Epidemiol. Infect. (1997), **119**, 313–318. Printed in the United Kingdom

A large localized outbreak of *Mycobacterium ulcerans* infection on a temperate southern Australian island

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(*Accepted 1 August 1997*)

SUMMARY

Mycobacterium ulcerans, the organism which causes Buruli or Bairnsdale ulcer, has never been isolated in culture from an environmental sample. Most foci of infection are in tropical regions. The authors describe the first 29 cases of *M. ulcerans* infection from a new focus on an island in temperate southern Australia, 1992–5. Cases were mostly elderly, had predominantly distal limb lesions and were clustered in a small region in the eastern half of the main town on the island. The authors suspected that an irrigation system which lay in the midst of the cluster was a source of infection. Limitation of irrigation was associated with a dramatic reduction in the number of new cases. These findings support the hypothesis that *M. ulcerans* has an aquatic reservoir and that persons may be infected directly or indirectly by mycobacteria disseminated locally by spray irrigation.

INTRODUCTION

Mycobacterium ulcerans infection causes slowly progressive, undermined skin ulceration [1]. Geographical foci of endemic disease due to *M. ulcerans* infection occur in many tropical and sub-tropical areas of the world [2], and have given rise to eponyms for the condition including Buruli ulcer (Uganda) [3] and Kumusi Ulcer (Papua New Guinea) [4].

The ecological niche of *M. ulcerans* is unknown. Humans appear to acquire infections from an environmental source. Foci of disease are typically related to substantial natural bodies of water but *M. ulcerans* has never been isolated in culture from an environmental site [5]. There are no known natural animal reservoirs. Koalas (*Phascolarctos cinereus*) are the only animal known to acquire *M. ulcerans* infection naturally [6], although this appears to be a rare event.

Sporadic cases of *M. ulcerans* infection (known locally as Bairnsdale ulcer) have been reported from the Gippsland region of temperate south-eastern Australia since the late 1930s [7]. During the 1980s cases were first reported from areas around Western Port, 140 km west of the Gippsland foci (Fig. 1), and since 1990 there have been 10 cases from another new

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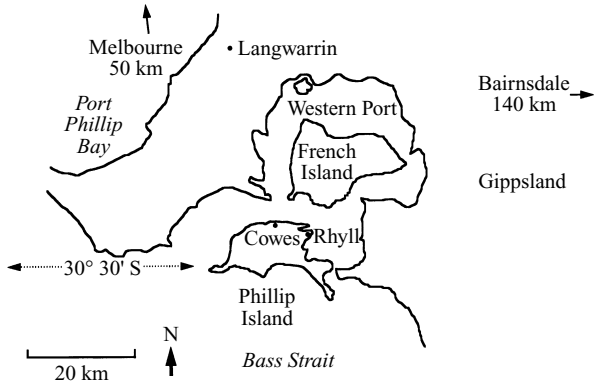

Fig. 1. The Western Port region, southern Victoria, Australia.

focus at Langwarrin, on the outskirts of southern suburban Melbourne [8].

Phillip Island (38° 30′ S) lies within Western Port, 75 km south-east of Melbourne (population 3·2 million). The climate is temperate. About half the permanent island population of 5000 live in the main town, Cowes. From Christmas to the end of January each year the island population increases to approximately 40000 with summer holiday-makers. No case of *M. ulcerans* infection had been associated with Phillip Island before a Phillip Island family physician (P. E. F.) diagnosed *M. ulcerans* infection in a permanent resident of Cowes in June 1993, and three further local cases in the following 2 months.

In this paper we describe the emergence of *M. ulcerans* infection on Phillip Island – the epidemiology of cases, their geographical and environmental associations, and the effect of a public health intervention.

METHODS

We established and maintained active surveillance for cases with an intense local campaign to educate residents and visitors and by sending information about this new focus of a rare infection to clinicians and diagnostic services state-wide.

The Victorian Mycobacterium Reference Laboratory cultured biopsies of ulcers from cases. *M. ulcerans* was identified as non-pigmented, cord-forming colonies which grew very slowly on Lowenstein–Jensen or Brown and Buckle media at 31 °C but not at 36 °C [9], *M. ulcerans* was distinguished from *M. haemophilum* by the dependence of *M. haemophilum* on ferric ammonium citrate in media [10].

Persons from whom positive cultures were not obtained were defined as having diagnostic histological features of *M. ulcerans* infection if sections showed acid-fast bacilli, features characteristic of mycobacterial infection (Langhans-type giant cells, macrophages with epithelioid change, and granuloma formation) and specific histological features of *M. ulcerans* infection (skin and fat necrosis, pseudoepitheliomatous hyperplasia, medial thickening and occlusion of small and medium sized arteries) [11, 12]. If specific features were present but acid-fast bacilli were not seen or cultured, the appearance was considered consistent with but not diagnostic of *M. ulcerans* infection. All histological specimens were examined by the one pathologist (J. A. H.).

A definite case of *M. ulcerans* infection associated with Phillip Island was a person who had visited or lived on Phillip Island since 1992, who had a skin ulcer or nodule from which *M. ulcerans* was cultured. Suspected cases were culture-negative or were not cultured but had diagnostic or consistent histological features of *M. ulcerans* infection. We excluded persons exposed to other foci of endemic *M. ulcerans* infection.

We asked cases to recall when they first recognized their skin lesion and attempted to define their whereabouts and activities in the preceding months.

We asked local wildlife officers to look for disease in koalas and to review autopsy records of koalas for ulcerative conditions.

RESULTS

Case characteristics

We cultured *M. ulcerans* from 18 cases. Eleven suspected cases comprised 7 culture-negative cases (one with diagnostic histological features and 6 with consistent histological features) and 4 persons with lesions clinically compatible with *M. ulcerans* infection whose biopsies were not cultured for mycobacteria (2 had diagnostic histology, 2 consistent histology). We consider these 18 definite and 11 suspected cases collectively for the remainder of this paper.

The median age at diagnosis was 66 years (range 3–90 years). Twenty cases were female, nine were male. Seventeen cases were retirees, but most enjoyed good health. Twenty-one cases (72%) had lesions on the lower limb, and eight cases had lesions on the upper limb. Twenty-five lesions (86%) were on the distal half of the limb.

The epidemic curve (Fig. 2) demonstrates that skin lesions were more commonly first recognized during the cooler months of April to September (21 cases),

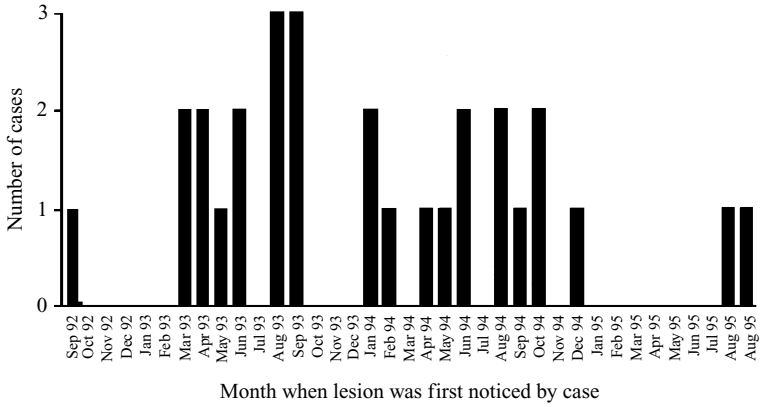

Fig. 2. Epidemic curve of cases of *M. ulcerans* infection associated with Phillip Island, September 1992–September 1995.

than during the warmer months of October to March (8 cases).

Because of the prolonged or frequent contact which most cases had with the outbreak area (Fig. 3), we could rarely estimate the incubation period of infection. In three cases the time from exposure to recognition of a distinct skin lesion was between 10 and 14 weeks. One case developed *M. ulcerans* infection within 2 weeks of exposure to Phillip Island, at the site of a lesion thought initially to be due to recent chicken pox. Another case developed infection within 3 weeks of an injury from the spiny branch of a sweet bursaria (*Bursaria spinosa*).

Case mapping

The town of Cowes lies along the northern shore of Phillip Island and extends approximately 3 km both to the east and west of the main street. The principal area of the outbreak was a 3×1 km region in eastern Cowes. Moving east from the main street, this area comprises medium-density suburban housing, a recreation reserve, golf course and lawn bowls club. In the easternmost part, known as Silverleaves, scattered holiday houses and some permanently occupied residences lie among low coastal scrub, bounded by the beach, an estuary, and low swampy ground.

We mapped most cases according to their residence in north-east Phillip Island. Most cases described a fairly stereotyped pattern of activities which brought them into frequent contact with the local environment for a few hundred metres around their residence. Except for a local general store there was no other focus of these perambulations. Hence, a case's residence represents a 'best guess' as to their main point of exposure to the general area.

Twenty-eight cases lived in or visited the outbreak area in Cowes (Fig. 3). Eleven cases were permanent residents of this area (2 played golf), 12 were holiday residents (2 played golf), and 1 visited the area for an afternoon only. One case lived just west of the main street but visited Silverleaves and played golf. Another case lived west of the main street and only had known contact with the outbreak area through working in the main street of Cowes. Three cases live in Rhyll (population 400) 6 km south-east of Cowes, but two of these visited the outbreak area to play golf or lawn bowls.

From September 1992 to January 1994, 10 cases were principally associated with Silverleaves, 4 with the streets adjacent to the golf course, 1 with visits to Silverleaves and the golf course, and 1 case had no direct contact with this area. In contrast, from February 1994 to September 1995, 11 of 13 cases were associated with the golf course area and only 1 with Silverleaves.

Environmental considerations

The golf course was irrigated by an extensive spray-irrigation system which drew most of its water directly from a large earthen dam in the north-east of the golf course. This dam water comprised ground water, and treated waste-water which had been supplied to the dam from the island's sewage treatment plant since the mid 1980s. The dam was not used for recreational activities. The frequency and volume of irrigation with water from the golf course dam were restricted in February 1995. Water from the dam was also piped 800 m west, to irrigate the recreation reserve, until this practice ceased in April 1994.

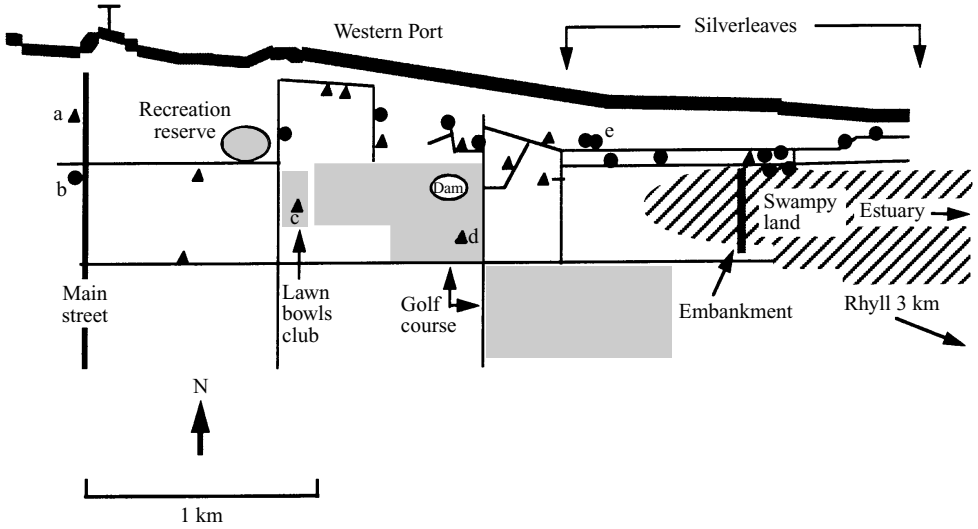

Fig. 3. Map of outbreak area, eastern Cowes, Phillip Island, showing residence of cases of *M. ulcerans* infection. Symbols represent permanent or holiday residence of case (except where specified). ● Onset September 1992–January 1994. ▲ Onset February 1994–September 1995. a, Workplace of case who had no other known contact with the outbreak area; b, frequently visited Silverleaves, and played golf; c, resident of Rhyll, played lawn bowls; d, resident of Rhyll, played golf; e, visited area for one afternoon only.

Filtered and chlorinated potable water is supplied to the outbreak area from a mainland source and is common to the rest of the island. Some properties also have sheet-metal rain-water storage tanks. Several properties in the outbreak area have large ornamental ponds filled by ground water. Most properties in Cowes are connected to the town sewerage system, except in Silverleaves, which is not served by this system and instead depends on household septic tanks.

From May 1991 to February 1992 unpaved dirt roads in Silverleaves were paved with bitumen. Excess material from the road-works was used to build an embankment across nearby swampy land, obstructing natural drainage. A company involved in road construction had a centre of operations and a quarry located within 500 m of an active mainland focus of *M. ulcerans* cases in Langwarrin [8].

There was no evidence of ulcerative disease among the closely monitored koala population, nor in koalas examined post mortem in the preceding 2 years.

DISCUSSION

New and unusual skin lesions are usually brought promptly to medical attention in Australia, so lesions due to *M. ulcerans* are usually excised with minimal morbidity. In some developing countries, however, *M. ulcerans* disease is an important public health problem, with hundreds of cases, limited therapy and many persons disabled by destructive lesions [13].

From September 1992 to September 1995, 29 definite or suspected cases of *M. ulcerans* infection occurred in persons who had lived in or visited Phillip Island. Cases were mostly elderly with limb lesions and all except one were exposed to an area of less than 4 sq km in eastern Cowes. Striking features of this outbreak included the sudden onset of disease on an island where the condition was unknown, and the tight geographical clustering of cases. From 1939 to the early 1980s fewer than 40 cases of *M. ulcerans* infection were reported from the sparsely populated far east of Victoria [14]. The Phillip Island cases therefore represent the largest localized outbreak of *M. ulcerans* infection reported in Australia. Where did the organism come from, and how? Where was it in Cowes, and how did cases become infected?

To understand this outbreak we depended on the descriptive epidemiology, observations of the apparent ecology of *M. ulcerans* in other endemic and epidemic foci of disease, and studies of other saprophytic mycobacteria with better defined environmental reservoirs and modes of transmission.

Foci of *M. ulcerans* infection are almost invariably located near substantial permanent swamps and slow-moving rivers [15, 2]. However, significant direct contact with the body of water is not always strongly associated with risk of disease [16]. Indirect routes of transmission from an aquatic reservoir have been

postulated, including exposure to contaminated soil [17], vegetation [18] and aerosol [2]. Person-to-person transmission of *M. ulcerans* appears to be a rare event [16].

Following skin contamination (and perhaps colonization) minor trauma may initiate infection by introducing the organism into the skin [19]. The protective effect of wearing trousers [13] supports the putative roles of contamination from an environmental source of *M. ulcerans* and trauma. The predominance of distal limb lesions among our cases is similar to the distribution of lesions among subsistence farmers in foci of infection in the developing world [16].

The localization of foci of *M. ulcerans* infection to a small area within larger ecosystems suggests that the mycobacterium only survives in numbers sufficient to cause human disease in the presence of certain unknown but geographically confined environmental factors or circumstances. Until January 1994 most but not all cases were associated with the Silverleaves area. We originally surmised that swampy land immediately south of Silverleaves was the source of infection for most of these cases [20]. Road-works in Silverleaves in 1991 and early 1992 caused considerable environmental disruption, and an embankment subsequently built across the swamp impeded natural drainage. The timing of cases in this area in relation to the road-works is consistent with previous reports of outbreaks following several years after major environmental disturbances, particularly flooding [2, 21]. Furthermore, road paving materials and equipment from a known mainland focus of disease may have inadvertently introduced the organism to this area.

Since February 1994 the principal focus of infection appeared to have moved to the west. Our suspicions therefore turned to the golf course dam and irrigation system. We propose that the golf course dam, its reticulation, or both, may have become colonized by *M. ulcerans*. Nutrients from treated waste-water may have facilitated the growth of mycobacteria in both the storage dam and the reticulation, and the spray irrigation efficiently dispersed *M. ulcerans* across the nearby environment.

Many species of mycobacteria have been isolated from water from man-made reticulations [22] and there is epidemiological and microbiological evidence that such reticulations may be the source of both sporadic [23] and clustered [24] cases of human non-tuberculous mycobacterial infection. Mycobacteria have been recovered from the biofilm of many such systems [25]. This milieu may provide sanctuary from the effects of disinfectants [26].

There is epidemiological evidence for dissemination of non-tuberculous mycobacteria in aerosols from aquatic environmental reservoirs [27]. *M. ulcerans* can be transmitted experimentally over short distances by aerosol [2]. We therefore surmise that transmission to humans on Phillip Island may have occurred from aerosols derived from the nutrient-rich surface layer [28] of the storage dam, from drift from the spray irrigation, or from transient micro-foci of organisms in the vicinity of the golf course.

Our estimates of incubation periods of 2–14 weeks are consistent with published accounts [29]. Incubation periods of this length may seem inconsistent with cases presenting in winter after exposure to irrigation water in summer. However, epidemiological and experimental studies have shown this to be quite variable – from 2 weeks [30] to many months [31, 32]. Moreover, if infection results not from direct exposure to contaminated irrigation water, but rather from exposure to an adjacent micro-focus of *M. ulcerans*, then a period of some months from peak summer irrigation to a peak in new cases is plausible.

The drainage of water throughout the outbreak area is inter-related by an extensive ground water system which surfaces at times as ponds in the swampy land to the south of Silverleaves. Therefore, *M. ulcerans* from the golf course area may reach contiguous areas via drainage of contaminated ground or surface water east, towards Silverleaves. This swampy land ultimately drains into an estuary which enters Western Port at Rhyll – the residence of the only case with no contact with the outbreak area.

Thus, contamination and proliferation of *M. ulcerans* within the golf course irrigation system may have been the source of organisms which later infected cases 'downstream' at Silverleaves. Alternatively, these cases may have been infected as they passed the golf course area on their way into the town centre.

In February 1995 local and state health authorities adopted a recommendation to restrict the use of the putatively contaminated irrigation system. In the following 12 months there were only two new cases of *M. ulcerans* infection associated with Phillip Island, and only one of these cases was exposed to the area which was associated with infections during 1993–4.

We hypothesize that colonization of a man-made water storage and reticulation with *M. ulcerans*, enrichment of this system with treated waste-water,

and dispersal by spray irrigation may explain this outbreak, which appears to have responded to a simple intervention. *M. ulcerans* may have joined the ranks of other environmental mycobacteria which have found favourable niches in man-made reticulations [5].

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