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**COMMENTARY** *(see article on pp. 489–490)*

# Buruli Ulcer – A Rapidly Changing Scene

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Buruli ulcer is a disabling cutaneous infection caused by *Mycobacterium ulcerans*, a slow growing environmental mycobacterium. The name originates from the district of Buruli in Uganda, where many of the early cases were reported in the late 1960s. Buruli ulcer is the third most common mycobacterial disease worldwide, after tuberculosis and leprosy (1). It is one of 17 Neglected Tropical Diseases prioritised for prevention and control by the World Health Organisation, in recognition of its extensive and increasing global burden of morbidity. Occasionally it is seen in visitors and migrants from endemic areas.

Clinically it presents as a painless skin papule or nodule most commonly occurring on a limb, often at a site of skin trauma. This progressively ulcerates with a characteristically underminded edge, often leading to massive local destruction of skin and soft tissue. There may be associated osteomyelitis, as in the case reported in this issue on p. 489–490 by Bessis et al. (2). Large lesions often result in scarring, contractural deformities, and limb amputation leading to functional disability, loss of education and work, and social stigma (3). The indolent clinical course contributes to delayed health-care seeking, and poorer treatment outcomes. Local traditions and fear of the consequences of this infection both further contribute to delays before presentation for treatment.

Buruli ulcer is most commonly found in rural communities near wetlands and slow-flowing rivers in tropical and sub-tropical countries. The mode of transmission remains unclear, although it is known to be linked to contaminated water (4). Focal outbreaks have reportedly been associated with human migration and environmental disturbance of surface water including flooding, dam construction and irrigation. Aquatic insects, adult mosquitoes and biting arthropods have been considered possible reservoir species and/or vectors (4). Secondary animal hosts such as possums have also been identified.

Cases have been reported from over 30 countries in Africa, Australia (where it is commonly known as Bairnsdale ulcer), Southeast Asia, China, Central and South America, and the Western Pacific (4). In addition, a number of cases have been reported in North America and Europe, resulting from international travel. Although Buruli ulcer may occur in any age group, most cases in West Africa occur in children aged between 4 and 15 years (5).

In this issue, Bessis et al. (2) report a case of Buruli ulcer in a 14-year-old girl living in an orphanage in Bamako, Mali. This is, to the best of our knowledge, the first reported case of Buruli ulcer in Mali, and the second reported case of Buruli ulcer in a Malian diagnosed outside the country. Previously, a 44-year-old farmer from Nioro in Mali, near the Mauritanian border, was diagnosed with Buruli ulcer during a visit to France for a training course (6). Although Mali is bordered by Buruli ulcer endemic countries, including Cote d'Ivoire to the south and Guinea to the southwest, it is not known to be an endemic zone. However, recent reports have highlighted the changing epidemiology of the disease, with increasing case numbers and geographic spread of cases in countries in West Africa. Migrating secondary hosts as well water schemes such as swamp drainage and irrigation projects have been suspected of contributing to this changing pattern.

Kanga & Kakou (7) reported a prevalence rate of 32/100,000 in Cote d'Ivoire. Similarly, the reported detection rate in Southern Benin and Ghana was 21.5/100,000, but focally as high as 151/100,000 in the most disease-endemic district of Ghana (8, 9). Epidemiologic studies such as these have employed widespread case searches to quantify the extensive disease burden, and serve to highlight frequent under-reporting of cases outwith these settings. The report by Bessis et al. raises the possibility of an unrecognised burden of Buruli Ulcer disease in Mali (2). As such, further epidemiological investigation is warranted to identify other cases in order to ensure optimal access to treatment for affected populations.

The other point of interest raised in the paper by Bessis et al. (2) relates to their use of PCR for diagnosis of Buruli ulcer. In endemic regions the diagnosis is often made clinically due to lack of access to laboratory services. The most widely available laboratory test for *M. ulcerans* is Ziehl-Neelsen staining to detect acid-fast bacilli (AFB) from an ulcer swab or punch biopsy. However, the presence of AFB does not differentiate *M. ulcerans* from other mycobacteria such as *M. tuberculosis* or environmental mycobacteria. *M. ulcerans* may be isolated from culture *in vitro* between 29–33ºC after 5 to 8 weeks incubation. Having said this, it is notoriously difficult to culture from clinical specimens, due to its slow growth rate (sometimes requiring a prolonged incubation of up to 6 months), low optimal growth temperature and restricted growth

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temperature range (10). Both microscopy and culture have low sensitivities, and indeed were negative in the case reported by Bessis et al. (2).

A study comparing direct smear (of punch biopsy specimens), culture, and histopathology with PCR for diagnosis of *M. ulcerans* reported sensitivities of 42%, 49%, 82% and 98%, respectively (11). Use of PCR for diagnosis of Buruli ulcer has been shown to be viable in a teaching hospital setting in Ghana (11), however high cost, and access to technical expertise and controls may be prohibitive at present. It may however prove an extremely useful tool in rapid, accurate diagnosis of *M. ulcerans,* as access to molecular based testing becomes more widespread, in order to gauge the scale of the problem in countries in West Africa such as Mali, and calculate the required public health response. Furthermore these tools would improve our capacity to implement prompt treatment measures such as the administration of rifampicin and streptomycin/amikacin plus surgery (10).

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