

# Buruli Ulcer

## A neglected disease

Menno Smit

*Victor is 25 years old and lives in Benin. He's the only member of his family that goes to school. During his final high school exams he was struck by a strange illness, starting with just a painless lesion on his right elbow.*

*Within a few weeks his whole right arm swelled, followed by hypesthesia and edema of his trunk, chest, scrotum and head. He believed it was black magic and tried herbals and spiritual rites, but his condition got worse. People were reluctant to come near him because of his appearance; the swellings had ruptured to ulcers and smelled terrible. The stench was horrible. Eventually he attended a hospital, but received neither a successful treatment nor a diagnosis.*

*After a few months his father brought him to a more specialized hospital in the south of Benin, a long distance from his village. For two years he was hospitalized and underwent more than eight surgeries, the cost of which placed a huge burden on his family. Although he now cannot bend his right elbow or lift his right shoulder, he is happy to be cured and to be able to continue his studies.*

### Introduction

Mycobacterium ulcerans disease, known as Buruli Ulcer, is a painless, necrotizing disease of the skin, subcutaneous tissue and bone. Left untreated it leads to severe handicaps, loss of livelihoods and social stigmata. The disease is endemic in more than 30 countries, but is most frequently found in the tropical

wetlands of West Africa. Worldwide it is the third most common mycobacterial infection after tuberculosis and leprosy. The mode of transmission and much of the pathology of Buruli Ulcer remains unknown. Last year, I spent 5 months in Benin doing research on this neglected disease.

“  
**The stench was horrible.  
I was alive but basically rotten.**  
”  
Victor (25yrs), patient



Benin



8 760 000  
inhabitants



\$1 250  
income per year



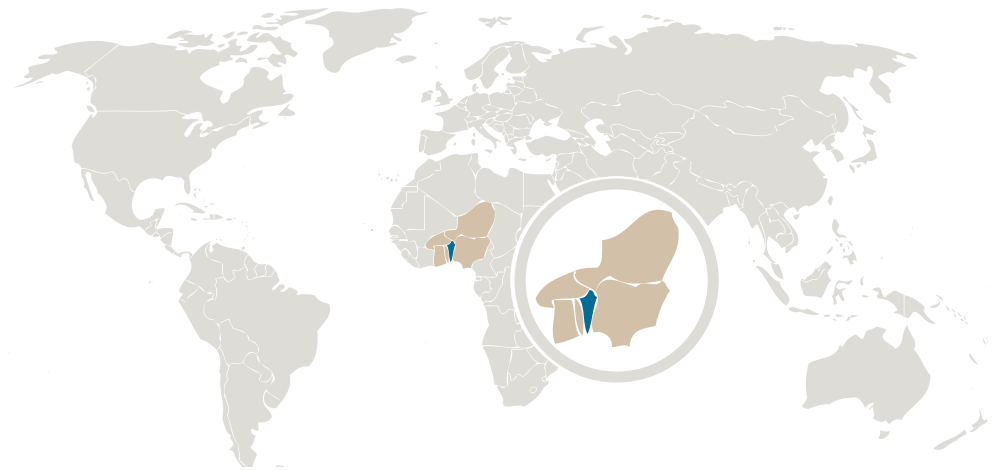
♂ 54yrs ♀ 55yrs  
life expectancy



5.3%  
of GDP for health



0.4  
doctors/10 000 people





Nodule



Papule



Small ulcer

### Epidemiology and transmission

The first case reports of *Mycobacterium ulcerans* disease, originating from Bairnsdale, Australia, were published in 1948. Later, hundreds of cases were reported along the Nile River in a region called *Buruli* in Uganda, giving the disease the name *Buruli Ulcer*. Currently Buruli Ulcer is endemic in five

continents, with the highest incidence in the rural wetlands of Benin, Côte d'Ivoire and Ghana. During the last decade more than 20 000 cases have been reported. In some West African countries the number of Buruli Ulcer cases may exceed those of tuberculosis and leprosy. Although all age groups are affected, children younger than fifteen years old represent more than half of the Buruli Ulcer burden of disease. It is commonly believed that *M. ulcerans* is an environmental pathogen related to slow-flowing and stagnant water (ponds, backwaters, and swamps). Recently, aquatic insects (Hemiptera) have been considered as potential vectors. Also the use of open water sources and penetrating skin injuries during fishing or farming activities have been proposed as possible modes of transmission. Clustering among families may reflect exposure to a common source and/or a genetic susceptibility.

mycolactone which can cause ulceration and even massive necrosis of the skin. Early (pre-) ulcerative lesions show large numbers of extracellular bacteria, extensive necrosis but very little inflammatory response. Over time some studies report an improved response while others demonstrate a persistent loss. Granuloma formation appears in later stages when there are less bacilli. In general the hypothesis is supported that T-helper 1 response is downregulated in early *M. ulcerans* disease. Most individuals exposed to *M. ulcerans* never develop the disease, while others develop lesions that heal spontaneously.



### Determinants of patients' delay in presenting to health care

- distance to hospital
- necessity for a family member to provide bedside care
- costs of treatment
- loss of income during admission
- limited knowledge of disease and treatment options
- fear of surgery and injections
- painless nature of the disease
- the hope of self-healing

### Pathogenesis

*M. ulcerans* is a slow growing mycobacterium, which grows optimally at 32°C. It produces the immunosuppressive and cytotoxic

### Clinical presentation

After an average incubation time of two to three months, Buruli Ulcer disease may appear in a localized form (nodule or papule) that eventually ulcerates or may disseminate directly.

The nodule is a firm, palpable, painless, spherical subcutaneous mass attached to the skin, and may attain a diameter of 2-4 centimeters.

The papule is a painless raised skin lesion less



Large ulcer

than 1 centimeter in diameter, with erythema of the surrounding skin. This form has only been observed in Australia.

Ulcers develop by perforation of the underlying necrosis through the epidermis and are surrounded with undermined edges and edema. Ulcers may enlarge and destroy large areas of skin and cause contiguous osteomyelitis, or may self-heal resulting in atrophic scars, leading to contractures and disabilities when located over joints.

Disseminated forms consist of progressive plaques, edema and metastases. Metastatic osteomyelitis develops in 10% of patients.

### Treatment

Before the introduction of the first effective antibiotic therapy in 2005, Buruli Ulcer could only be treated by radical surgical excision and successive skin grafting. Presently the use of streptomycin-rifampicin combination therapy heals up to 47% of cases within eight weeks of treatment. The other 53%, especially those who appear in a late stage of disease, require surgery.

After treatment, recurrence (5.9%) and



Skin graft

functional limitations (24%) remain a major problem. Aside from vaccine development, additional effort needs to be made to find more effective, oral antibiotic therapies that can be administered through rural health care posts.

### Prevention

Primary prevention remains impossible due to a lack of both knowledge regarding transmission and vaccines. For this reason secondary prevention methods to enhance early case detection, including active case finding and education of healthcare workers and at risk populations, are even more important. Tertiary prevention methods, such as physiotherapy to reduce disease related complications, are essential in maximizing quality of life post-treatment.

### About the author

Menno Smit, a sixth year medical student in Groningen, spent five months following-up patients treated for Buruli Ulcer to establish recurrence and functional limitation rates in Benin.



Contractures

### Further reading

- T.S. van der Werf. Bulletin of the World Health Organization 2005 Oct;83(10):785-91.
- F. Portaels. Clinical Dermatology 2009 May;27(3): 291-305.
- Video: The Legacy of Buruli (<http://www.who.int/buruli/information/videos/en/>)

### Global Medicine presents Neglected Diseases

About one billion people in the world are affected by one or more neglected tropical diseases (NTDs). Neglected, because these diseases persist exclusively in the poorest and the most marginalized communities, and have been largely eliminated and thus forgotten in wealthier places.

[www.who.int/neglected\\_diseases](http://www.who.int/neglected_diseases)

This is the fourth article in a series on neglected diseases. In our next issue we will discuss *Schistosomiasis*. For more information, check [www.globalmedicine.nl](http://www.globalmedicine.nl)