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 (*Isoodon 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.

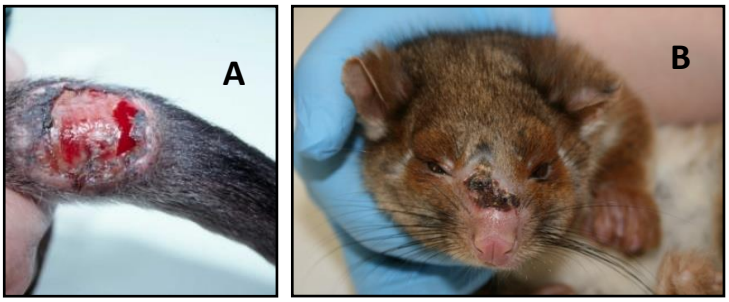

Figure 1. A. Long-footed potoroo with large lesion at the base of the tail. B. Ringtail possum with lesion on the nose

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.

Acknowledgements

We are grateful to the people who had input into this fact sheet and would specifically like to thank the Victorian Infectious Diseases Reference Laboratory (VIDRL), Christina McCowan, Caroline Lavender, Janet Fyfe, John Hayman and Emma Hobbs who have a special interest in this condition in Australia.

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.

Updated: January 2024

References

1. Vic Department of Health (2022) Buruli ulcer (*Mycobacterium ulcerans* infection). 8 Nov 2022; Available from: https://www.health.vic.gov.au/infectious-diseases/mycobacterium-ulcerans-infection
2. Tai AY, Athan E et al. (2018) Increased severity and spread of *Mycobacterium ulcerans*, southeastern Australia. *Emerging Infectious Diseases*, **24**(1): 58
3. McOrist S, Jerrett IV et al. (1985) Cutaneous and respiratory tract infection with *Mycobacterium ulcerans* in two koalas (*Phascolarctos cinereus*). *Journal of Wildlife Diseases*, **21**(2): 171-173
4. Fyfe JA, Lavender CJ et al. (2010) A major role for mammals in the ecology of *Mycobacterium ulcerans. PLOS Neglected Tropical Diseases*, **4**(8): e791
5. Röltgen K, Pluschke G et al. (2017) *Mycobacterium ulcerans* DNA in bandicoot excreta in Buruli ulcer–endemic area, Northern Queensland, Australia. *Emerging Infectious Diseases*, **23**(12): 2042
6. Carson C, Lavender CJ et al. (2014) Potential wildlife sentinels for monitoring the endemic spread of human Buruli ulcer in south-east Australia. *PLOS Neglected Tropical Diseases*, **8**(1): e2668
7. O'Brien C, Handasyde KA et al. (2014) Clinical, microbiological and pathological findings of *Mycobacterium ulcerans* infection in three Australian possum species. *PLOS Neglected Tropical Diseases*, **8**(1): e2666

8. Singh A, William McBride J et al. (2019) Survey of local fauna from endemic areas of Northern Queensland, Australia for the presence of *Mycobacterium ulcerans. International Journal of Mycobacteriology*, **8**(1): 48-52

9. Blasdell KR, McNamara B et al. (2022) Environmental risk factors associated with the presence of *Mycobacterium ulcerans* in Victoria, Australia. *PLoS One*, **17**(9): e0274627

10. Vic Health (2022) Beating Buruli in Victoria. 4 May 2022; Available from: https://www.health.vic.gov.au/infectious-diseases/beating-buruli-in-victoria#buruli-ulcer-in-victoria-%E2%80%93-past-and-present

11. Nohrenberg M, Wright A et al. (2023) Non-tuberculous mycobacterial skin and soft tissue infections in the Northern Territory, Australia, 1989-2021. *International Journal of Infectious Diseases*, **135**: 125-131

12. Southern NSW Health District (2023) Locally transmitted Buruli ulcer cases identified on the NSW south coast. 8 Sept 2023; Available from: https://www.snswlhd.health.nsw.gov.au/about-us/newsroom/media-releases/locally-transmitted-buruli-ulcer-cases-identified

13. Ban S, Cox-Witton K et al. (2020) *Mycobacterium ulcerans* in a ringtail possum in a new location. *Animal Health Surveillance Quarterly*, **25**(3): 13-17

14. Vic Health (2022) Buruli ulcer bacteria identified in inner north Melbourne. 4 May 2022; Available from: https://www.health.vic.gov.au/health-advisories/buruli-ulcer-bacteria-identified-in-inner-north-melbourne

15. Vic Health (2022) Local Government areas surveillance report. Available from: https://www.health.vic.gov.au/infectious-diseases/local-government-areas-surveillance-report

16. Trubiano JA, Lavender CJ et al. (2013) The incubation period of Buruli ulcer (*Mycobacterium ulcerans* infection). *PLOS Neglected Tropical Diseases*, **7**(10): e2463

17. Debacker M, Zinsou C et al. (2003) First case of *Mycobacterium ulcerans* disease (Buruli ulcer) following a human bite. *Clinical Infectious Diseases*, **36**(5): e67-e68

18. Mee PT, Buultjens AH et al. (2024) Mosquitoes provide a transmission route between possums and humans for Buruli ulcer in southeastern Australia. *Nature Microbiology*. 10.1038/s41564-023-01553-1

19. Röltgen K, Johnson PD et al. (2022) Epidemiology of Buruli Ulcer. In 'Leprosy and Buruli Ulcer.' pp. 541-550. (Springer)

20. Xu RW, Stinear TP et al. (2022) Possum bites man: case of Buruli ulcer following possum bite. *Medical Journal of Australia*, **216**(9): 452-453

21. Vandelannoote K, Buultjens AH et al. (2023) Statistical modeling based on structured surveys of Australian native possum excreta harboring *Mycobacterium ulcerans* predicts Buruli ulcer occurrence in humans. *eLife*, **12**: e84983

22. Johnson P and Lavender C (2009) Correlation between Buruli ulcer and vector-borne notifiable diseases, Victoria, Australia. *Emerging Infectious Diseases*, **15**(4): 614-615

23. Johnson P, Azuolas J et al. (2007) *Mycobacterium ulcerans* in mosquitoes captured during an outbreak of Buruli ulcer, southeastern Australia. *Emerging Infectious Diseases*, **13**(11): 1653-1660

24. Quek TY, Athan E et al. (2007) Risk factors for *Mycobacterium ulcerans* infection, southeastern Australia. *Emerging Infectious Diseases*, **13**(11): 1661-6

25. Wallace JR, Mangas KM et al. (2017) *Mycobacterium ulcerans* low infectious dose and mechanical transmission support insect bites and puncturing injuries in the spread of Buruli ulcer. *PLOS Neglected Tropical Diseases*, **11**(4): e0005553

26. Johnson P (2019) Buruli ulcer in Australia. In 'Buruli Ulcer.' (Eds G. Pluschke and K. Röltgen) pp. 61-76. (Springer: Tokyo)

27. Singh A, McBride W et al. (2018) Potential animal reservoir of *Mycobacterium ulcerans*: A systematic review. *Tropical Medicine and Infectious Disease*, **3**(2): 56

28. Fyfe JA, Lavender CJ et al. (2007) Development and application of two multiplex real-time PCR assays for the detection of *Mycobacterium ulcerans* in clinical and environmental samples. *Applied and Environmental Microbiology*, **73**(15): 4733-4740

29. Booth R (1994) Medicine and husbandry: dasyurids, possums and bats. *Wildlife: The TG Hungerford Refresher Course for Veterinarians Proceedings*, **233**: 423-41

30. Vogelnest L, Stewart S et al. (2012) Poxvirus infection outbreak in common ringtails (*Pseudocheirus peregrinus*). *Australian Veterinary Journal*, **90**(4): 143-145

31. Johnson R and Hemsley S (2008) Gliders and possums. In 'Medicine of Australian mammals.' (Eds L. Vogelnest and R. Woods) pp. 395-437. (CSIRO)

32. Eden JS, Rose K et al. (2017) *Francisella tularensis* ssp. *holarctica* in ringtail possums, Australia. *Emerging Infectious Diseases*, **23**(7): 1198-1201

33. Elsner L, Wayne J et al. (2008) Localised *Mycobacterium ulcerans* infection in a cat in Australia. *Journal of Feline Medicine & Surgery*, **10**(4): 407-12

34. O'Brien C, McMillan E et al. (2011) Localised *Mycobacterium ulcerans* infection in four dogs. *Australian Veterinary Journal*, **89**(12): 506-10

35. van Zyl A, Daniel J et al. (2010) *Mycobacterium ulcerans* infections in two horses in south-eastern Australia. *Australia Veterinary Journal*, **88**(3): 101-106

To provide feedback on Fact Sheets

Wildlife Health Australia welcomes your feedback on Fact Sheets. Please email admin@wildlifehealthaustralia.com.au. We would also like to hear from you if you have a particular area of expertise and are interested in creating or updating a WHA Fact Sheet. A small amount of funding is available to facilitate this.

Disclaimer

Wildlife Health AUSTRALIA

Find out more at **wildlifehealthaustralia.com.au**

Email: **admin@wildlifehealthaustralia.com.au**

Or call +61 2 9960 6333