Main issues arising from the open meeting

Control group

Christian Johnson reported that there was concern over the reduction in detection rates in various areas, which in some places related to reduced surveillance rather than a real reduction in incidence. It was agreed that along with improvement in surveillance, it is desirable that there should be an increase in the proportion of laboratory-confirmed cases in order to get a truer picture of the incidence of Buruli ulcer. The aim should be for at least 70% confirmation rate (implying at least 70% PCR-positive cases out of the total number of cases reported). Endemic countries will be encouraged to improve their rates of detection of confirmed cases and to not report patients from whom samples were sent for confirmation but not confirmed positive.

The facility will soon exist (https://who.telederm.org) for centres where there is internet access to upload clinical data and lesion photographs for secondary remote confirmation. Countries will be strongly encouraged to make use of this facility to improve diagnosis.

Access to WHO-recommended antibiotics, particularly streptomycin, has been limited by procurement problems in the recent past. It was agreed that clarithromycin may be substituted at such times, although there are no immediate plans to change the guidelines. Shortening the duration of treatment to less than 8 weeks is strongly discouraged.

The WHO guidelines for training will be revised and tailored to meet the needs of individual treatment centres.
Research group

Tim Stinear selected some illustrations of advances made since the last meeting in 2011 from the many excellent papers and posters presented during the meeting.

- Transmission: Improvements in the method for culturing *Mycobacterium ulcerans* from environmental samples together with access to ever cheaper genome sequencing were pointing to new ways of tracing the source of human cases. An almost complete match in the genome of *M. ulcerans* isolated from a human case with that from an environmental sample is necessary in order to conclude that there was a transmission link and that has not yet been observed, for example in the isolate described by Tony Ablordey. His isolation method will be further refined and simplified to make it suitable for wider application.

- Detailed mapping of the environment in and around endemic villages is expected to lead to better insights into how villagers are exposed to *M. ulcerans*. Pam Small emphasized the need for the transmission research community to embrace scientific methods of environmental sampling, including guidelines on sample replicates and establishing spatially defined sampling sites in order to introduce rigour to the field and to develop datasets that can be compared between communities; ‘Systematic review and consensus guidelines for environmental sampling of *Burkholderia pseudomallei*’ (*PLoS Neglected Tropical Diseases* e2105, 2013) is an example of a good model for studying a pathogen in the environment.

- Diagnostics:
  - An improvement in the Kishi fluorescence TLC method for detecting mycolactone has been tested in a mouse model of *M. ulcerans* infection in the footpad. This may be applicable to diagnosis in human lesions if the problems of non-specific bands can be eliminated.
  - Other methods for detection of *M. ulcerans* are being developed including antigen detection but currently they lack sufficient sensitivity (antigen detection) or specificity (LAMP).

- Mechanism of action and kinetics of mycolactone:
  - Major advances have been made by Caroline Demangel’s group towards understanding how mycolactone disrupts cell adhesion through its binding to the nWASP protein.
  - The kinetics of mycolactone production in the mouse footpad model have been described together with the effect of antibiotic treatment in this model.

- Vaccine development: The BuruliVac project has led to many new findings, but a satisfactory vaccine candidate has not yet been identified. Among the spin-offs from the consortium project have been a better understanding of the mode of action and kinetics of mycolactone; definition and testing of *M. ulcerans* specific proteins; and live vaccine candidates.

- Clinical trial: A control trial of conventional RS treatment compared to RC for 8 weeks has started in Benin and Ghana. During the meeting, it was agreed
that the feasibility of adding patients from Togo and Côte d’Ivoire should be explored with a view to adding both countries as trial centres.

**HIV**

The TAG noted the need to increase the knowledge of Buruli ulcer and HIV coinfection, and called for provisional guidelines to help health workers to manage coinfected patients.

**Priorities**

It was agreed that the top priority for funding will be the clinical trial during the next 2 years. Among the above research areas, the greatest impact is likely to come from advances in understanding the mode of transmission of *M. ulcerans* and from improved diagnostic methods.

**Future meetings:** The next meeting will be in March 2015 in Geneva, Switzerland.

Mark Wansbrough-Jones

Chair, WHO Technical Advisory Group for Buruli ulcer

2 April 2013