



BURULI ULCER

ENDING THE NEGLECT OF A DISEASE THAT IMPACTS THE YOUNG

Buruli ulcer disease is a serious skin infection which if untreated can lead to disfiguring and disabling lesions. This neglected tropical disease is mainly endemic in western Africa, although it has been reported elsewhere in Africa, the Americas, Australia and Japan. It affects communities living along slow-flowing bodies of water such as ponds, swamps and lakes. People with HIV and the young appear to be most at-risk, with most patients being under 15 years of age.

Around 5,000 new cases of Buruli ulcer are reported every year worldwide. But the number of people affected by this disease is estimated to be much higher. Many cases are believed to go undiagnosed, as knowledge of the disease is limited and it hits poor, rural communities the hardest.

Like tuberculosis and leprosy, Buruli ulcer is caused by a type of mycobacteria (called *M. ulcerans*). The disease can affect any part of the body, but most lesions are found on the limbs, mainly the lower limbs. The exact mode of transmission is unknown and still being investigated. Some research suggests that in Africa aquatic insects can harbour the mycobacteria in their salivary glands. More recent studies from Australia and Cameroon suggest that a type of mosquito may be a vector; if this were confirmed, Buruli ulcer would be the only known mycobacterial disease to be transmitted by insects.

Médecins Sans Frontières (MSF) has treated more than 800 patients with Buruli ulcer in Akonolinga in Cameroon since 2002.



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MSF Access Campaign

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A SIMPLE TOOL IS NEEDED FOR EARLY DIAGNOSIS

It is possible to make laboratory diagnoses by looking through a microscope for the presence of the mycobacteria in samples from the lesions, but this method is not very accurate. Alternatively, diagnosis can be confirmed by growing the bacteria in a culture sample, or by relying on DNA amplification techniques known as PCR, but these are sophisticated tools that require access to a high-tech laboratory.

Given that many of the people affected by Buruli ulcer live in remote or resource-poor settings with no access to laboratory services, these diagnostic tools are not widely available to those that need them most. What is needed is a simpler, more efficient diagnostic

tool that could be used in the field, particularly in remote settings.

In the absence of a user-friendly and accurate test, MSF in Cameroon is currently developing a very simple clinical score system to help detect Buruli ulcer cases. Clinical scoring does not require any diagnostic platform and could be adapted for settings with a very limited health infrastructure. Ideally, the scoring system should be so simple that it could be used by the traditional healers that most patients with lesions initially consult. The final results will be available in 2014 and if the study concludes this clinical score system is useful, partners in areas known to be endemic for Buruli ulcer will be encouraged to use it at community and primary health care levels.

Developing more simple and accurate diagnostic tools is all the more important given the need for early diagnosis – if a person with Buruli ulcer show signs of complications or is referred at the very late stage of the disease, they may require extensive debridement or, in extreme cases, amputation. Early diagnosis reduces the likelihood of deformities or the need for amputations, and simplifies or eliminates the need for the surgery that may be required to remove necrotic tissue, cover skin defects, and correct deformities. Diagnosing Buruli ulcer earlier can also help alleviate the economic burden borne by patients and their families, and limit the stigmatisation and ostracism they can face in their communities.

LIVING WITH BURULI

“The healer gave me dressings made of tree bark. The wound continued to grow, but the healer told me this was normal. I followed the traditional treatment for almost a year, but [because of the ulcer] I was unable to finish my year at school.”

Like many others with Buruli ulcer, Serge Bitete, a teenager from a village not far from Akonolinga, Cameroon, only sought treatment from MSF after living with the disease for over a year. In spite of awareness campaigns, there is still limited knowledge within communities that ulcerative skin lesions may be due to an infectious disease which can be effectively treated with drugs and dressings.

With ulcers on his left foot and right hand, Serge attended an MSF awareness campaign in his village in 2010. “The team immediately saw I had Buruli ulcer and they explained that it was

in an advanced stage. They offered to take me to MSF’s Buruli Pavillion inside the district hospital of Akonolinga but I didn’t want to go. I did not believe that doctors could actually cure it.”

Delays in seeking help from modern medicine explain why many patients present at treatment centres with large ulcers. This makes treatment more complex; in late-stage cases, antibiotic therapy and dressings will not remove the need to undergo surgery.

Noa François, a 56-year old from Yaoundé, went to MSF’s treatment centre in Akonolinga in July 2011 – where he has been receiving treatment

ever since – more than three years after the first signs of the disease. He was operated on to receive a skin graft but unfortunately the graft hasn’t taken; he will need to be operated on again. “I have been here for a long time and my family needs me. I wish my treatment had been shorter. I can only hope that the graft will work this time. But I remain optimistic.”

MSF has been diagnosing and treating Buruli ulcer in Cameroon since 2002, offering antibiotic treatment, dressings, physiotherapy, surgery and general medical care. Over 800 people have been treated in the project to date.

SIMPLE, SAFER AND AFFORDABLE TREATMENTS ARE NEEDED

Surgical intervention has been the main approach for the treatment of Buruli ulcer for many years. Only relatively recently in 2004 did the World Health Organization (WHO) recommend an eight-week course of antibiotics to treat the disease. Chemotherapy has made the delivery of care for Buruli ulcer easier and treatment more accessible for patients. There is solid evidence that early and limited lesions can be effectively treated with antibiotics alone, without any need for surgery and hospitalisation.

But the current recommendations still present significant disadvantages. The most commonly used treatment is a combination between rifampicin, an oral drug, and streptomycin, which requires daily intramuscular injections for a long period of time, and is difficult and costly to administer in remote settings. The drugs also have significant side effects, including kidney and liver damage, loss of balance and vertigo, making treatment cumbersome on patients.

To respond to the urgent need to identify simpler and more patient-friendly

treatment options for Buruli ulcer, WHO is sponsoring a trial to assess the first all-oral treatment regimen developed, combining rifampicin and clarithromycin. This initiative is welcomed, and, if successful, could provide an important incremental improvement. This oral combination is already used in the field by several organisations, including MSF.

Alternative regimens are needed to overcome these major obstacles to wider implementation of care.

What is needed for Buruli ulcer is a treatment regimen that is more effective, shorter, does not require injections and daily visits to hospitals, can be safely used in children and adolescents, and can be taken by people who are living with HIV. The future of Buruli ulcer case management depends on early diagnosis and an oral drug that can be taken safely at home. Both developments will reduce the need for hospitalisation.

ACCESS TO MODERN DRESSINGS

MSF undertook a review of existing dressings, selecting five which are suitable for chronic wounds and have proven effective in speeding up healing, if combined with antibiotic treatment and physiotherapy.

The main problem with these dressings is their high price. If ministries of health are to use modern dressings for wound management in Buruli ulcer, prices will have to be substantially reduced.

LOOKING TO THE PIPELINE

Because Buruli ulcer typically affects children living in poor communities, where medical services are unavailable, there is almost no research and development funding dedicated – either by pharmaceutical companies or by governments – to study the disease, its diagnosis, or its treatment.

In addition to the WHO-sponsored trial on rifampicin and clarithromycin, further research is critical to identify and evaluate new treatment candidates. Several drugs and drug candidates have demonstrated potential efficacy against Buruli ulcer. These would be easier for people

to take and would cause fewer side effects. But data is lacking and rigorous conclusions can't be drawn. The anti-tuberculosis drug research and development pipeline also represents an important and potentially rich source of novel compounds for Buruli ulcer treatment.

WHAT NEEDS TO HAPPEN

ENDEMIC COUNTRIES SHOULD:

- ❖ Invest in educational campaigns to promote early diagnosis along with treatment programmes for Buruli ulcer
- ❖ Ensure that the drugs and dressings needed to treat Buruli ulcer are available by including them in national essential medicines lists
- ❖ Support research efforts that aim to test the efficacy and safety of new drug candidates and combinations

THE WORLD HEALTH ORGANIZATION SHOULD:

- ❖ Rapidly evaluate the changing clinical evidence base and create evidence-based guidelines to enable countries and health workers to improve treatment of Buruli ulcer
- ❖ Ensure that the drugs needed to treat Buruli ulcer, including newer medicines, are available by including them in the WHO Essential Medicines List

RESEARCHERS AND PHARMACEUTICAL COMPANIES SHOULD:

- ❖ Intensify research efforts to identify the mode of transmission of the disease
- ❖ Intensify research efforts aimed at developing simple and accurate tests for early detection of cases
- ❖ Systematically evaluate potential drugs for efficacy against *M ulcerans*, including drugs developed for other purposes
- ❖ Support clinical trials to evaluate the most promising candidate drug combinations, especially those that are all-oral, have minimal side effect profiles, and offer shorter treatment
- ❖ Ensure that drugs for Buruli ulcer are both available and affordable for those living in resource-poor environments
- ❖ Identify if Buruli ulcer is an opportunistic infection for HIV patients



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