Buruli ulcer (BU) is a neglected tropical disease (NTD) that causes a debilitating skin and soft tissue infection, mainly in children aged 15 years or younger. It is caused by Mycobacterium ulcerans, a bacterium that belongs to the same group as those that cause tuberculosis and leprosy.

The disease is endemic in at least 33 countries around the world, and is a serious public health problem in rural communities in sub-Saharan Africa, particularly in Benin, Cameroon, Côte d’Ivoire, the Democratic Republic of the Congo (DRC) and Ghana. Other important foci outside Africa are Australia, French Guiana, Japan, Papua New Guinea and Peru. When BU is in the advanced and late stages, treatment is extremely difficult and outcomes are poor, resulting in disfigurement and disability that is often stigmatized.

There are no primary preventative measures to control BU, mainly due to poor understanding of its epidemiology. The current control strategy emphasizes early diagnosis and prompt treatment, with the goal of preventing the complications associated with advanced stages of the disease.
At the end of 2013, a meeting of BU experts, convened by FIND and WHO in Geneva, reviewed the unmet diagnostic needs for the disease. The team explored various options for development of novel tests including, among others, detection of bacterial proteins or bacterial DNA, and toxins produced by *M. ulcerans* known as mycolactones. The meeting outputs informed the development of the FIND strategy on BU diagnosis and, since then, FIND has been working with partners to develop and evaluate three BU diagnostic tools.

There is no diagnostic test for BU appropriate for the rural health facilities that see most cases. Surveillance of the disease is also poor due to the absence of effective diagnostic services. Clinical diagnosis is very often inaccurate and complicated as other infections that have a similar presentation to BU.

Health personnel refer samples for confirmation by complex methods at tertiary level laboratories, while relying on non-specific clinical signs to initiate treatment. This can lead to over/under treatment due to misdiagnosis. Yet disease management, which is based on a combination of antibiotics (rifampicin and streptomycin for 8 weeks) as a first-line treatment, is quite effective, with a cure rate of around 80%.

The best outcomes occur with early treatment, when lesions measure less than 5 cm. Unfortunately, most cases are diagnosed once the disease has reached advanced stages. The laboratory methods in routine use for confirmation of BU include culturing of the bacteria, histopathology, smear microscopy for acid-fast bacilli and polymerase chain reaction (PCR). New diagnostic tools to accurately identify BU patients at district health facilities or point-of-care tests in primary healthcare facilities would significantly contribute to early treatment and control of the disease.

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**PROTEIN ANTIGEN CAPTURE ASSAY**

A point-of-care test for diagnosis at the community level would transform surveillance and control of the disease. The Swiss Tropical & Public Health Institute (Swiss TPH) has developed monoclonal antibodies specific to *M. ulcerans* that could be used as targets in the development of a simple, instrument-free assay. These have been used to develop an ELISA test, whose sensitivity is comparable to current reference methods.

**CURRENT STATUS AND FUTURE PLANS**

Alere/Standard diagnostics is using monoclonal antibodies discovered by Swiss TPH to develop a rapid diagnostic test (RDT) that can be deployed at the primary healthcare level where the majority of patients first seek care. Together with Swiss TPH, Institut Médical Evangélique of Kimpese, the Democratic Republic of the Congo (DRC) and other partners, FIND is testing RDT prototypes and optimizing a sample preparation protocol. During the development process, clinical trials will be carried out by FIND, together with Swiss TPH and endemic country partners. Further research is being carried out to develop improved versions of the RDT for future uptake.
In partnership with the Department for Infectious Diseases and Tropical Medicine (DITM/KUM, Germany) and the Noguchi Memorial Institute for Medical Research (NMIMR, Ghana), FIND is carrying out studies to determine the best primers, dyes and LAMP chemistries to produce a dried reagents based LAMP kit to detect BU that can be stored at ambient temperature. The data generated will be used to develop a diagnostic kit for BU. Research is also being carried out to improve methods for collecting, preparing and storing samples before they are used to perform the test. Instrument-guided detection methods, using a field amenable fluorimeter, are also under evaluation.

DETECTION OF BACTERIAL DNA WITH LAMP

Polymerase chain reaction (PCR), a technology with limited implementation, as it can only be performed by experts in sophisticated laboratories, is currently the most accurate method for diagnosing BU. A better option to PCR is loop-mediated isothermal amplification (LAMP) of DNA, a technology being exploited by FIND and partners for diagnosis of several infectious diseases. Unlike PCR, no specialized training or equipment is required.

CURRENT STATUS AND FUTURE PLANS

In March 2016, FIND and Anesvad signed a Memorandum of Understanding to collaborate in support of the WHO integrated strategy on skin NTDs, such as Buruli ulcer. This partnership will support the development, evaluation and introduction of diagnostic tools and strategies for early detection of BU. This will result in improved management of BU and other skin diseases. The specific activities related to BU will link with FIND’s ongoing activities that are supported by UBS Optimus Foundation, the Swiss Agency for Development and Cooperation, and the German Federal Ministry of Education and Research.

DETECTION OF MYCOLACTONES BY FLUORESCENCE THIN LAYER CHROMATOGRAPHY

Mycolactones are unique toxins produced by M. ulcerans. The toxins destroy the skin and soft tissues, forming large ulcers. They can be detected by fluorescence thin layer chromatography (f-TLC), a technique commonly used for identifying compounds in a mixture.

CURRENT STATUS AND FUTURE PLANS

The World Health Organization (WHO), FIND and Harvard University are now working with a number of laboratories in Ghana, Benin and the DRC, to evaluate the test. The evaluation study is also determining whether the test can be used to monitor the efficacy of treatment. Initial results from recent field trials in Benin and Ghana have shown that f-TLC is more sensitive than microscopy and can be carried out by technicians with minimal training in district hospital laboratories.

FIND is also working closely with WHO to support the BU research and control community by improving access to specimens, supporting advocacy and regular meetings, and setting joint goals and priorities.