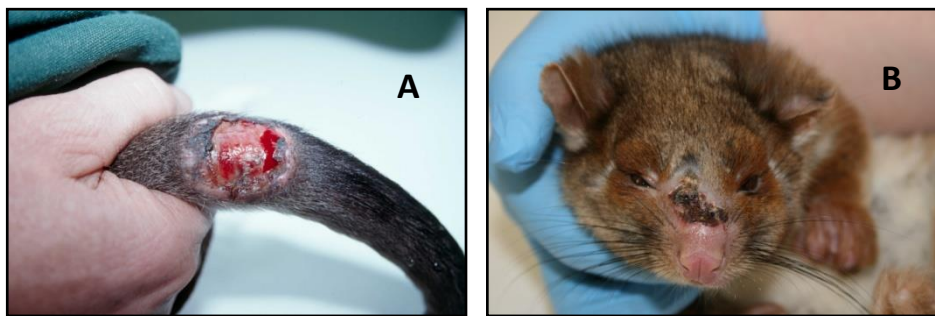


Figure 1. A. Long-footed potoroo with large lesion at the base of the tail. B. Ringtail possum with lesion on the nose

Diagnostic criteria include:

- animal lives in an endemic area
- animal has an ulcer with no other apparent cause, usually on an extremity, and which may have undermined edges
- acid-fast bacilli demonstrated in diagnostic specimens.

Laboratory diagnostic specimens and procedures

Collect:

- swabs (dry or in transport medium)
- fresh tissue
- paraffin-embedded fixed tissue sections.

Diagnostic procedures:

- direct smear examination for acid fast bacilli (AFB)
- culture for *M. ulcerans*
- polymerase chain reaction (PCR)
- histopathology.

PCR is the most rapid, sensitive and specific method for the diagnosis of *M. ulcerans* disease [28]. This test is performed at the Victorian Infectious Diseases Reference Laboratory (address: 792 Elizabeth St, Melbourne 3000, phone: 03 9342 9379, www.vidrl.org.au). It is advisable to contact the laboratory prior to sending a specimen for testing.

Clinical pathology and pathology

Most cases of *M. ulcerans* in wildlife exhibit cutaneous ulcerative lesions, sub-cutaneous nodules or swelling of paws, limbs or digits. There may be an undermined skin ulcer, with necrotic fat frequently visible at the base (Fig. 1). There may be minimal inflammatory response. Systemic infection is also known to occur. Necropsy examinations of a long-footed potoroo, koalas and ringtail possums have revealed the presence of *M. ulcerans* in internal organs as well as cutaneous lesions. The bacterium produces mycolactone toxin, which causes tissue damage and hinders the local immune response.

Differential diagnoses

Other causes of skin ulcers in Australian mammals include trauma, other mycobacterial and infectious skin ulcers; sarcoptic mange or other external parasite infestations [29]; poxvirus infections [30]; fungal infections and exudative dermatitis of possums [31]; and tularaemia [32].

Treatment

Various medical and surgical methods have been used to treat MU disease in domestic animals, including antibiotic treatment, surgical excision and cryosurgery [33-35]. In wildlife, the infection has been known to resolve without treatment, as in the case of a mountain brushtail possum from Bellbird Creek (Fig. 2) and a brushtail possum from Point Lonsdale (unpublished). In severe cases, animals have been euthanased. Human treatment is not addressed in this Fact Sheet.



Figure 2. Mountain brushtail possum with lesion (A) at diagnosis and (B) later without treatment.

Prevention and control

Effective strategies for prevention and control of the disease in wild animals are not considered feasible. People working with wildlife in endemic areas of Australia should be alert to the possibility of this disease if they encounter native mammals with skin ulcers. Referral of diseased animals for treatment or euthanasia by veterinarians experienced in the diagnosis of this condition is recommended.

People are advised to adopt a range of precautions in endemic areas, including covering up when outdoors, avoiding insect (in particular mosquito) bites, protecting skin wounds with occlusive dressings and promptly disinfecting any new scratches or cuts. More information is available at: www.health.vic.gov.au/infectious-diseases/mycobacterium-ulcerans-infection. Early diagnosis in humans is critical for treatment ^[10]. More information on mosquito control and bite prevention is available at: www.betterhealth.vic.gov.au/protect-yourself-mosquito-borne-disease.

Research

The WHO has identified six main priorities for research into BU: mode of transmission; development of simple diagnostic tests; drug treatments and new treatment modalities; development of vaccines; social and economic studies; and studies to determine the incidence and prevalence.

In Australia, much research has focused on determining the mode of transmission and environmental source of MU. Further work is needed to gain a better understanding of the potential role of ringtail and brushtail possums, if there are any epidemiological interactions between these two species, and whether the relative population density of ringtail and brushtail possums influences endemicity and/or emergence of BU in humans. Possum faecal surveys may provide a useful public health monitoring tool and may act as sentinels for incidence in humans.

Work is required to better understand the prevalence of MU lesions in possums in human endemic areas, the susceptibility of different Australian marsupial species to MU infection, the possibility of gut amplification in marsupial species and whether MU disease poses a risk to populations of possums or other marsupial species.

Genomic studies could help to explore whether different pathogen strains are associated with different virulence, and whether strains are evolving and changing in virulence over time ^[2].

Surveillance and management

There is no targeted surveillance program for MU disease in wildlife. A greater awareness of the disease among veterinarians and wildlife carers, particularly in endemic areas of Vic, as well as active case finding as part of research, has led to increased reporting of cases in wildlife and domestic animals.

The WHO Collaborating Centre for MU – based at the Victorian Infectious Diseases Reference Laboratory (VIDRL) in Melbourne – maintains records of all known human and animal cases of MU disease in Australia. In Victoria, the Department of Health publishes statistics on notifiable infectious diseases (in humans), including MU infection, on its website www.health.vic.gov.au.

Wildlife Health Australia administers Australia's general wildlife health surveillance system, in partnership with government and non-government agencies. Wildlife health data is collected into a national database, the electronic Wildlife Health Information System (eWHIS). Information is reported by a variety of sources including government agencies, zoo based wildlife hospitals, sentinel veterinary clinics, universities, wildlife rehabilitators, and a range of other organisations and individuals. Targeted surveillance data is also collected by WHA. See the WHA website for more information <https://wildlifehealthaustralia.com.au/Our-Work/Surveillance> and <https://wildlifehealthaustralia.com.au/Our-Work/Surveillance/eWHIS-Wildlife-Health-Information-System>. There are over 30 cases reported in eWHIS from free-living marsupials from endemic areas of Vic, mostly in ringtail possums.

WHA is interested in hearing from anyone with information on this condition in Australia, including laboratory reports, historical datasets or survey results that could be added to the National Wildlife Health Information System. If you can help, please contact us at admin@wildlifehealthaustralia.com.au.

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Wildlife Health Australia recognises the Traditional Custodians of Country throughout Australia. We respectfully acknowledge Aboriginal and Torres Strait Islander peoples' continuing connection to land, sea, wildlife and community. We pay our respects to them and their cultures, and to their Elders past and present.

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