

**ABSTRACTS**

**DRAFT**

**ANNUAL MEETING  
OF THE WHO GLOBAL BURULI ULCER  
INITIATIVE**

**15-17 MARCH 2006**

**GENEVA, SWITZERLAND**

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## **ENDEMIC COUNTRIES ACTIVITIES**



# **BURULI ULCER IN CAMEROON: ACTIVITIES CARRIED OUT IN 2005**

*Dr Charles Nsom Mba, National Buruli Ulcer Control Programme, Cameroon*

## **Introduction**

In 2005, the Cameroonian National Buruli Ulcer Control Programme was able to carry out the activities described in the outlook for that year: i.e. activities in the existing foci of Ayos and Akonolinga and their extension to new sites. All these activities are coordinated at the national level. This presentation will follow the main lines of strategy adopted at the previous meeting of the Global Buruli Ulcer Initiative, as well as providing an overview of activities scheduled for 2006.

### **1. Community-level early case detection, Information, Education and Communication**

These activities were carried out in the Ayos and Akonolinga foci by health area staff and officials from the integrated health centres who had been trained in 2004. As a result, a large number of new cases were recorded in the two foci in 2005.

### **2. Observance of the case-management protocols (antibiotics, surgery, prevention of disabilities and rehabilitation)**

Since 2004, when antibiotics were introduced into the treatment of Buruli ulcer, the national programme has complied with this strategy, which is systematically applied in accordance with the WHO protocols. As a result, the strategy has been applied to all patients, and has made it possible rapidly to cure patients and to shorten hospital stays. Initially, both foci received support from partners with supplies of antibiotics. At present, negotiations are under way with the National Tuberculosis Control for joint orders of streptomycin and rifampicin on account of the number of patients expected.

### **3. Case confirmation**

Case confirmation was provided for all patients by the Cameroonian Pasteur Centre; in 2005, approximately 253 examinations were carried out on patients; 113 Ziehl-Neelsen stains and 89 PCR which confirmed the presence of *Mycobacterium ulcerans*. We should mention that the Cameroonian Pasteur Centre carries out these examinations as part of its public health activities.

Table 1 : **Cases of Buruli ulcer in Cameroon in 2005**

	<b>Ayos</b>	<b>Akonolinga</b>	<b>Total</b>	<b>Percentage</b>
<b>Total number of cases</b>	83	109	192	100
<b>New cases</b>	82	96	178	92,70
<b>Recurrent cases</b>	1	13	14	7,29
<b>Children</b>	35	62	97	50,52
<b>Women</b>	35	57	92	47,91
<b>Disability on diagnosis</b>	12	32	44	22,91
<b>Ulcerative or mixed forms</b>	73	82	155	80,72
<b>Sited on lower limbs</b>	52	64	116	60,41
<b>Sited on upper limbs</b>	26	41	67	34,89

#### **4. Strengthening the health system**

Thanks to the support of partners, **ALES and MSF**, improvements have been made to health facilities in the Ayos and Akonolinga foci. Equipment has been procured for the new Buruli ulcer sites and handed over to health facilities. As regards logistics, thanks to ALES, Sud-Ouest province now has a vehicle with which to start Buruli ulcer control activities.

#### **5. Training for health workers, teachers and village volunteers**

During 2005, the Programme was called on to provide training in case management and programme administration for health workers in new Buruli ulcer foci, with the support of ALES. The staff concerned included 10 physicians and 90 nurses who will be responsible for the Programme at the new sites. Refresher training was also provided for staff at existing foci. Training for teachers and village volunteers is due to begin shortly.

#### **6. Standardization of the case recording and reporting system using the BU 01 and BU 02 forms and the HealthMapper**

Since activities began, data on Buruli ulcer cases has been collected using the WHO Buruli ulcer forms. Thanks to the GPS provided by WHO two years ago, map coordinates for the villages in the two districts are being determined for use with the Health Mapper.

#### **7. Follow-up and evaluation.**

Follow-up of the Programme's activities is regularly undertaken by the central level down to the peripheral level by means of supervisory missions and missions to monitor the activities scheduled.

## **8. Other activities**

The Programme received a visit from David Karashima of the Nippon Foundation who was deeply impressed by our programme and promised to provide it with support.

In March 2005, we took part in the meeting of the WHO advisory group at Geneva and in the workshop to finalize the Buruli ulcer training modules for staff, which was held at Ouidah in Benin in October 2005.

## **Cameroun, Buruli ulcer: activities planned in 2006**

In 2006, the Programme intends to consolidate its achievements at Ayos and Akonolinga and to extend them to new foci, where we have started by training staff.

### **1. Community-level early case detection, Information, Education and Communication**

The Programme intends to improve community-level early case detection by involving primary school teachers and community intermediaries in the Ayos and Akonolinga foci. Public information campaigns are also planned.

### **2. Compliance with the case-management protocols (antibiotics, surgery, prevention of disabilities and rehabilitation)**

Strict compliance with the case-management protocols will be systematically ensured, with a focus on prevention of disabilities and rehabilitation. Negotiations will take place with the tuberculosis programme regarding joint orders of streptomycin and rifampicin, which are already subsidized by the Government.

### **3. Case confirmation**

This will be systematically provided by the Pasteur Centre in Cameroon. The possibility of involving other laboratories in the Programme will be considered.

### **4. Strengthening the health system**

There are plans to develop the infrastructure in the new foci, and in particular at NGOANTET, in Centre province and at MBONGUE, in Sud-Ouest province with the support of ALES.

### **5. Training for health workers, teachers and village volunteers**

We plan to provide training for health workers, teachers and community intermediaries in both existing and new Buruli ulcer foci. We count on support from WHO to carry this out.

## **6. Standardization of the case recording and reporting system using the BU 01 and BU 02 forms and the HealthMapper**

The WHO forms will be used in conjunction with the continuation of data collection from the villages and districts in which the disease is endemic for use with the HealthMapper.

## **7. Monitoring and evaluation.**

Follow-up and monitoring missions are planned, together with a national meeting to coordinate the Programme's activities.

# **COTE D'IVOIRE - ANNUAL OVERVIEW 2005**

*Dr Moussa Diabaté, National Buruli Ulcer Control Programme, Côte d'Ivoire*

## **Introduction**

Buruli ulcer, an endemic, disabling cutaneous mycobacterial infection has been present in Côte d'Ivoire since 1978 and constitutes a public health problem. In 1997, cases were confirmed in 56 of the country's 58 departments. The National Buruli Ulcer Control Programme, which was set up in 1995, has introduced a control plan in order to reduce morbidity and disabilities caused by the disease. Clear progress had been made until 2002, when the war wiped out everything that had been achieved. In 2005, a new BU control team was set up. As a result, new orientations have been defined on the basis of priorities. After one year's operation, here is the overview of our activity in 2005.

## **I. Objectives**

The objectives of PNLUB in 2005 were as follows:

### **I1 Overall objective**

- To reduce morbidity and disabilities caused by Buruli ulcer

### **I2 Specific objectives**

These may be summarized under seven headings :

- To press ahead with decentralization of treatment
- To enhance awareness
- To intensify active case detection
- To improve treatment of Buruli ulcer patients
- To promote research into Buruli ulcer
- To improve the programme's management and coordination
- To develop collaboration between sectors

## II. Outcomes

The expected outcomes were the following :

- Everyone was to be familiar with Buruli ulcer;
- The skills of staff responsible for treating Buruli ulcer were to be improved;
- Detection of non-ulcerative forms was to be enhanced (at least 45% of cases);
- Incidence was to be reduced by at least 10%;
- 85% of active cases registered or detected were to receive medical treatment;
- Standardized treatment of Buruli ulcer was to be introduced nationwide;
- At least one additional integrated Buruli ulcer treatment centre was to be operational;
- At least one research project was to be carried out;
- At least 10% of post-treatment disabilities were to receive physical rehabilitation;
- At least 10% of persons with disabilities caused by Buruli ulcer were to be reinserted into the social and economic fabric;
- The Programme's management and coordination was to be enhanced and it was to have an operational and operating organization chart.

## III. Contributions from the services

### A. Epidemiological surveillance service

Table 1- **Distribution of Buruli ulcer in Côte d'Ivoire in 2005**

	<b>North and East</b>	<b>South</b>	<b>West</b>	<b>Centre</b>	<b>Total</b>
<b>Number</b>	35	245	332	952	1564
<b>Percentage</b>	2.23	15.54	21.23	61	100

Distribution of Buruli ulcer in 2005 was identical to 2004.

Table 2 - Comparison of results 2004–2005

	2004	2005
<b>Aggregate number</b>	22000	23564
<b>Incidence</b>	1110	1347
<b>under 15yrs</b>	46.46%	50.12%
<b>Sex ratio</b>	1.08	1.00%
<b>Case fatality rate</b>	1.72%	0.56%
<b>Disability</b>	NP	16%

The cumulative number of Buruli ulcer cases rose from 22 000 cases in 2004 to 23 564 cases in 2005. This increase is attributable to improved reporting of cases thanks to the distribution of new reporting tools.

It should also be mentioned that the proportion of children under 15 years of age affected increased to 50% and the case fatality rate fell considerably. This reduction was attributable to better treatment thanks to the distribution of drugs to case management facilities, which benefited from several missions. The increase in incidence made it necessary to improve the number of case-management facilities.

### B. Diagnosis and treatment service

#### B1 - Decentralization of case management

Several case-detection missions were carried out in the interior of the country in order to identify pilot public health facilities for decentralization.

These missions allowed us to identify several treatment facilities able to offer the following skills:

Table 3 - Distribution of health facilities by skills available

Centres	Activities	Hospitalization	Dressing	Surgery	Lab.
<b>Djékanou Gen. Hosp.</b>		Yes	Yes	Excision	Yes
<b>Taabo General Hospital</b>		Yes	Yes	Nodulectomy	No
<b>San-Pedro Regional Hospital</b>		No	No	Excision	Yes
<b>Tiassale General Hospital</b>		No	Yes	No	Non
<b>Bondoukou District Hospital</b>		Yes	Yes	Excision	Yes
<b>Zouan-Hounien General Hospital</b>		No	Yes	No	No

At Zouan-Hounien, an Italian clinic has agreed to build a BU ward within the general hospital.

## B2 - Case-management activities

- A permanent supply of drugs is available for treatment facilities, either by replenishing their account at PSP or by direct supply by the Programme from its own stocks.
- WHO-recommended antibiotic treatment effectively began in Côte d'Ivoire in May 2005.
- We have reinforced the capacity of the Angré and Zoukougbeu centres by assigning physicians and anaesthetists to the operating theatres (select table)

## B3 - Research activities

- Project for the confirmation of BU cases in association with the Institut Pasteur in Côte d'Ivoire
- In March 2006, the results of the project involving treatment with green clay, which is near completion, could be presented at Geneva.
- Research project on the BU rapid diagnosis test in collaboration with the BU Programme, the Institut Pasteur and Professor Collizzi's department is under preparation

## B4- Follow-up of the Programme's activities

- Lack of logistic and financial resources to undertake the different research projects
- Inadequate collaboration with the teaching hospital

## C- Communication, training and supervision

In 2005, Dr Abo N'takpé and Dr Son Jérôme gave five lectures on the following topics under the supervision of the Director-Coordinator in different regions of Côte d'Ivoire:

- Topic 1 : *Buruli ulcer : epidemiology and impact on the population*
- Topic 2 : *Buruli ulcer, the 3<sup>rd</sup> millennium's leprosy*
- Topic 3 : *Buruli ulcer : symptoms and treatment*
- Topic 4: Case-management of Buruli ulcer patients

Information missions were organized in six sub-prefectures in Côte d'Ivoire : Djékanou, San Pédro, Bouaké, Yamoussoukro, Adzopé, Taabo

During 2005 :

1. The Director-Coordinator followed a training course for trainers in Benin in December 2005.
2. All the health workers responsible for treatment of Buruli ulcer at the church-operated centres at Angré and San Pédro followed refresher courses.

3. A series of meetings was organized between nuns from Kongouanou (Yamoussoukro) and the inhabitants of the neighbouring villages.
4. In January 2006, Zogba Gervais presented a paper on the social perception of Buruli ulcer in Taabo sub-prefecture 2006.
5. The staff of public health facilities opened in 2005 were provided with training.
6. We provided training on application of the streptomycin-rifampicin protocol for nurses from Taabo general hospital.

## **IV. Analyzes and comments**

### **A. Analyzes**

This overview shows a number of objectives that we have not been able to attain:

- Sufficient trained staff to provide case management.
- Properly equipped technical facilities for all treatment centres.
- Sufficient supplies of drugs for all our patients.
- Satisfactory communication.
- Availability of a reliable source of documentation.
- Availability of a pool of trainers to train health workers in treatment of Buruli ulcer.

### **B. Comments**

The difficulties encountered in carrying out our different activities were essentially attributable to a wholly inadequate budget.

## **V. Prospects for 2006**

We have selected the following activities for 2006:

1. Organization of a national day for Buruli ulcer control;
2. Production and distribution of information material at public talks;
3. Production of a documentary film on BU in Cote d'Ivoire by the Programme;
4. Preparation of a programme for active case-detection;
5. Organization of a national day to mobilize resources for Buruli ulcer control in Côte d'Ivoire;
6. Continuation of training for staff in public facilities
7. Improvement of the technical facilities in all centres providing treatment;

8. Continuation of the effort to set up treatment centres in public health facilities;
9. Preparation and provision of Buruli ulcer treatment kits;
10. Introduction of standardized treatment for Buruli ulcer in all treatment centres;
11. Development of a set of rules for treatment of Buruli ulcer per level 1,2, 3;
12. Provision, with the assistance of MAP International, of a virtual library;
13. Participation, from 13 to 17 February 2006, in a training session for health professionals on prevention of disabilities at Taabo;
14. Enhanced participation by staff in the different activities of the Programme.

## **Conclusion**

This overview of the Programme for gives an idea of the progress made on several fronts: improved reporting of cases, an increase in the number of centres providing treatment and a drop in the case-fatality rate in comparison with 2004.

However, considerable efforts are still called for, as the number of cases is clearly on the increase. The Programme's shortcomings are largely attributable to the war and to the budgetary restrictions deriving from it.

# **NEW BURULI ULCER CONTROL ACTIVITIES CONDUCTED IN 2005 IN THE DEMOCRATIC REPUBLIC OF THE CONGO (DRC): CONFIRMATION OF BURULI ULCER CASES BY POLYMERASE CHAIN REACTION (PCR) IN FORMER FOCI (CASES IN BANDUNDU PROVINCE).**

*Authors: Anatole Kapay Kibadi, Jackie Nyota Singa, Leontine Nkuku, Emmanuel Kiangala, Tamfum Muyembe and Françoise Portaels*

## **Introduction**

Buruli ulcer is endemic in DRC. Only samples from the Bas-Congo province and the town of Kinshasa had been confirmed by PCR up to 2004. We felt it was important to conduct new activities to confirm the presence of Buruli ulcer in old foci by PCR testing in other endemic provinces of DRC. The objective of this undertaking is to confirm by PCR testing the presence of Buruli ulcer in the province of Bandundu with a view to control Buruli ulcer in DRC.

## **Methodology**

First we developed research projects aimed at confirming cases of Buruli ulcer and then we sought funding. The research component was spread over three phases:

- Phase 1: On-site preparation of at least 1 month by community contact points.
- Phase 2: The "mission": Identification of patients, sample-taking, patient care.
- Phase 3: Analysis of samples using Ziehl-Neelsen stain (on-site) Ziehl-Neelsen and culture (INRB-Kinshasa), Ziehl-Neelsen stain, culture and identification, PCR (ITM Antwerp), and histopathology (AFIP).

## **Results**

Two research missions were conducted in the province of Bandundu in 2005:

- The first mission, financed by the World Health Organization, was conducted in April 2005 in Gungu territory. We detected 31 clinical cases of Buruli ulcer: DRC (10 positive Ziehl-Neelsen stains), ITM Antwerp (3 positive Ziehl-Neelsen stains, cultures contamination +++ and 2 positive cases by PCR: Ref. 05-0894, 05-0929).
- The second mission, financed by the Damien Foundation Belgium, was conducted in August 2005 in Idiofa territory. We detected 20 clinical cases of Buruli ulcer: DRC (10 positive Ziehl-Neelsen stains), ITM Antwerp (2 positive Ziehl-Neelsen stains, cultures: contamination +++ and 1 positive case by PCR: Ref. 05-2835).

## **Discussion**

For the first time ever samples from Bandundu province are being confirmed by PCR. The report on this province produced in 1974 by Meyers and Coll. was based on Ziehl-Neelsen staining and histopathology. But these two short missions are inadequate to determine the scale of this affliction in this endemic foyer of Bandundu.

## **Conclusions**

Our two research projects were completed and allowed us to confirm the presence of Buruli ulcer by PCR in the province of Bandundu where the first case of Buruli ulcer had been reported by Van Oye and Baillon in 1950.

## **Future prospects**

We should pursue our research with a view to confirming cases of Buruli ulcer by PCR in other former Buruli ulcer foci in DRC (Kasongo, Waatsa, etc.) but to date, we have been unable to find funding to continue these missions aimed at enhancing Buruli ulcer control in DR Congo.

# THE BURULI ULCER SITUATION IN GABON

*Dr Bayonne Manou, Dr Orema Patrick, Mr Zikoko Loba*

Activities to detect Buruli ulcer in Gabon began two years ago thanks to close collaboration between the Ministry of Public Health and the World Health Organization on the one hand and non-governmental organizations such as ANESVAD Aide aux Lépreux Emmaüs-Suisse (ALES), Switzerland on the other.

The activities focus mainly on active case-detection, a training workshop to raise awareness for health workers and the provision of medical and surgical equipment for the Estuaire (Libreville hospital centre), and Moyen Ogooué (Lambaréné hospital centre) provinces to provide surgical treatment for patients.

## Epidemiological situation in Gabon in 2005

### Case detection and data analysis

During 2005 we reported 91 cases, which were detected in three provinces:

- 83 cases in Moyen Ogooué province;
- 3 cases in Woleu-Ntem province
- 5 cases in Ngounié province

Table 1 : **Distribution of cases**

	<b>Moyen Ogooué</b>	<b>Ngounié</b>	<b>Woleu-Ntem</b>	<b>Total</b>
<b>Men</b>	40	1	0	41
<b>Women</b>	26	1	2	29
<b>Children</b>	17	3	1	21
<b>Total</b>	83	5	3	91

Table 2 : **Clinical forms**

	<b>Moyen Ogooué</b>	<b>Ngounié</b>	<b>Woleu-Ntem</b>	<b>Total</b>
<b>Nodules</b>	2	0	0	2
<b>Papules</b>	0	0	0	0
<b>Plaques/oedema</b>	0	0	0	0
<b>Ulcers</b>	81	5	3	89
<b>Total</b>	83	5	03	91

Table 3 : **Site**

	<b>Moyen Ogooué</b>	<b>Ngounié</b>	<b>Woleu-Ntem</b>	<b>Total</b>
<b>Upper limbs</b>	37	1	0	38
<b>Lower limbs</b>	42	4	3	49
<b>Other sites</b>	4	0	0	4
<b>Total</b>	83	05	3	91

## **Geographical distribution**

All the cases reported are from three regions : Moyen Ogooué, Ngounié and Woleu-Ntem (which lies on the border with southern Cameroon and Equatorial Guinea)

## **Activities carried out and results achieved**

### **1. Survey**

A case-detection survey was conducted in Moyen Ogooué province for the purpose of:

1. Confirming the presence of an active disease focus;
2. Determining the prevalence of the disease in the province.

Samples were taken from patients of both sexes of all ages. Eighty-three of the 121 samples were positive, a prevalence of 68.59%.

The eight other cases were from Ngounié and Woleu-Ntem; it should be mentioned that 7 of the 83 Buruli ulcer cases were also HIV-positive.

### **2. Training workshop**

In August 2005, a training and awareness workshop was held at Libreville for health officials; it was attended by 49 participants, and was taught by 4 international WHO consultants (from Cameroon, Cote-d'Ivoire, Benin, and Geneva).

The workshop was designed to:

1. Mobilize health staff at the central level;
2. Provide comprehensive information on Buruli ulcer;
3. Form a pool of national trainers in case detection and treatment of Buruli ulcer;
4. Set up a data base for the purpose of identifying all Buruli ulcer patients.

Three of the four international consultants travelled to Lambaréné to evaluate the facilities there.

### **3. Donation**

A Spanish non-governmental organization (ANESVAD) made a donation of medical and surgical supplies to Gabon. The donation was handed over to the Central hospital in Libreville and to the hospital in Lambaréné in December 2005.

### **4. Difficulties**

1. Under-reporting of cases;
2. Lack of training of health staff;
3. Lack of facilities in which to provide treatment for patients;
4. Difficulties in conducting evaluation missions (vehicle);
5. Mobilization of national and WHO resources for awareness-raising, communication and the system of epidemiological surveillance, organization of provincial workshops, essentially on account of lengthy formalities.

## **Prospects for 2006**

January – June:

- Introduction and strengthening of the system of epidemiological surveillance;
- Training community intermediaries in Buruli ulcer control.

March – June:

- Prepare educational messages for the population in high-risk areas.

March 2006-October 2004 :

- Organize 4 case-detection surveys in 4 health regions.

July 2006 – June 2007 :

- Conduct supervisory missions for health staff in endemic foci.

## **Acknowledgements**

To WHO and ANESVAD, for funding the survey in Lambaréné, the training workshop for officials in Libreville and for the donation of the audiovisual equipment.

To ANESVAD for the donation of the medical and surgical equipment;

To Aide aux Lépreux Emmaüs-Suisse (ALES) for its moral support;

To the Institute for Tropical Medicine, Antwerp, Belgium for analyzing a number of samples.

## **PROGRAMME ACTIVITIES: BURULI ULCER – GHANA, 2005**

*Dr Edwin Ampadu*

Ghana, for effective implementation of the global strategic areas, the Buruli ulcer programme concentrated in the following areas;

1. Surveillance and early case detection
2. Surgical capacity development
3. Health resource development
4. Rehabilitation

### **1. Surveillance and early case detection.**

A total of 1005 new cases were recorded. This was from 26 endemic districts currently reporting on the disease.

In the age distribution analysis, patients below 15 years continue to dominate with 53% followed by 38% for ages above 15 – 49 years and lastly above 50 years took 12%.

Laboratory confirmation of diagnosis has improved from 4.1% last year to 14.4% in 2005. This is mainly due to the introduction of antibiotics in case management and as a prerequisite condition to treatment, confirmation of cases must also be established. National programme also continues to remind clinicians to confirm diagnosis before treatment.

Community based volunteers were trained in 4 districts to strengthen the early case detection activities. This was supported by some of the NGOs; ANESVAD, World Vision International.

Nodule/ulcer ratio was 1:3 .

### **2. Surgical capacity development**

Surgical case management has been a big challenge to National programme and most endemic centres. In 2005, two major trainings were organized. In addition to that, four specialist support visits were undertaken to some of the Buruli ulcer treatment centres.

The surgical training which lasts for a week brought together some selected health workers [doctor, anaesthetist (nurse) theatre nurse, ward nurse, laboratory personnel and another worker responsible for rehabilitation activities] from Buruli ulcer centres.

The strategy adapted is Teamwork Approach to case management. In all 8 treatment centres were trained.

Some of the centres visited include:

1. Goaso Government Hospital
2. Bechem Government Hospital
3. Dadiesoaba Health centre
4. Nkawie Government Hospital
5. Bekwai District Hospital

### **3. Health Resource Development**

Strengthening of health facilities especially those in the Buruli ulcer endemic areas has become an integral part of the national programme control activities.. In 2005, the main activities were in the direction of 2 major constructions.

These include the construction of a surgical theatre, wards for Buruli ulcer patients with a 30 bed capacity, and a physiotherapy hall for rehabilitation of Buruli ulcer patients.

Dunkwa and Nkawie Government Hospitals have benefited from this support – ANESVAD Spain, ILFO, Italy.

In addition to structures, equipment and instrument package will be provided. They are expected to be completed by the end of 2006.

Other NGOs have also contributed to equipment support to National Programme. The Tri-State Hospital Supply Corporation, Michigan, USA through Mr. Steve Smith & Prof. Richard Merritt donated surgical instruments to the Programme. A local NGO, Mother & Child Foundation also supported National Programme with drugs; antibiotics (streptomycin and rifampicin), surgical dressings and hospital beds.

### **4. Rehabilitation**

This area is very important but poorly resourced to operate. As institutions get new structures to improve services, physiotherapy and rehabilitation shall be added to it.

Hopefully, by the close of 2006, 4 endemic treatment centres would have been equipped to provide such services.

Finally, 4 severely affected patients were supported whiles on admission at the teaching hospital when referred to 3 institutions.

### **Acknowledgement**

The National Programme is privileged to mention the following stakeholders for their contributions and immense support in the course of the year.

Table 1: at local level

<b>Contributors</b>	<b>Type of contribution</b>
<b>Ministry of health [GHS]</b>	<ul style="list-style-type: none"> <li>• Funds</li> <li>• Surgical dressings</li> <li>• Vehicle – Nissan Patrol</li> </ul>
<b>Mother &amp; child foundation, Ghana</b>	<ul style="list-style-type: none"> <li>• Drugs (streptomycin and rifampicin)</li> <li>• Surgical dressings</li> <li>• Hospital beds</li> </ul>
<b>Rotary club, Accra</b>	<ul style="list-style-type: none"> <li>• Funds – to pay for surgery for a patient</li> </ul>
<b>ILFO, Italy</b>	<ul style="list-style-type: none"> <li>• Funds to support theatre construction at Dunkwa and equipment</li> </ul>
<b>DFID, Ghana</b>	<ul style="list-style-type: none"> <li>• Funds – to programme activities £30,000</li> </ul>
<b>World Vision Ghana</b>	<ul style="list-style-type: none"> <li>• Funds for community case control and management</li> </ul>
<b>Noguchi Memorial Institute for Medical Research</b>	<ul style="list-style-type: none"> <li>• Animal experimentation</li> </ul>
<b>Kumasi Centre for Collaborative Research into Tropical Medicine (KCCR), Kumasi</b>	<ul style="list-style-type: none"> <li>• Support some treatment centres with laboratory works</li> </ul>

Table 2: at international level

<b>ANESVAD, Spain</b>	<ul style="list-style-type: none"> <li>➤ Financial</li> <li>➤ Equipment</li> <li>➤ Infrastructure</li> </ul>	<ul style="list-style-type: none"> <li>• Early case detection and surgical training</li> <li>• Theatre , physiotherapy, laboratory</li> <li>• Physiotherapy/classroom</li> <li>• Surgical Theatre</li> <li>• vehicle</li> <li>• Incinerator and accessories</li> </ul>
<b>World Health Organization</b>	<ul style="list-style-type: none"> <li>➤ Educational materials, technical support</li> <li>➤ Transport</li> </ul>	<ul style="list-style-type: none"> <li>• Toyota Land Cruiser Prado</li> </ul>
<b>Tri-State Hospital Supply Corporation, Michigan USA</b>	<ul style="list-style-type: none"> <li>➤ Surgical instrument and dressings</li> </ul>	
<b>SASAKAWA, Japan</b>	<ul style="list-style-type: none"> <li>➤ Technical support</li> </ul>	
<b>American Leprosy Mission</b>	<ul style="list-style-type: none"> <li>➤ Rehabilitation support</li> </ul>	

# BURULI ULCER CONTROL IN GUINEA DURING 2005

*Dr Adama Marie Bangoura*

## I. Background

- The whole country provides a favourable environment for the development of the disease
- The disease is present in the Forestière region and there are strong suspicions that it is present in Basse Guinée
- The number of cases is under-reported
- Cases are detected late, with the consequent risk of permanent disability

## II. Epidemiological situation

- National prevalence is unknown
- Aggregate number of cases from 1993 to 2005: 843
- Number of clinical cases detected in 2005 : 208

### Distribution of cases by sex

Women : 113 i.e. 54 %

Men : 95 i.e. 46%

### Distribution of cases by age

Under 15 yrs : 23 %

16 - 45 yrs : 63 %

45 yrs and above : 14 %

### Distribution of cases by clinical form

Pre-ulcerative : 10%

Ulcerative : 85%

Sequelae : 5%

### **III. Activities carried out**

#### **III.1. Advocacy and resource mobilization**

From 25 to 29 March 2005, a joint mission was carried out by the coordinating office of the National Buruli Ulcer Control Programme (PNLUB), the Secretary-General of the Guinean Raoul Follereau Association (AGUIRAF) and by Mr Robert KOHLL, the Luxembourg Raoul Follereau Foundation (FFL) Projects Director at N'Zérékoré.

In May 2005, a draft agreement was signed by the Ministry of Public Health and the Luxembourg Raoul Follereau Foundation. The agreement covers the construction and fitting out of a Buruli ulcer treatment centre at N'Zérékoré, assistance with the supply of drugs and consumables and research.

Thanks to a coordination meeting organized on 19 December 2005 to strengthen partnership for Buruli ulcer control, it was possible to make available extensive information on the disease and to raise partners' awareness with a view to achieving greater commitment to its control. The meeting which was chaired by the Minister of Public Health, was attended by a total of 53 participants representing the diplomatic and consular corps, international institutions and NGOs, by executives from cooperation agencies, the Ministries of the Economy and Finance, Communication, Planning and of Public Health.

#### **III.2. Community awareness**

- Projection of the WHO documentary on Buruli ulcer « The mystery disease » and dissemination of educational messages on BU by the Guinean Radio and TV channel (RTG), the rural radio stations in Boké and Kindia and by the Kamsar community radio station.
- Distribution of comic strips, posters and leaflets in schools and health facilities.

#### **III.3. Laboratory case confirmation**

Ziehl-Neelsen stain is the only technique that can be used in all the selected treatment facilities. A total of 137 samples were analysed and 58 found to be positive.

The following improvements were noted:

- Better biological case confirmation at the national level thanks to an increase in the number of tests carried out
- Better collaboration between surgical services and laboratories and improved data collection.

However, the following difficulties were also noted:

- Lack of funds to pay for the transport of samples abroad for confirmation by culture and PCR;
- The poor conditions of transport and storage of samples on account of the remoteness of endemic areas (a journey of 2 to 3 days).

### III.4. Case management

Treatment is essentially by surgery and is mainly carried out at the hospitals in N'Zérékoré, Lola and Yomou, at the Philafricaine mission's medical centre in Macenta, the Catholic clinic in Samoé and at the Palé health centre. MSF Switzerland collaborates with Lola and N'Zérékoré for case detection and referral of suspected Buruli ulcer cases from the Lainé refugee camp at Lola.

Table 1: case management situation in 2005

Category	Number of cases
Cured without sequelae	92
Cured with sequelae	06
Total	98

### III.5. Improvement in the provision of care and use of services

- **Better equipment:** Donation by ANESVAD of a considerable amount of surgical equipment to the N'Zérékoré, Lola and Yomou hospitals. The equipment was handed over to the N'Zérékoré Regional Health Directorate on 28 June 2005.
- **Infrastructure development :** This has benefited from a major effort in order to provide proper care for more patients. A Buruli ulcer treatment centre is under construction by FFL at N'Zérékoré in association with the Guinean Raoul Follereau Association. The foundation stone was laid on 21 August 2005.

### III.6. Training for health workers, teachers and village volunteers

A total of seven training workshops were held nationwide, most of them in the Forestière region and at Kamsar, for health personnel, community health workers and teachers.

### III.7. Standardization of the case recording and reporting system using the forms (BU 01, BU 02 and the HeathMapper)

Data-collection tools were prepared and distributed to treatment facilities providing case management. Although Buruli ulcer has priority for surveillance, it has not yet been incorporated into the national health information and management system (SNIGS).

### **III.8. Supervision of control activities**

In June and October 2005, two supervisory missions were organized by the coordinating office in N'Zérékoré region. The aim of the missions was to:

- Evaluate case-management activities in health facilities and the use of the management tools provided by PNLUB ;
- To encourage biological case detection and confirmation.
- These exercises identified the following problems :
  1. The inability of the facilities currently providing case management to provide treatment for many of the patients detected (shortage of drugs and consumables, problems of cost recovery and use of a single form of treatment (surgery) which requires surgical skills and proper equipment).
  2. The inability of the ECDS and ERS to supervise BU in the health facilities for lack of training.

### **III.9. Prospects for 2006**

- Follow-up to the meeting with partners in order to ensure mobilization of the resources needed to carry out activities ;
- Continuation of training activities for health personnel in order to spread information on the disease as widely as possible, and research ;
- Improving health facilities and equipment and in particular completion of the building and fitting out of the BU treatment centre in N'Zérékoré and discussions concerning the extension of the prefecture hospital in Dubréka ;
- Improving epidemiological surveillance and laboratory case confirmation (extension of control activities to other areas, especially to Basse Guinée, and revision of the data-collection tools with a view to their integration into SNIGS).

## **Conclusions**

Buruli ulcer is a public health problem. Progress has been made and there is the potential to improve control activities in Guinea, despite the problems

However, case detection and laboratory confirmation of cases need to be improved. Regular contacts and multi-sectoral collaboration should be continued with all national and international partners to encourage them to commit themselves to and support the control effort. A greater commitment is needed by the State and its development partners if this disabling disease is to be brought under control. In this respect, the coordination meeting with partners has raised high hopes for the PNLUB coordinating office.

**Our thanks** are due to all our partners, and in particular to WHO, ANESVAD, FFL/AGUIRAF and the Philafricaine mission.

# **ESCALATING BURULI ULCER SITUATION IN NZARA; SOUTHERN SUDAN**

*Dr Ireneaus Sindani*

## **Introduction**

BU was unknown in South Sudan until ICRC reported 3 cases in 1990s from Upper Nile and Bahr El Ghazal regions. In July 2002 CARE international made an alert of sudden outbreak of tropical ulcer among IDPS in Mabilia (Tambura County in Western Equatoria). An emergency Field investigation team of WHO, KEMRI and CARE went to Mabilia to manage cases and collect specimens in July/August 2002 and Mycobacterium ulceran, the causative agent for BU, was isolated in 3 cases in September 2002. Since then cases have continued to be detected in both Tambura and Nzara. However, the trend of BU case has recently changed. The epicenter of the disease seems to shift from Tambura to Nzara. While no cases of BU have been reported in Tambura in 2005, 23 new BU cases and one recurrent case were reported in Nzara alone.

## **Objective of the BU program in Southern Sudan**

This is to reduce BU morbidity through effective case management.

## **Methodology**

Training of health workers in case detection and management is the key in meeting the objectives of the BU program in Southern Sudan. This is coupled with uninterrupted supply of BU drugs to all areas where cases are detected and creation of community awareness about the disease.

## **Cases detected in 2005**

In 2005, 24 BU cases were diagnosed in Nzara compared to a total of 13 proven cases diagnosed from 2001 to 2004. Out of these cases 23 were new cases while one was a recurrence. Of all 24 cases, 11 (45.8%) were males while 13 (54.2%) were females. 9 of the cases had single lesions while 15 had multiple lesions. Of these lesions 17 patients had lesions affecting the upper part of the body while 7 cases had lesions affecting the lower part of the body. The lesions ranged from single nodules to plaques. 3 patients had single nodules, 6 patients had single ulcers while another 3 patients had both nodule and oedema. Combination of oedema and ulcer was found in 7 patients (majority of the patients) while a triple combination of oedema, ulcer and plaque was found in 5 patients. Of all cases 7 had complication of deformity.

## **Conclusion**

There is a sudden emergency of BU in Nzara area. It is not clear whether this sudden increase in case numbers in Nzara is due to a stable epidemic in the area or due to better knowledge of the disease among health workers who are now able to diagnose the disease because of continuous training being offered to these health workers coupled with the people becoming aware of the disease and are now capable of coming for medical treatment unlike previously when they associated these lesions to witchcraft and could not seek medical treatment. Therefore, this finding begs for more intensification of the BU program not only in Nzara but also in other parts of Southern Sudan.

## **Future plan of action**

In 2006, the BU program in Southern Sudan intends to scale up the BU program in Southern Sudan through:

- Promotion of early detection of cases through training health workers to diagnose cases early
- Standardization of case management both surgical and laboratory
- Strengthening laboratory services for confirmation of cases
- Renovation of health institutions in Nzara and Tambura and strengthening them by providing surgical kits, medicines and drugs.
- Training Health Workers, school teachers and village volunteers for community awareness
- Standardization recording and reporting system
- Creating public awareness by providing of IEC materials
- Ensuring proper implementation through effective supervision and monitoring.

## **STATUS OF BURULI ULCER DISEASE IN MOYO AND ADJUMANI DISTRICTS, UGANDA**

*Henry Wabinga, Francis Lulu, Ben Khing and Pieter Stragier*

Buruli ulcer disease (BUD) has been confirmed in Adjumani and Moyo districts and during 2005 extensive sensitization among health workers and active search for cases were undertaken in these two districts. The outcome of these two activities revealed that health workers were well aware of BUD that is also locally referred to as Lupi Lupi. Visits made by one of us (Peter Steiger) found 72 cases of BUD in the two districts in a period of two months. These two districts are sparsely populated (about 200000 people) and with this high number of cases, BUD can be considered a public health problem. There is also a strong belief that this is still an underestimation of the magnitude of BUD and this calls for continuous surveillance and sensitization of the community.

# REVIEW OF THE SITUATION OF *MYCOBACTERIUM ULCERANS* INFECTION (BURULI ULCER) IN FRENCH GUYANA IN 2005.

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<sup>1</sup> Dermatology service, Cayenne Hospital Centre;

<sup>2</sup> Health Centre, Cayenne Hospital Centre;

<sup>3</sup> Parasitology Service, Cayenne Hospital Centre;

<sup>4</sup> Institut Pasteur, French Guyana

The points addressed concern data from surveillance in 2005, the possibilities of association with cutaneous leishmaniasis, the results of a study of the etiology of leg ulcers leading to consultation in the Dermatology Service at Cayenne and detection of *Mycobacterium ulcerans* (MU) in the environment.

## Surveillance

Two new cases of *M. ulcerans* infection (MUI) were diagnosed in 2005 in comparison with 17 in 2004.

## Association IMU-cutaneous Leishmaniasis

We describe 3 situations : 1) identification in a single skin lesion of *M. ulcerans* (direct Ziehl+; PCR+) and of *Leishmania guyanensis* (direct MGG stain, culture+, PCR+) in a young 18-year old female patient ; 2) presence in a pregnant 31-year old patient of ulcerated lesions on an upper limb with detection of *Leishmania spp.* by MGG stain smear examination and of a foot nodule with identification of *M. ulcerans* (direct Ziehl+ ; PCR+, culture+) ; 3) isolation of *M. ulcerans* (direct Ziehl+ ; PCR+, culture+) from an ulcer on a 12-year old child and simultaneous diagnosis in two of the child's sisters of leishmaniasis (direct MGG+ ) from skin ulcers. These three observations should incite practitioners working in areas in which these two diseases are endemic to be vigilant when making a precise diagnosis of a nodular skin lesion and/or ulcer.

## Prospective study of the causes of lower limb ulcers in French Guyana

A descriptive prospective study carried out in the Dermatology Service of Cayenne hospital centre from April 2003 to April 2004. The following inclusion criteria were applied : 1<sup>st</sup> consultation for a skin ulcer on a lower limb. Samples for biological examination were taken on the basis of epidemiological and clinical data. Results : 143 patients (median age 40.5 yrs) were included. Etiology of the ulcers, in decreasing order of frequency : infectious (57.4%); vascular (17.5%); injury (16.1%); miscellaneous (9%). The 57.4% of infectious origin broke down as follows : leishmaniasis :32.9% ; pyoderma :16.8% ; MUI : 3.5% (i.e. 5 out of 143 cases of ulcer) ; others :4.2%. Ulcers are the commonest form of detection of MUI worldwide and differential diagnosis must be used judiciously for MUI on account of the numerous possible causes of lower limb ulcers in a tropical environment.

## **Study on isolation of *M. ulcerans* in the environment**

Samples were taken between November 2004 and February 2005 at Javouhey (the west coast region). A total of 303 insect and fish specimens were taken and identified, together with nine plant specimens. All the PCR (IS2404) carried out on the samples proved negative. This geographical area was chosen because it has the highest incidence of MUI in French Guyana. However, during the months that followed, the number of cases of MUI was very low (2 in French Guyana in 2005, none of them in this region); this suggests that the presence of the bacterium in the environment varies considerably from one year to the next in French Guyana.

# ***MYCOBACTERIUM ULCERANS* IN AUSTRALIA – 2005 REPORT**

*Paul Johnson,<sup>1,2</sup> Janet Fyfe,<sup>2</sup> Caroline Lavender,<sup>2</sup> Maria Globan,<sup>2</sup> John Hayman<sup>2</sup>*

<sup>1</sup>Infectious Diseases Department, Austin Health and University of Melbourne

<sup>2</sup>Victorian Infectious Diseases Reference Laboratory, Melbourne, Australia

## **Definitions and data sources**

Cases are those that have been confirmed by culture or PCR (or both) at the Mycobacterium Reference Laboratories in Victoria or Queensland.

## **Report**

Forty-six cases of PCR and/or culture confirmed *Mycobacterium ulcerans* infection were recorded in Australia during the calendar year 2005, compared with 34 in 2004. The majority were adults, but several children also required treatment. Only 6 cases in 2005 were from Queensland, however an unknown (but probably small) number of cases are diagnosed by histology alone in this state (John Hayman, personal communication).

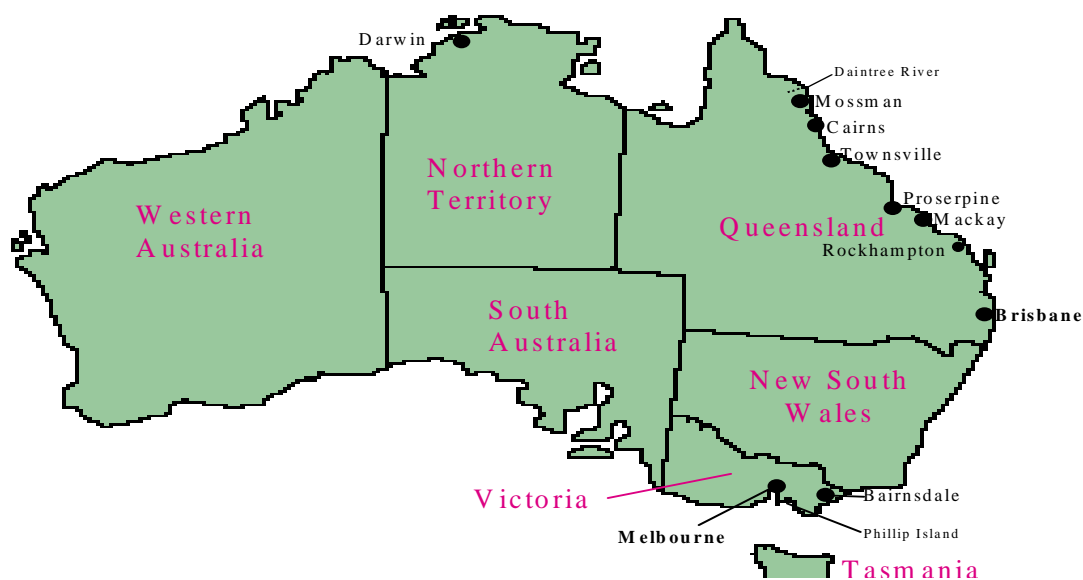
One confirmed case was diagnosed in New South Wales but the patient had a history of regular visits to New Guinea and molecular typing suggested that the infection was not locally acquired.

Of the 6 Queensland cases, 3 were from the known Mossman/Daintree focus and a fourth case was linked to Port Douglas, just to the south of Mossman. However 2 infections occurred near Rockhampton, 700 km further south. This area has been active in the past but had been considered “burnt out” for many years.

In Victoria there were 40 cases, compared with 25 for 2004. Half were linked to the small coastal resort town of Point Lonsdale, where there has been an intense outbreak since 2002. Of the remaining 20 cases, only 4 were linked to the traditional endemic area around Bairnsdale. These 16 patients had contact with either the Bellarine Peninsula, the Mornington Peninsula or the south-eastern bay side suburbs of Melbourne. This latter focus is newly recognised, and is in an area of high population density only 35 km from the centre of Melbourne.

Table 1: Cases of *Mycobacterium ulcerans* infection in Australia, 2005

State	Likely place of acquisition	Cases
Victoria	East Gippsland (Bairnsdale)	4
	Mornington Peninsula	3
	St. Leonards	2
	Point Lonsdale	20
	Bellarine Peninsula other	5
	Bay (south-eastern suburbs of Melbourne)	6
Queensland <sup>1</sup>	Mossman/Daintree	2
	Port Douglas	1
	Rockhampton/Yeppoon	2
	Other	1
Australia	All	46



<sup>1</sup> We thank Chris Coulter and Chris Gilpin from the Queensland Mycobacterium Reference Laboratory, Brisbane, for providing data for this report.

## **NGO ACTIVITIES**



# **ACTIVITIES RELATED TO BURULI ULCER CONTROL CARRIED OUT BY ALES IN 2005 IN CAMEROON**

*Dr Alphonse Um Boock*

## **1. Organization of the National Control Programme**

- In collaboration with the Ministry of health and WHO , we have organized the national workshop for planning UB programme control for the period from 2006 to 2009.
- Epidemiological national survey in BU.
- Providing vehicle and motor bicycle for some provinces.
- Technical and financial support for activities of supervision.

## **2. Treatment of patients**

Focused in three aspects : Rehabilitation of infrastructures , equipment and training.

### **Rehabilitation of infrastructures**

1. Mbonge hospital in endemic province of south – west has been rehabilitated.

### **Equipment of services**

1. The following hospital has been equipped with medico-chirurgical and anaesthesia material: Mbonge, Ayos, Mbalmayo, Mfou , Bandam, Ntui, Eseka , Abong Mbang.
2. The room for physiotherapy has been completely equipped.

### **Training for medical staff**

A total of 156 health personnel divided into six endemics provinces (Centre, South, South-west, extrême-north, East et Adamaoua) has been trained to management of Buruli ulcer.

## **3. Physiotherapy**

The training of 8 health personnel in physiotherapy has been completed.

## **4. Sensitization of the population**

- A media programme using all media available ( radio, television, news, etc.) has been set up.
- Distribution of posters of Buruli ulcer for health centre.

## **5. Schooling**

Development of schooling activities.

## **6. Research**

Three subjects was conducted :

1. Direct cost of Buruli ulcer programme.
2. Social cost of Buruli ulcer programme.
3. Thermotherapy ongoing.

## **7. Early case detection**

Three mass campaign of screening in schools.

## **8. Coordination**

1. National : support to the organization of the national meeting coordination.
2. International : Sponsoring of Ayos DMO to Geneva meeting.

## **9. Future plan: 2006**

1. To Maintain infrastructures and equipments .
2. Improvement of the quality of treatment of patients.
3. Providing drugs.
4. Sensitization of population
5. Surveillance of the disease.
6. To extend the programme into all endemics provinces.
7. Training of the community.
8. Advocacy in favour of Buruli ulcer.
9. Mass campaigns for early cases detection.
10. Cartography of the disease.
11. Building of Ngoantet health centre.
12. Equipment of new Buruli ulcer services.

13. Thermotherapy in collaboration with the Universities of Heidelberg and Basel.

14. Strengthening of reinsertion activities.

### **Activities in Gabon 2005**

Participation to the launching of Buruli ulcer activities in Gabon.

### **Future plan: 2006**

1. To define the collaboration with the country.
2. To support the national programme in many ways.

## **ACTIVITIES RELATED TO BURULI ULCER CONTROL, CARRIED OUT BY ALM (2005-2006)**

*Dr Paul Saunderson*

By tradition, ALM works through local non-government partners, in order to reach the affected communities most effectively. Government programs may also be assisted, but generally through the local NGO partner.

ALM seeks to work where it can contribute resources or expertise not otherwise available. At present, a major contribution is in the field of disability prevention (POD), in which ALM's consultant, Ms Linda Lehman, has a leadership role. In 2005, ALM contributed, with other NGOs, towards the publication by WHO of a POD Manual for BU – publication date is expected to be March, 2006.

Geographically, ALM works in three centers:

- 1) **Ghana, Ashanti Region:** we support three activities in the Region, coordinated by Dr Pius Agbenorku (consultant plastic surgeon):
  - a. Training of doctors in District Hospitals to manage BU
  - b. Training of regional health staff in the prevention of disability (POD)
  - c. Early case detection in one sub-district (Bomfa), as a pilot project
- 2) **Côte d'Ivoire:** we support early case-finding activities as a pilot project in one district (Taabo) through a partner organization, MAP International.
- 3) **Democratic Republic of the Congo, I.M.E./Kimpese Hospital, Bas Congo:** we support case management at this referral hospital.

### **Activities**

#### **Ghana**

The surgical training continued during 2005, concentrating on the towns of Obuasi, Nyinahin and Manikraso, where there are government district hospitals and a private hospital belonging to the gold mine. In addition, supervisory visits were paid to other hospitals where training had been given in previous years. Prevention of disability training by Linda Lehman also took place, to consolidate the start made in 2004.

A community-based project was started in Bomfa sub-district with the aim of promoting community awareness of the disease and increasing early case detection. Sixty patients have been detected and treated. There have been a number of unforeseen difficulties with this project, including high staff turnover, so that the methods and approach need to be re-thought for 2006.

The major problem facing all these projects in Ghana is the lack of reimbursement of patients' hospital fees, contravening an earlier commitment by the government to underwrite free treatment of BU. Many hospitals in Ashanti Region, both government and private, are owed tens of thousands of dollars in exempted fees, so a crisis is looming.

### **Ivory Coast**

Two building projects were completed in 2005. One involved a ward for BU patients at the University Hospital in Treichville, Abidjan. At present, it is underused as a referral center because patients find it difficult to get there, for a variety of reasons; the national program is aware of the problem and intends to take action to facilitate the movement of patients within the country.

The second building is also a ward for Buruli ulcer patients, this time in an endemic rural sub-district named Taabo, about 100 miles from Abidjan. Our partner organization in Ivory Coast, MAP International, has initiated a community-based program for health promotion and early case detection in the sub-district. Over 200 patients were identified and treated in the area, during 2005. The activities in the community have been very successful. The major challenge at present is that there is no surgeon at Taabo Hospital, so the more severe cases cannot be treated adequately there: referral to Treichville is the correct procedure on paper, but rarely feasible in practice.

### **IME Hospital, Kimpese, DR Congo**

The diagnosis and treatment of Buruli ulcer cases continues at Kimpese, which is a well-functioning mission hospital, four hours drive from Kinshasa. Some community mobilization takes place in the most endemic areas to promote early presentation. Individual case management, including antibiotics, surgery and POD, is well established at Kimpese.

### **Future plans**

**In Ghana**, to continue training staff of district hospitals (in surgery and POD), so that BU cases in Ashanti Region are well managed. To develop further the pilot project in Bomfa for early case detection, after initial setbacks due to high staff turnover. To support organizational capacity building for project expansion. Subsequently, other early detection projects can be started. To start some community-based rehabilitation projects, which will include socio-economic rehabilitation.

**In Côte d'Ivoire**, to work on providing effective case management (surgery and POD) for cases found in Taabo District. To expand the successful early case detection work to other areas. To start some community-based rehabilitation projects, which will include socio-economic rehabilitation.

**In Bas Congo**, to develop activities in endemic villages aimed at early case detection. To start some community-based rehabilitation projects, which will include socio-economic rehabilitation.

## **ANESVAD**

*Ms Verónica Malda*

The strategy followed by ANESVAD in the field of Buruli ulcer control in 2005 has continued to develop along the following 6 major lines of action:

1. Case management and treatment for patients, comprising the following activities:
  - Improvement and construction of facilities and provision of equipment;
  - Support for surgical operations in case-management centres;
  - Help feeding hospitalized patients;
  - Provision of drugs to treat hospitalized and out patients.
2. Information and early detection campaigns
3. Training for staff, and in particular for health workers and teachers
4. Help with schooling and literacy classes for hospitalized patients
5. Prevention of disabilities and rehabilitation of hospitalized patients
6. Preparation of information, education and communication aids (IEC) for health facilities, case-detection campaigns and awareness-raising activities.

We maintained the same pattern of intervention as in previous years:

- First of all, direct support for case-management activities in Côte d'Ivoire, Benin, Ghana and Cameroon
- Secondly, collaboration between ANESVAD and the national Programmes in Benin and Ghana
- Lastly, support for certain activities of the WHO Global Initiative.

### **Côte d'Ivoire and Benin**

One new feature of our activity has been the implementation of comprehensive projects in the case-management centres in Côte d'Ivoire and Benin: this comprises support for activities connected with patient case management itself, (treatment, laboratory case confirmation, food, etc.) including, as an integral part of treatment, the prevention of disabilities and rehabilitation, assistance with schooling and literacy and social reintegration. In addition, some case-management centres organize awareness-raising and early detection activities in the surrounding villages and schools. Training sessions and refresher courses are also organized for health personnel.

This comprehensive arrangement has been implemented:

1. in Côte d'Ivoire, in the following case-management centres:

- The Kongouanou dispensary ;
- The Saint Michel centre in Zoukougbeu ;
- The Demi-Emile Buruli ulcer centre in Angré ;
- The Notre Dame du Carmel centre in Sakassou ;
- The Sainte Famille Centre in Yamoussoukro ;

2. and in Benin, in the following centres:

- Gbèmontin in Zagnanado ;
- Saint Camille in Davougon ;
- La Croix hospital in Zinvié.

In addition to these activities, we ought to mention the disability-prevention and rehabilitation programme under way in Côte d'Ivoire and in Benin. Fabrizio Bonifacio has been collaborating with ANESVAD since 2004. After having carried out, during an initial phase, case-detection missions in Côte d'Ivoire and in Benin in 2005, the main activities in this area have been:

- Implementation of the training programme for staff in case-management centres. In each centre, the training sessions last two months and cover topics such as mobilization techniques, prevention of contractures, making orthoses and other tools, mainly using locally available material.
- So far, the training has been provided in the Saint Michel centre in Zoukougbeu and the Demi-Emile centre in Angré, in Côte d'Ivoire and in the Gbèmontin centre in Zagnanado and the Saint Camille centre in Davougon, in Benin. At present, in Benin Fabrizio is continuing to train staff from the Lalo and Allada health centres and from Zinvié hospital.
- Another activity in this area was the edition of a first manuel entitled "*Manual on techniques for preventing and treating disabilities caused by Buruli ulcer,*" Which is used in the training courses. On completion of Fabrizio's mission in Benin, the manual will be completed with new illustrations.
- And to complete this activity, new rehabilitation rooms were build and equipped in in the case-management centres in Côte d'Ivoire and Benin. Workshops for making orthoses are being built close to the rooms. These new buildings follow standard designs for all the centres.

Noteworthy among the projects carried out in 2005 in Côte d'Ivoire was the training-retraining course organized by Professor Assé in the case-management centres with which we collaborate. In recent years, treatment of Buruli ulcer has advanced both as regards surgery and multi-drug treatment and elements such as rehabilitation have been included in the treatment provided for patients.

These new features of case management are of direct concern to the centres' health personnel, as they are the patients' first contacts. In most cases, they have not received any training to improve their knowledge and skills. The training course involves a series of training seminars for the purpose of updating, retraining and standardizing the knowledge and practices used to treat patients, on the basis of the WHO recommendations. The courses were provided in the centres themselves and included a theoretical and a practical component.

Collaboration with the national Programme in Benin has made it possible to introduce training and early case-detection activities in the departments of Zou, Atlantique and Couffo. The training was intended for physicians, nurses and community health workers and consisted of the following modules : introduction to the disease, diagnosis and case-detection, treatment, social and economic consequences and disease prevention and surveillance. The training courses lasted five days and included a theoretical and a practical component.

With regard to activities planned for 2006, generally speaking we intend to maintain the same level of activity in Côte d'Ivoire and in Benin, while extending the comprehensive case-management projects to all the centres. We plan to terminate the disability-prevention and rehabilitation programme in the centres in Benin and, political circumstances permitting, to complete the training in this area for staff from the centres receiving support from ANESVAD in Côte d'Ivoire.

## **Ghana**

In Ghana, ANESVAD's collaboration in 2005 involved continuing to improve facilities at the Saint Martin d'Agroyesum and Nkawie hospital in Atwima in the Ashanti region, and at the government hospital in Dunkwa in the central region, through IALO (International Anti-Leprosy Organization). At these centres, we have built operating theatres, wards, rehabilitation rooms and classes in which literacy classes and tuition are provided for hospitalized patients.

In Amansie West district, ANESVAD continued its activities for a second year by supporting the early case-detection programme which involved training 172 community volunteers, 400 teachers, 110 "chemical sellers", 96 traditional healers, 40 health workers and 16 nurses from the 40 communities with the highest level of endemicity. The programme includes visits to 27 communities during which we show the WHO film in the evening and examine inhabitants the following morning. This year, the programme includes the purchase of 86 bicycles to help village volunteers monitor the cases in villages.

In 2006, we plan to step up our action in Ghana in areas where we are already present and to expand our collaboration to other regions such as that of the Agogo hospital.

## **Cameroon**

ANESVAD started operating in Cameroon in 2005 via MSF–Switzerland, by providing support for a programme to improve case-management at the Akonolinga hospital. In 2006, we intend to continue to provide support for this programme and to determine our future strategy in Cameroon.

## WHO

Throughout 2005, ANESVAD funded the publication of new IEC documents to raise awareness and educate people about Buruli ulcer, essentially at the community level. The actual documents are a documentary film for use in community education activities and over 35 000 documents (more than 9 000 in English and over 25 000 in French) in different formats (brochures, posters and leaflets) for distribution to community health workers in 16 countries.

In addition to its work in the field, ANESVAD seeks to inform the public about problems such as Buruli ulcer besetting developing countries. To this end, we conduct information campaigns in Spain.

ANESVAD became involved in Buruli ulcer control in 1999; from the outset we appreciated the importance of providing information on the disease to the Spanish public, and we were the first organization to provide information on Buruli ulcer in Spain.

### **1. Awareness campaigns using the media.**

In order to raise awareness of the disease, we have conducted media campaigns, essentially using television. It needs to be borne in mind that we are talking about a virtually unknown disease that occurs in remote locations, and this entails certain difficulties. During this period, our efforts mainly involved providing information on the disease, its symptoms, treatment, sequelae and the countries in which it is endemic, rather than on ANESVAD's efforts to control it.

Since 1999, ANESVAD has launched seven campaigns to raise awareness, some of which have been presented here at WHO. Thanks to these efforts, the disease has become better known. Proof of this is the fact that the media get in touch with us to request data, documents and interviews.

Individuals also get in touch with us to organize activities themselves to raise awareness of Buruli ulcer among their acquaintances. For example, pupils at a small school in Alicante asked us for a video on Buruli ulcer. The twelve-year-old pupils watched the film and prepared a presentation on the disease which they used in the other classes to talk about it to their schoolmates. They also organized activities with the parents' association, the municipal authorities and the town's market etc. Ultimately, almost the whole town had heard about the disease.

### **2. Awareness-raising activities.**

TV campaigns are very effective because they are seen by many people. However, on account of their short format, they are unable to provide detailed information. Consequently, they need to be completed by information activities which not only make it possible to get directly into touch with the target audience, but which also provide far more detailed information.

Buruli ulcer is part of all ANESVAD's general activities (lectures, exhibitions, and workshops in educational establishments) because it is one of our main areas of activity. However, we have also endeavoured to organize ad-hoc activities on the disease.

For example, we have developed a model intended for medical faculties and nursing colleges, during which we organize at the same time a lecture and a photographic exhibition. Our aim is

to inform future health professionals about two diseases: leprosy and Buruli ulcer. These are two diseases in which ANESVAD is involved and which – especially in the case of Buruli ulcer - are not included in the regular curriculum despite the number of people afflicted by them worldwide. The lecture and exhibition are entitled "Forgotten diseases: leprosy and Buruli ulcer".

We aim to reach a specialized audience concerned by questions related to health. The lecture is delivered to students and lecturers: this means that we address future health professionals and those responsible for training them. The latter will then be able to introduce the diseases into their lectures, thus helping to spread the message.

The exhibition is usually presented in the university entrance hall, thus making it accessible to everyone. In addition, the main local media are informed of the events and their location, in order more widely to publicize them.

These events have so far been organized in four universities. The experience has been a positive one, and we plan to get in touch with other venues.

## **Conclusion**

As you can see, raising awareness completes the activities carried out by ANESVAD in the field. It is only when people are interested that they are able to absorb information, to become aware of the problem and as far as possible to become involved. This has been our aim: to try to provide information about Buruli, in order to combine the efforts of all.

## **SUPPORT PROVIDED BY LUXEMBOURG RAOUL FOLLEREAU FOUNDATION (FFL) TO BURULI CONTROL ACTIVITIES IN BENIN IN 2005 AND PROSPECTS FOR THE FUTURE.**

*China E.,<sup>1</sup> Sopoh G.<sup>2</sup>*

<sup>1</sup>Beninese Raoul Follereau Association, Cotonou, Benin

<sup>2</sup> « Le Luxembourg » Centre for Buruli Ulcer Screening and Treatment (CDTUB), Allada, Benin

The Luxembourg Raoul Follereau Foundation provides support for Buruli ulcer control in Benin via its local partner, the Beninese Raoul Follereau Association. Its support is channelled essentially to the Allada CDTUB, which was built and equipped by FFL and handed over to the Beninese authorities, who have been responsible for operating it since July 2002.

Year by year, the Centre has improved its performance in order to attain its objectives for the treatment of Buruli ulcer, thanks to the support it continues to receive from FFL.

In 2005, support for the Allada CDTUB in 2005 was based on five projects:

- strengthening the centre's capacity,
- helping to supply drugs,
- assistance with psychological and social case-management and tuition of hospitalized children,
- Assistance with the provision of medical and surgical supplies and
- Funding for activities to raise awareness.

The total cost of this support amounts to CFAF 267 870 655 i.e. €408 366.

FFL has every intention of continuing to provide its support in the following areas:

- construction of additional facilities,
- epidemiology,
- assistance with drug supplies,
- training staff,
- monitoring hospitalized patients,
- awareness campaigns for different target groups,
- procurement of specialized medical equipment.

## **UPDATE ON THE PROJECT TO TREAT BURULI ULCER USING HYPERBARIC OXYGEN THERAPY, ALLADA, BENIN**

*Dr Franco Poggio*

Participants in TUBA, which was held at Cotonou from 5 to 7 December 2005, were able to observe that the project to treat Buruli ulcer using hyperbaric oxygen therapy, which was proposed at the WHO meeting and implemented at the Allada Buruli Ulcer Treatment Centre (CTUB) in Benin, is now operational.

We were impressed by the high quality of the facilities provided by the Luxembourg Raoul Follereau Foundation, which is undertaking major extension work to the hospital in order to provide more beds and a pathology laboratory, which will be monitored by our own Dr C. Clemente.

Special thanks are due to Mr Kohll and to Professor Kiniffo from the Follereau Foundation, to the various Rotary Clubs of Districts 2040 and 2050, and in particular to the north Bergamo and New York Manhattan Rotary Clubs and to Admiral Martines, who heads the Italian Naval medical services; all of them have supported my own Milan Aquileia Rotary Club and contributed to this project in an exemplary Rotarian spirit.

Our sincere thanks are also due to Drs Christian Johnson, Ghislain Sopoh and Ange Dossou, who are here with us today, and who have given dedicated support to the project on the spot, in collaboration with a team of paramedical staff.

Should the results confirm the efficacy of hyperbaric oxygen therapy as a treatment for Buruli ulcer, our Rotary group is prepared to examine the possibility of providing a second hyperbaric chamber alongside the existing one.

As regards medical and scientific aspects, my colleagues Professor Giorgio Leigheb and Dr Ange Dossou will present their report to you themselves.

We are confident that the Minister of Health of Benin, Ms Dorothée Akoko Kindé GAZARD, will pursue this collaboration in order to try to solve this serious health problem.

Thank you for your attention.

## **ANTIBIOTIC TREATMENT AND OTHER TREATMENTS**



## ANTIBIOTIC TREATMENT AT THE POBÈ CENTER, BENIN – UPDATE

*Dr Annick Chauty*

In 2005, the Pobè Buruli ulcer Diagnosis and Treatment Centre (CDTUB) intensified case-detection and treatment in peripheral health centres.

A total of 284 patients were diagnosed and treated.

Treatment is in compliance with the WHO protocol : streptomycin and rifampicin are administered for at least 4 weeks before offering surgery, which is carried out at the CDTUB during the fourth week if possible, although frequently later.

The size of the lesions was noted when the cases were detected:

- 68 patients had small of less than 5cm, 80% of them did not require surgery.
- 133 patients had lesions of from 5 to 15cm, 50% of them were cured without resorting to surgery.
- 83 patients had lesions of over 15cm, 33% of them refused surgery but were nevertheless cured.

The following severe forms were detected :

- Three patients with multiple skin sites on detection: They were treated with SR and adjunct surgery. None of them developed further lesions after treatment.
- Six patients had multiple skin and bone lesions (2,1%): They were treated with SR and surgery. Removal of the bone sequestrations was performed only after the periosteum had responded sufficiently to permit removal of the sequestration. Two patients developed lesions elsewhere during treatment or in the weeks that followed. One of them has active hepatitis B and the other is HIV-positive.
- Eight HIV-positive patients (2,8%) had skin lesions on admission ( HIV was detected during the examinations on admission). Two patients with lesions of less than 5cm cured under SR without surgery and developed no further lesions. Five who had lesions of more than 15cm were treated by SR and surgery; two of them developed further bone lesions. One patient with a lesion of more than 15 cm absconded to traditional healers. After we had visited him several times he decided, seven months later, to return to the CDTUB; his lesion had spread over the whole limb.

CD4 counts were carried out on these HIV-positive patients and they were placed under ARV.

As things stand, the results of the laboratory case confirmation examinations are as follows:

- 64% of patients have at least one positive smear examination,
- Out of 197 patients examined by PCR, 152 (77%) had at least one positive PCR.

## **Conclusion**

It is important to continue with case detection at patients' local health centre and to provide them with streptomycin and rifampicin as soon as the disease is diagnosed.

The smaller the lesion, the lesser the need for surgery. If patients refuse to undergo surgery, it is important to offer them simple clean dressings as many of them will develop scars without sequelae under antibiotic treatment.

Case management of forms with bone involvement is improved by prior administration of a four-week course of SR which enables patients to develop a response in the periosteum, permitting removal of the sequestrum.

Dissemination of lesions, especially in the bone, is a source of concern in the case of patients with co-morbidity, especially chronic hepatitis B, or HIV infection.

# **ROLE OF TREATMENT WITH TOPICAL ANTIBIOTICS (RIFAMPICIN AND STREPTOMYCIN) IN THE TREATMENT OF *MYCOBACTERIUM ULCERANS* INFECTION ON A FACIAL SITE**

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Buruli ulcer is a disabling and disfiguring disease.

The treatment generally recommended for case management of Buruli ulcer involves excision of the necrosed tissue followed by restorative procedure with or without skin graft.

Although *Mycobacterium ulcerans* is sensitive to several anti-mycobacterial drugs *in vitro*, their role in treatment of the disease has yet to be demonstrated.

In view of the numerous difficulties with which surgical treatment is associated in endemic areas, since the launch of the Global Buruli Ulcer Initiative the World Health Organization has always given research priority to the development of a drug-based treatment.

Extensive oedematous forms of the disease sited on the face or which threaten to spread, especially in children, are difficult to treat by surgery alone, which often results in serious deformities resulting from extensive excision.

In response to an invitation from the Global Buruli Ulcer Initiative for all health professionals applying the provisional recommendations to inform it of their comments and experience, we are submitting some preliminary observations on the role of topical treatment with antibiotics (rifampicin and streptomycin) in treatment of *Mycobacterium ulcerans* infection sited on the face.

# CLINICAL RESPONSE AND BACTERIAL KILLING DURING ANTIBIOTIC TREATMENT OF *M. ULCERANS* DISEASE

*Authors: Phillips R, Sarfo FS, Osei-Sarpong F, Lartey A, Adentwe E, Ampadu E, Adjei O, Wansbrough-Jones M.*

## Introduction

Recently the combination of rifampicin with streptomycin was evaluated for its ability to kill *M. ulcerans* in early human lesions of *M. ulcerans* disease. Cultures for *M. ulcerans* were positive at baseline with no treatment and after treatment for 2 weeks but negative thereafter, indicating that this combination of antibiotics might be useful for management of nodules and plaques, the only types of lesion included in the study. Further encouragement came from clinical observation and measurement showing that no lesions enlarged and most became smaller during treatment. We have compared the clinical response and bacterial killing during treatment with standard daily streptomycin and rifampicin to that with alternate day streptomycin and rifampicin or daily moxifloxacin and rifampicin using punch biopsies to quantify viable bacteria.

## Methods

30 subjects with early lesions (nodules, plaques, ulcers <10 cm in maximum diameter and oedema) were recruited serially and allocated randomly. Only those above 35kg in weight were allocated to receive moxifloxacin since it is only available in one dose of 400mg. Six subjects received moxifloxacin 400mg and rifampicin 10mg/kg daily (MR), 5 received streptomycin 15mg/kg and rifampicin 10mg/kg on alternate days (SRA) and 19 received streptomycin 15mg/kg and rifampicin 10mg/kg daily (SRD). All patients received treatment for 8 weeks. 4 mm punch biopsy samples were taken from lesions for ZN stain, PCR for *M. ulcerans* and semi-quantitative culture at baseline and further culture 4 or 6 weeks after starting antibiotics. The surface area of lesions was measured by taking tracings alongside punch biopsies. All patients will be followed up for 12 months.

## Results

To date all of 8 patients on SRD had negative cultures after treatment for 4 or 6 weeks and their lesions were completely healed after 3 months. 5 more patients had >50% and 1 <50% healing but culture results are not yet available. 3 of 4 patients on SRA for 4 weeks had negative cultures and 1 patient had complete healing so a biopsy was not done. Of the 4 patients, 3 had >50% healing but 1 had recurred at 12 months follow up. Of 6 patients treated with MR, 3 had negative cultures after 4 weeks and in 1 there was a 3 log reduction in colony count but there was no significant reduction after 4 weeks in 2 patients. There was complete healing in 1 patient, >50% in 3 patients and <50% in 2 of which 1 was still not healed after 12 months. Cultures were negative before and after treatment in 14 cases despite positive clinical diagnosis and PCR.

## Conclusions

These results confirm that daily rifampicin and streptomycin is an effective combination for treatment of early *M. ulcerans* disease and that punch biopsy samples can be used to evaluate new antibiotic combinations in humans. More data are needed to fully evaluate the SRA and MR regimens but the clinical response and culture results to date are encouraging. The time before taking the second biopsy for culture may have been too short in early patients treated with MR or SRA and a 6 week time interval will be used in future. These pilot studies have an important role in testing antibiotic regimens before proceeding to full scale clinical trials.

**THE *IN VITRO* AND *IN VIVO* ACTIVITIES OF RIFAMPICIN, STREPTOMYCIN, AMIKACIN, MOXIFLOXACIN, R207910, LINEZOLID AND PA-824 AGAINST *MYCOBACTERIUM ULCERANS*.**

*Baohong Ji, Sébastien Lefrançois, Jerome Robert, Aurélie Chauffour, Chantal Truffot, Vincent Jarlier.*

Bactériologie-Hygiène, Faculté de Médecine Pierre et Marie Curie, Université Paris, France.

Seven antimicrobials were tested *in vitro* against 29 clinical isolates of *Mycobacterium ulcerans*. R207910 demonstrated the lowest MIC<sub>50</sub> and MIC<sub>90</sub>, followed by moxifloxacin (MXF), streptomycin (STR), rifampicin (RIF), amikacin (AMK), linezolid (LZD), and PA-824. All but PA-824 demonstrated an MIC significantly smaller than the clinically achievable peak serum level. Administered as monotherapy to mice, RIF, STR, AMK, MXF, R207910 and LZD demonstrated various degrees of bactericidal activity, whereas PA-824 failed to prevent mortality and to reduce the mean number of CFU in the footpads. Because 4 or 8 wk of treatment by the combinations RIF-MXF, RIF-R207910 and RIF-LZD displayed bactericidal effects similar to those of RIF-STR and RIF-AMK, these three combinations might be considered as orally administered combined regimens for treatment of Buruli ulcer. Taking into account the cost, potential toxicity and availability, the combination RIF-MXF appears more feasible for application in the field; additional mouse experiments to define further its activity against *M. ulcerans* are warranted.

# CLINICAL AND THERAPEUTIC TRIAL OF HYDRATED ALUMINIUM SILICATE TO TREAT BURULI ULCER

*Dr Jérôme Son*

Buruli ulcer is a mycobacterial infection of the skin which has been endemic in our tropical regions for several decades and which has highly disabling sequelae. The disease is very difficult to cure, even with numerous medical and surgical interventions. This situation has led to the emergence of a number of approaches to treatment, one of which involves treatment with hydrated aluminium silicates (clay).

The title of the project in this presentation is <<*Clinical and therapeutic trial of hydrated aluminium silicate to treat Buruli ulcer*>. Our main purpose is to evaluate the contribution of clay to treatment of Buruli ulcer.

The main inclusion criteria were:

1. Confirmed case of BU
2. Age < 55 years
3. HIV negative patient

Patients were divided into two groups:

1. **Group A**, comprising 1/3 of the patients, who were treated in the conventional manner (dressing, surgery)
2. **Group B** comprising the other 2/3 of the patients, who were treated using clay.

Samples were taken from all the patients at the beginning of treatment, and a second sample was taken during the second month of treatment.

We were able to include 46 patients, 20 of whom were given conventional treatment 26 treatment using clay. Eight of the latter group underwent surgery to manage scarring; these formed the third group, **group C**.

After six months, we obtained the following results.

Evolution	Group	Group A %	Group B %	Group C %
Cure		18.75	46.67	50.00
Satisfactory evolution		62.50	40.00	50.00
Poor evolution		18.75	13.33	00.00

Samples taken after four months' treatment from patients cured or whose evolution was satisfactory, and whose samples had been positive at the outset of treatment were negative.

From the clinical angle, clay achieves a much more rapid detergent effect.

Medium-sized lesions cure far more spontaneously.

The results show that hydrated aluminium silicate could effectively help in case management of Buruli ulcer patients. We need further to pursue the trials in order to determine exact indications and the different ways in which clay acts.

## **CASE MANAGEMENT**



## **THE BENEFITS OF CONTROLLED SCAR FORMATION IN SURGICAL CASE MANAGEMENT OF BURULI ULCER**

*Pr Henri Assé, Dr Patrick Meredith, Dr Rémy Zilliox*

"Controlled" scar formation (CS) is a deliberate treatment procedure whose purpose is to achieve epidermization of a wound using the three phases of second-line scar formation : cleansing, budding, epidermization.

It may also be used to improve the result of incomplete first-line scar formation (excision suture).

Controlled scar formation is not an act of negligence or an overlooked unapplied dressing. It is a carefully managed alternation of pro-inflammatory and anti-inflammatory dressings.

The detersion phase may be performed using local topical agents or debridement with a (pro-inflammatory dressing)

Budding will take place in a pro-inflammatory humid environment with treatment of any local microbial infections.

Hypertrophied budding will be controlled by an anti-inflammatory dressing (corticosteroid) or surgical de-budding.

Epidermization will spread from the edges of the wound. Epidermal cells will grow from the outside to the inside or from epidermal "inclusions" to the edge: centrifugal and centripetal scarring. If such spontaneous scarring is not longer possible, surgical scarring must be considered, i.e. split skin graft.

# **ORGANIZATION OF CASE MANAGEMENT OF BURULI ULCER IN THE DEMOCRATIC REPUBLIC OF THE CONGO: THE CASE OF THE IME/KIMPESE HOSPITAL IN BAS-CONGO PROVINCE.**

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## **Introduction**

Buruli ulcer is still endemic in the Democratic Republic of the Congo, where cases have been reported in every province, with the exception of west and east Kasai. The province of Bas-Congo is the site of the most important foci, which are located in the Cataractes district and more precisely in Songololo territory.

The IME/Kimpese hospital, which is located in Songololo territory some 220 kilometres south of Kinshasa, regularly admits cases of *Mycobacterium ulcerans* infection. This hospital is the general referral hospital for Kimpese rural health district, which covers an area of 3900 Km<sup>2</sup> and has a population of 160 442.

On account of its location in Bas-Congo province, its position with regard to the Buruli ulcer map, its facilities and the reputation it has built up since 1950 throughout the province as a missionary and medical training centre and its leading position in leprosy and tuberculosis control, the IME/Kimpese hospital is called on to play a key role in controlling Buruli ulcer in Bas-Congo province.

## **Development of the Buruli ulcer control project**

### **1. Composition of the team**

A multi-disciplinary team has been in place since 2004; it comprises a histopathologist, a surgeon, two trained physicians, three nurses, three laboratory technicians, two x-ray technicians, two physiotherapists, a nutritionist, a chaplain and two administrative staff.

### **2. Priorities for control strategies**

These fall into five control elements, as advocated by the Global Buruli Ulcer Initiative:

1. Strengthening the case management capacity of facilities in the areas affected ;
2. Prevention of disabilities and physical rehabilitation ;
3. Feeding patients and providing psychological and social support for those affected;
4. Enhancing IEC for the general public and community-based surveillance ;
5. Training and research.

### **3. Partners**

At the national level, the Buruli ulcer project at the IME/Kimpese hospital collaborates with the National Buruli Ulcer Control Programme, the leprosy/TB Coordination Bureau, the National Institute for Biomedical Research and the University of Kinshasa...

Internationally, our activities are supported in different degrees by WHO, the IMT/Antwerp, ALM, the EU (BURULICO), MSV, PCD, the «F.MIULLI» regional hospital in Italy and the Sasakawa Memorial Foundation.

### **4. Preliminary results**

Since well before independence, Bas-Congo province has been the site of one of the largest foci in our country: Songololo.

At present, the data available on case notification at the IME/Kimpese hospital confirm that the main origin of Buruli ulcer patients is still Songololo territory in Cataractes district ;

- Improved clinical case management of BU patients (excision, graft, prevention of sequelae, corrective surgery and medical treatment);
- There are virtually no absconders;
- Gradually improved access to information in the areas affected ;
- The annual admission rate has trebled, from 16 to 50 patients ;
- Confirmation of active forms is 70% ;
- Post-admission follow-up after one year of more than 70% of patients ;
- Recognition by the political, administrative and health authorities that Buruli ulcer is a public health problem in endemic areas.

### **5. Outlook**

- Determination of the scale of the disease in the province ;
- Institution of an operational community-based surveillance system ;
- Establishment of up-to-date mapping of Buruli ulcer ;
- Strengthening care facilities to provide providing local case management ;
- Clinical, epidemiological and environmental study ;
- Development of a regional mycobacteriology laboratory.

## **ADVANCES IN THE TREATMENT OF BURULI ULCER WITH HYPERBARIC OXYGEN THERAPY IN THE CDTUB OF ALLADA (BENIN) – PILOT STUDY**

*Leigheb G, Poggio F, Clemente C, Martines V, Leigheb F, Johnson RC, Sopoh GE, Dossou A, Barogui Y*

Hyperbaric oxygen therapy (H.O.T.) in association with antibiotics and surgery when necessary has been employed in the CDTUB “Le Luxembourg” of Allada in the treatment of Buruli ulcer (BU). Since 2005 we follow a scientific protocol proposed to evaluate by a controlled clinical trial the efficacy of oxygen to improve the healing of the lesions with a consequent reduction of the destructive surgical excisions and possibly with a shortening of the days of hospitalization for BU patients. A provisional analysis of this pilot study concerning three groups of cases of BU classified in different clinical stages has been performed. The cases treated with recommended standard antibiotic therapy (streptomycin and rifampicin), surgery when necessary, and H.O.T. (for a total of 28 days), compared with three control groups (BU in treatment with antibiotics without H.O.T.), demonstrate during the follow up (T28, T60, T90) an impressive clinical improvement of cutaneous lesions with shortened times of healing. A number of clinical pictures which we present will give the confirmation of our successful efforts.

Waiting for a greater number of BU cases to submit to our therapeutic protocol and for a definitive statistical analysis we express our satisfaction for the very promising clinical results obtained with HOT.

# COMBINATION OF SURGERY AND CHEMOTHERAPY IN THE MANAGEMENT OF BURULI ULCER: THE BENEFITS.

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## Background Information

Buruli ulcer, a tropical swampy climate disease, is one of the commonest diseases associated with most typical villages such as those in the Bomfa sub-district of Ejisu-Juaben District in the Ashanti Region of Ghana. These villages are inhabited mainly by the “*poor of the poor – the poorest of the poor*” who are mainly subsistence farmers.

All the Buruli ulcer patients had a combination of surgery and chemotherapy as the mode of treatment. This was in the quest of finding the most effective ways of treating the disease among these people and in a response to World Health Organization’s guidelines on the use of chemotherapy in the treatment of Buruli ulcer. A study was therefore conducted using *Patients’ Intake and Engagement Form* as database to find factors including the combination of surgery and chemotherapy that would enhance the total treatment of the patients and subsequent eradication of the disease from the area.

## Aims of Study:

- To find out the role of surgery combined with chemotherapy in the management of Buruli ulcer in an endemic area.
- To find out the effect of this “dual therapy” on the duration of hospital admission.
- To find out the most effective approach in the control of Buruli ulcer in an endemic area (Pius, this aim is not reflected in the results? Already inferred from the first point).

## Method and subjects

Random sampling of “*Patients’ In -take and Engagement Form*” filled for all patients were used as the main source of information.

Buruli ulcer patients within the Bomfa sub-district of the Ejisu-Juaben District in the Ashanti Region of Ghana from January 1, 2005 till December 31, 2005.

## Results

- Sixty-two (62) patients from the Bomfa sub-district were treated with the combination of *surgery* and *chemotherapy* at the Global Evangelical Mission Hospital between January 1 till December 31 2005.
- The ages of the 62 patients ranged from 4 to 79 years.
- There was a reduction in the number of multiple surgeries as compared to the pre-chemotherapeutic era.
- Sizes of edematous forms reduced considerably as a result of chemotherapy thereby enabling lesser area of excision as compared to the pre-chemotherapy era.
- Follow-up of these 62 patients up to date have shown no signs of recurrence observed (follow up continuing).
- Forty-five (45) out of the sixty-two (62) patients had their lesions on their lower limbs representing 72.6% of the total number of patients treated.
- No complication was observed in the use of Buruli chemotherapeutic drugs (streptomycin and rifampicin).

## Conclusion

- The application of Buruli chemotherapy has resulted in “minimal” surgery as against the traditional extensive tissue debridement in the pre-chemotherapeutic era.
- Currently the combination of surgery and chemotherapy is the main stay of treatment for Buruli ulcer patients.
- The recommended dose of rifampicin and streptomycin was strictly adhered to.
- The “dual” mode of treatment (surgery + chemotherapy) reduced hospital admission period which directly reduced the cost of treatment (no evidence is provided in the results to lead to this conclusion).
- Surgery and chemotherapy play a major role in the control of Buruli ulcer.

## Recommendations

- All the 62 patients in the series need regular and long term follow-ups so as to look for any signs of recurrences.
- The combination of chemotherapy and surgery is recommended to Buruli ulcer management centres.



## **PREVENTION OF DISABILITIES**



# **PRESENTATION OF A TOOL TO FACILITATE SHARING OF KNOWLEDGE AND KNOW-HOW FOR THE PREVENTION OF DISABILITIES LINKED TO BU**

*Ms Valérie Simonet*

## **1. Background**

In Cameroon, Buruli ulcer control is currently organized around 5 referral centres providing case management in the main regions affected. At one of these centres, Ayos district hospital, a pilot project, which is being jointly carried out by the Ministry of Health and Aide Aux Lépreux Emmaüs-Suisse, is at a fairly advanced stage. Training in prevention of disabilities from Buruli ulcer is part of the comprehensive strategy currently being implemented in this country and which comprises:

1. Training for medical staff and community health workers
2. Reinvigorating the district management teams in the districts concerned
3. Strengthening the referral and counter-referral systems
4. Strengthening community-based case-management activities
5. Fitting out case management facilities and providing vehicles
6. Providing drugs and other consumables
7. Active case detection

In 2005, several strategies were introduced in order to strengthen each of the above elements, and more specifically prevention of disabilities; for example, a multi-disciplinary weekly visit was organized to all BU patients in hospital at Ayos and a district management team was set up to monitor the routing of patients and their follow-up as outpatients.

This presentation focuses on one of the strategic elements introduced to prevent disabilities: training.

## **2. Aims and main achievements in 2005 in terms of training to prevent disabilities from BU**

### **a. Training providers specialized in prevention of disabilities caused by BU**

The third and final training module, which lasted three and a half weeks between May and June 2005, taught providers elementary techniques for preventing disabilities caused by Buruli ulcer. Follow-up was provided in the form of reports and correspondence between the rehabilitation team at Ayos and the trainer in Switzerland.

An evaluation of the programme was carried out in December and showed highly encouraging results, both in terms of the efficacy of the treatment and of the integration of disability prevention into comprehensive case management of Buruli ulcer patients. The main weaknesses were identified and led to the introduction of new strategies which are due to be re-evaluated in the spring of 2006.

**b. Introduction to prevention of disabilities for health workers in integrated district health centres and from other endemic regions**

As part of the training activities on comprehensive case management of Buruli ulcer, the providers from Ayos who were trained in prevention of disabilities themselves organized and provided basic training on treatment of oedemas and other deformities caused by joint and other contractures.

**3. Training in prevention of disabilities caused by BU: aims and goals for 2006**

**a. Improvement of the quality of disability prevention activities at Ayos**

An in-service training system has been introduced; it comprises regular collaboration with a physiotherapist from Yaoundé who has been integrated into the programme, one or two annual visits to Ayos by the trainer and monitoring of reports using the Internet. We plan to introduce precise treatment protocols, and to evaluate the skills acquired once or twice a year using a document which has already been tested in the field and which adopts precise and benchmarked indicators.

**b. Sharing knowledge and know-how with other health workers from other centres which are strategic for prevention of disabilities**

Ayos has become the location of choice for providers to attend practical training courses, the first of which is due to take place in April 2006. The aims and duration of the training course will be determined for each trainee on the basis of their expected level of performance having regard to the task of his or her health centre. These new rehabilitation specialists will be regularly supervised in the field by one of the providers trained during the initial training session. The trainer will herself supervise these centres at least once a year; she will also evaluate the skills acquired during the course at Ayos. In addition to the manual published by WHO on prevention of disabilities, case management protocols will assist the new providers responsible for prevention of disabilities in their task.

**c. Sharing skills for prevention of disabilities at the community level**

The practice of rehabilitation specialists making rounds of the integrated health centres (IHC) or even, if appropriate, directly to the villages, provides confirmation of the decisively community-based orientation of disability prevention. This strategy has a threefold purpose: to enable patients to be monitored on an outpatient basis, to enhance the disability-prevention skills of providers at IHCs and to provide families with ongoing training in how to care for their relatives affected by Buruli ulcer. In this case too, precise case-management protocols will be of considerable use in helping those concerned to perform their tasks.

#### **4. Aims and types of protocols that contribute to prevention of disabilities from Buruli ulcer**

Case-management protocols serve several purposes: in addition to facilitating the implementation of the main disability prevention activities, they ensure the uniformity of teaching and help to preserve the quality of treatment. They may take several forms. ALES has decided to adopt that of a practical field handbook containing several modules suited to individual requirements. In the past, WHO and Handicap International have already published highly satisfactory handbooks of this type intended for both health workers and families. In the same way, this handbook, which specifically focuses on the problems posed by Buruli ulcer, could prove a valuable field version of the keenly-awaited manual on prevention of disabilities caused by Buruli ulcer, which is due to be published this year.

# HOW TO ORGANIZE AND DEVELOP POD ACTIVITIES IN BURULI ULCER MANAGEMENT

*Ms Linda F. Lehman*

This presentation will discuss the process and challenges of organizing and developing Prevention of Disability (POD) activities within Buruli Ulcer (BU) management. Strategies are needed for local health services as well as for referral centers which first establishes a solid foundation with the implementation of essential POD activities and then expands to include more complex interventions. It requires leadership, political, technical and financial support from government, community and non-government organizations. The use of a multidisciplinary technical team with a public health, clinical and rehabilitation perspective is important in planning, monitoring and evaluating the development and implementation of POD activities at all levels. This team is more effective if the members themselves have had experience in organizing and implementing POD within their own BU control activities.

Below are important steps which have already been obtained in organizing and developing POD Activities in BU Management.

1. The political recognition and support provided by WHO's Global Buruli Ulcer Initiative which has included POD as an essential component of BU management along with surgery and antibiotics.
2. The development of a POD manual, a poster and a brochure by WHO's Global Buruli Ulcer Initiative to give health managers and workers a better understanding about POD and the essentials to implement.
3. The clarification of essential POD activities to be taught, implemented and supervised at local health services managing BU cases.
4. The recognition that POD requires a team effort which includes the collaboration and participation of persons affected by BU, their community and all health workers.
5. The inclusion of a POD module within the WHO's Global Buruli Ulcer Initiative International Surgical Training curriculum
6. The development of additional rehabilitation training materials and courses for specialist (physical and occupational therapist) working in BU referral centers.

On the Job Training (OJT) may be one of the most effective and efficient training strategies to teach essential POD activities. Experiences with OJT in the Taabo area of the Ivory Coast and Ashanti region of Ghana during 2005 and 2006 will be shared. OJT utilizes the existing health service and resources to teach workers the knowledge and skills to prevent disability with the BU patients managed by their service. The opportunities to problem solve utilizing local resources, followed by the immediate opportunity to monitor and observe change, encourages the health worker and persons affected by BU to appreciate the practical ways they can prevent disability daily.

The exclusion or limited inclusion of wound dressers and surgeons within previous POD training has limited or interfered with the implementation process of POD within BU management. The important roles that the surgeon, the wound dressers and the persons affected by BU have in preventing and managing disability will be demonstrated. The presentation will challenge the participant to evaluate their teaching methodology, the benefit of theoretical discussions and practical experiences which integrate theoretical concepts.

The challenge to the trainer / supervisor will be to become a facilitator who provides a participatory learning experience which gives the knowledge, skills and attitudes needed to implement activities that prevent disability.

Periodic supervision includes planned OJT and will be the key to assuring that POD activities are developed and implemented according to the local situation and resources. Identification of referral centers and the process for referring needs to be clearly understood. Criteria for referral can be developed by a technical team. Care needs to be given to assure that local health services are able to provide the essential POD activities and that referral is only done for activities requiring specialty training. Referral centers should demonstrate good quality implementation of essential POD activities by a multidisciplinary team within their service. An expanding bank of technical support persons (management and treatment) should evolve from both local and specialty centers as POD services are implemented.

# **ADEQUATE POSITIONING TO PREVENT DISABILITIES IN BURULI ULCER**

*Ms Linda F. Lehman*

Inadequate positioning in Buruli Ulcer(BU) management is one of the leading causes of disability and deformity. Skillful anti-deformity positioning is fundamental to successful management outcomes. Combined with adequate control of oedema, good wound management and skin care, adequate management of scars, early exercise and activity, skillful anti-deformity positioning can prevent complications and facilitate function. Anti-deformity positioning can help produce successful outcomes when understood by all members of the team: surgeons, clinicians, nurses, wound dressers, therapists, the person affected by BU and their caregivers. Indeed, all need to understand the vital importance of anti-deformity positioning. Further, all need to work together to ensure that adequate positioning is obtained early in treatment and maintained until wound healing and scar maturity is obtained.

Training and supervision must include opportunities to improve knowledge and skills in anti-deformity positioning. Local materials and resources need to be utilized and adapted to ensure that adequate positioning is consistently obtainable by both health workers and persons affected by BU. The most frequent problems observed have been the prolonged immobilization of affected body parts and the inadequate or inappropriate positioning of the hand, e.g., metacarpal phalange (MP) joints neglected in extension by health workers, before and after skin grafting. This too, has caused much dysfunction and deformity.

Briefly, normal tissue healing processes will be reviewed with a focus on positioning that is best used during the active inflammatory phase, the repair or proliferation phase and the maturation or remodeling phase. Positioning aims to control edema, maintain full soft tissue and joint range of motion, and facilitate function. The strong disabling forces of contracting tissues may require much attention to control until the scar is mature (1-2 years) . Wound contraction is an ongoing process influenced by myofibroblasts. Excessive production of collagen, called fibrosis, can cause stiffness and interfere with function.

Examples of positions which cause oedema and facilitate soft tissue and joint contractures will be demonstrated. Conversely, this will be followed by a demonstration of anti-deformity positions which can decrease oedema and improve soft tissue length, joint movement and function. The purpose of this presentation is to increase the participant's awareness that much of the disability seen in Buruli Ulcer is the direct result of inadequate positioning and prolonged immobilization. Improved knowledge and skills in anti-deformity positioning are expected to reduce the disabilities caused in BU in the future.

## **LABORATORY CONFIRMATION OF CASES**



## HOW A DIAGNOSTIC SYSTEM OPERATES IN GHANA

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In order to strengthen diagnostic capacities, efforts were undertaken to establish a diagnostic network initially comprising two major treatment centres in two endemic regions in Ghana, one local reference laboratory and two external reference laboratories.

### **Case finding and inclusion criteria**

Case finding utilized the services of community based volunteers to refer suspect cases to treatment centres. After examination by the local surgeon clinically diagnosed patients with pre-ulcerative and ulcerative lesions and a duration of the disease of less than 6 month (“early lesions”) were selected for laboratory diagnosis. Only complete sets of diagnostic specimens with accompanying clinical information were processed in the laboratory.

### **Standardized collection of patient information**

Relevant patient information (clinical, epidemiological, treatment, specification of specimens) was collected on a laboratory data entry form and the BU1 form.

### **Standardized specimen collection bags**

In order to provide optimal conditions for storage and transport of specimens and to facilitate specimen collection, standardized specimen collection bags were distributed to the hospitals. Besides an empty laboratory data form, swabs, sterile surgical disposable scalpels and forceps, the bags contained test tubes with storage and transport media for the respective specimens/laboratory tests:

<b>Pre-ulcerative specimens</b>	<b>Ulcerative specimens</b>	<b>Transport/storage medium</b>	<b>Diagnostic test</b>
-	swab	5 ml PANTA medium	microscopy/culture
-	swab	700 µl Cell Lysis Solution	DRB-PCR
-	swab	700 µl Cell Lysis Solution	standard PCR
tissue	tissue	5 ml PANTA medium	microscopy/culture
tissue	tissue	700 µl Cell lysis solution	DRB-PCR
tissue	tissue	700 µl Cell lysis solution	standard PCR
tissue	tissue	5 ml 10 % buffered neutral formalin	histopathology

In view of limited refrigerating facilities, storage of specimen bags was carried out at room temperature. Unused specimen bags were replaced by reference laboratory staff after six months in order to avoid degrading of media. Once diagnostic specimens were in the bags refrigerated storage was recommended.

### **Standardized collection of specimens**

Swabs were taken by circling the entire undermined edge of ulcers before surgery. Tissue specimens with a maximum size of 10 x 10 mm were obtained from surgically excised tissue after surgery. In case of pre-ulcerative lesions the tissue specimens were taken from the centre of the lesion by cutting the centre longitudinally and horizontally in four equal segments. The tissue specimens for ulcerative lesions were taken from the edge of the lesions below the end of the undermined edge containing necrotic tissue sections. All four tissue specimens were located adjacent to each other to guarantee comparable results in all diagnostic tests conducted. For diagnostic purposes it was mandatory that tissue specimens contained subcutaneous adipose tissue, otherwise the specimen was rejected.

### **Transport of specimens to the reference laboratories**

KCCR laboratory staff collected the specimen bags on a regular basis (depending on the availability of patients, at least once monthly) using local transport. Upon arrival at the treatment centre KCCR staff examined the specimen bags for completeness of content. Upon arrival at the laboratory patients data were entered in a laboratory data base and specimens were processed. Slides, standard PCR and histopathology specimens were sent to the external reference laboratories for quality assurance and differential diagnosis on a regular basis.

## **Diagnostic tests**

The local reference laboratory carried out swab smear microscopy, swab culture, swab DRB-PCR, tissue microscopy, tissue culture, and tissue DRB-PCR. Histopathology and quality assurance testing (re-reading of slides, standard reference PCR) was carried out at the external reference laboratories.

## **Handling of diagnostic laboratory results and quality assurance procedures**

In the context of the study a laboratory test was defined positive if the test result could be confirmed by quality assurance testing, i.e. re-reading of slides for microscopy, parallel testing of specimens by the standard method for PCR, and confirmation of positive cultures by ZN and PCR. In case of contradicting results between two laboratories, the tests were repeated at both laboratories and considered “not determined” if no consensus result was achieved.

## **Communication with hospitals**

The results obtained at KCCR on first analysis were communicated to the surgeons as “preliminary results”. Once microscopy and PCR quality assurance results from the external laboratory were available a final result report was issued. Histopathology results were communicated to the surgeons separately depending on availability.

## **Specimens processed**

Between January 2003 and August 2005 diagnostic specimens from 205 clinically diagnosed BU patients were collected. According to the inclusion criteria 20 incomplete sets of specimens were rejected. Subsequently 185 sets of specimens (ulcers: n= 115, nodules: n=70) were subjected to laboratory analysis.

### *Laboratory confirmation of pre-ulcerative lesions*

65 % of the pre-ulcerative lesions were confirmed by tissue microscopy (40 %) and tissue DRB-PCR (additional 25 %). The remaining 35 % were subjected to histopathology.

## **Laboratory confirmation ulcerative lesions**

70 % of the ulcerative lesions were confirmed by swab smear microscopy (30 %) and swab DRB-PCR (additional 40 %). Thus, laboratory analysis of swabs allowed a non-invasive pre-surgical laboratory diagnosis for the majority of patients. The additional diagnostic yield of tissue microscopy and tissue DRB-PCR was 5 %. The remaining 25 % were subjected to histopathology.

## **External Quality Assurance**

### *Microscopy:*

Blinded re-reading of 287 slides (swab smears: n=106, tissue smears: n = 181) resulted in a concordance rate of 81 % between local and external reference laboratory. Second blinded re-reading increased the concordance rate to 97.9 %

### *PCR:*

Simultaneous testing of 265 PCR specimens (swab: n= 98, tissue: n=167) by DRB-PCR and the standard reference method resulted in a concordance rate of 84 % between local and external reference laboratory. Second re-testing in both laboratories increased the concordance rate to 95 %.

This project was supported by the Volkswagen foundation.

## **BENEFITS AND DRAWBACKS OF PATHOLOGICAL DIAGNOSIS OF BURULI ULCER: PARTNERSHIP WITH AN NGO IN BENIN**

*Dr Ph Chemaly<sup>1</sup>, Dr AR Wann<sup>2</sup>, Pr MT Akpo<sup>3</sup> and Dr MC Ballé<sup>4</sup>*

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We recall the role played by pathology in positive and differential diagnosis of Buruli ulcer (BU). Ischaemic necrosis of the dermis and hypodermis, the presence of acid-fast bacilli and the discrete nature of the inflammatory reaction are characteristic features of the initial and fully active phases. Diagnosis may also be performed in a few days by local physicians in any laboratory with standard equipment for routine examinations.

Unfortunately, pathological examination is not easily available in the countries in which BU is widespread.

From 1 to 10 December 2005 we carried out a needs evaluation mission in Benin in collaboration with colleagues responsible for BU control. The needs proved to be considerable, and we drew up a list at Cotonou hospital and at the Padre Pio Centre. The equipment was occasionally inadequate or antiquated. Stains and reagents were often not available. The laboratory would occasionally cease operating because of a broken item of equipment. Equipment is costly and an additional difficulty is the cost of transport and customs hassle

Despite these difficulties, pathological examination is cheaper than PCR or culture.

The *Pathologie Cytologie Développement* association has been active for twelve years in promoting pathology in Africa, a number of south-east Asian countries and the former USSR.:

- Provision of equipment collected in public or private laboratories; this equipment is overhauled, repaired and delivered free of charge;
- Provision of emergency 'kits' of reagents and stains;
- Provision of books and journals on pathology;
- Assistance with traineeships in France for our colleagues;
- Since 2004, organization in Africa of local further-training modules for pathology technicians;
- Participation in cytological screening for cervical cancer using image transmission for difficult cases in three countries ( Cambodia, Mali and Algeria) in collaboration with the LEDA–Med group (Liaison-Education-Diagnostic –Médecine) and the French Ministry for Research.

We are in contact with most teaching hospitals in French-speaking Africa. With regard to BU in particular, a second evaluation mission has just been carried out in the Democratic Republic of the Congo. A report on the mission will be provided at a later date.

The different aspects of our NGO's activity and its presence in Africa may contribute to BU control thanks to early diagnosis in support of existing pathology facilities. We have the equipment and dedicated and skilled men and women.

Beninese pathologists are keen to receive our support and the health authorities are enthusiastic. The system set up by Benin's National Buruli Ulcer Control Programme for the collection of samples greatly facilitates the task, but we nevertheless would appreciate assistance in continuing to fulfil our mission.

## **SURVEILLANCE AND TRAINING**



# ORAL PRESENTATION AT THE ANNUAL MEETING OF THE GLOBAL BURULI ULCER INITIATIVE – INTEGRATING BU CONTROL IN PERIPHERAL LEVEL HEALTH FACILITIES

*Dr Alexandre Tiendrebeogo*

## **Abstract**

BU is a Neglected Tropical Disease (NTD) and most BU affected countries are in Africa where the disease is afflicting poor rural communities, with low health service coverage. In 2004, the confirmation of the effectiveness of combined antibiotics against *M ulcerans* opened the way to medical non invasive case management of BU. To improve BU control, case finding and case management activities must be:

- Extended and decentralized from reference and district hospitals to peripheral level health facilities.
- Integrated to other communicable disease control activities in these facilities and at health district levels.

To that effect, the WHO African Region:

- Produced guidelines for controlling BU in the Region in 2004.
- Developed and finalized training modules for BU organization and management at health district level in 2005.

The presentation is showing how African countries can use these two tools to decentralize BU control activities and integrate it to other communicable disease control activities, mainly leprosy elimination (LEP) and Guinea worm eradication programmes (GWE).

# **THE VALUE OF COMMUNITY MOBILIZATION FOR BURULI ULCER CONTROL: THE CASE OF THE PILOT PROJECT IN TAABO, CÔTE D'IVOIRE**

*Dr Julien Aké Aké, Mr Aubin Yao*

## **Background**

In Cote d'Ivoire, Buruli ulcer is endemic in 80% of health districts. In order better to control the disease, a pilot control project is under way in the sub-district of Taabo. The purpose of the project is to test a means of integrating into Cote d'Ivoire's public health system a method of Buruli ulcer control that is both efficient and suitable for application in all districts in which the disease is endemic. The project relies on mobilization of the network of community intermediaries (Community Health Workers – CHW) which has developed around health facilities. To this end, the CHWs have been trained in communication to persuade the members of their communities to change their behaviour and to contribute to early detection and referral of cases. This study is intended to measure the impact of the activities carried out under this project for the benefit of these community intermediaries.

## **Objectives of the study**

To measure the contribution made by community intermediaries to early case detection in 2005.

## **Methodology**

Analysis of data from periodic activity reports and project management documents

## **Results**

The following indicators were calculated:

- Number of cases referred by the community intermediaries: 144
- Proportion of successful referrals: 96 cases i.e. 67%.
- Proportion of pre-ulcerative forms detected by the community intermediaries: 38%.
- Proportion of the cases referred by the CHWs confirmed by health professionals after clinical examination: 85%.

## **Remarks**

The number of cases detected increased to 213 in 2005 from 20 in 2001, 19 in 2002, 73 in 2003 when the national programme carried out a case detection mission and 39 in 2004 when the project was implemented.

The number of cases detected at an early stage increased gradually (38%), with a consequent decline in the number of cases detected at a late stage. The proportion of early cases is approximately 30% in the literature. It is gradually improving with time. The trend is towards a reversal of the figures, with a higher number of pre-ulcerative than ulcerative forms.

The quality of detection was satisfactory: 85% were confirmed by health professionals after clinical examination.

## **Conclusion**

Community mobilization can make an undeniable contribution to Buruli-ulcer control. Action targeting community intermediaries can have a definite impact.



**ECONOMIC AND SOCIAL RESEARCH**



# **BURULI ULCER, POVERTY, AND POVERTY REDUCTION IN RURAL GHANA, 2003**

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## **Introduction**

Buruli Ulcer (BU) is a neglected disease of primarily poor, neglected populations. Most BU-affected countries are still developing and therefore lack adequate resources to implement national BU surveillance, education, and treatment programs. In 2004, 80% of the 30 countries reporting cases of BU were classified by the World Bank as low or lower middle income. In 2003, Ghana, a BU endemic country, had a gross national income per capita of U.S. \$320 and an external debt that was 106% of the country's gross national income. Although the Ghanaian government, public, and private donors subsidize some of the treatment costs for BU, a large proportion of BU-associated costs are borne by BU victims and their households. There are no studies assessing how much the cost of BU care consumes the incomes or earnings of the BU-affected households.

## **Methods**

In October 2003, we conducted a retrospective survey to determine the cost of BU care for BU-affected households. We asked the heads and members of BU-affected households in three endemic districts of rural Ghana: Amansie West, Upper Denkyira, and Atwima about their socioeconomic and demographic status, and the BU patient's disease characteristics. A cost-of illness approach was used to calculate the annual total (direct and indirect) costs of BU care per patient in BU-affected households. We used self-reported household earnings per capita to calculate quartiles for annual earnings per capita (earnings quartiles) for the poorest to the richest households. The cost per patient of BU care per household was determined for each earnings quartile from poorest to richest. Also, the total costs per patient of BU care were calculated as a percentage of the BU-affected household's earnings per capita. We examined changes in the costs of BU care using multivariate regression analysis. All calculations were converted from Cedis, the local currency, to 2003 U.S. dollars (U.S. \$). Costs incurred in 2003 were annualized by a constant weight of 4/3. Data were entered into Microsoft Access and analyses were performed using STATA.

## **Results**

We enrolled and interviewed persons from 390 households in which 468 BU patients resided. Of these 468 BU patients, 83 were excluded from analysis due to incomplete survey responses and outlying responses. The median age of the 385 BU patients included in the analysis was 15 years of age (range: 1.5-88 years), 55% were females, and median duration of illness was 3 years (range: 0.08-15 years). Cut-off annual earnings quartiles for 2003 were U.S. \$32.83, \$88.80, \$329.35, and \$2,008.27 for the poorest, second, third, and fourth or richest quartiles, respectively. The cost per patient of BU care per household by earnings quartile was \$153.12 (95% CI: \$99.14 - \$207.09) for the poorest, \$215.86 (95% CI: \$153.79 - \$277.94) for the second, \$229.50 (95% CI: \$153.53-\$305.48) for the third, and \$466.90 (95% CI: \$268.31 - \$665.50) for the richest quartile. Multivariate regression analysis showed that the cost per patient of BU care per household for the richest earnings quartile was 93.5% (95% CI: 89.2-104.9%) of the annual household earnings per capita. The cost per patient of BU care per household for the poorest earnings quartile was 242.1% (192.6-314.8%) of the annual household earnings per capita.

## **Conclusions**

Among BU-affected households, the poorest spent the highest portion of their reported earnings on caring for a BU-affected member in 2003. BU has significant to catastrophic economic consequences for BU-affected households in rural Ghana. BU-affected households must be borrowing from sources (such as from other family members' earnings) that they can ill afford to care for BU patients because BU care costs per household for most patients is more than 100% of the reported earnings per capita. This may be causing these households to fall into poverty, and be pushed deeper into poverty

# DETERMINANTS OF BURULI ULCER (BU) COSTS FOR HOUSEHOLDS AND TREATMENT FACILITIES, GHANA, 2000-2003

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## Introduction

Buruli Ulcer (BU) causes skin destruction that may require prolonged and expensive treatment and result in long-term disability. The costs of BU per patient for affected households and health care systems are substantial. However, few studies have examined the factors influencing these costs. Knowing these factors may assist BU program managers in health care and management planning.

## Methods

To examine the costs of BU for affected households, we retrospectively surveyed households affected by BU from 1998 to 2003 in three endemic districts of Ghana, Amansie West, Upper Denkyira, and Atwima about their socioeconomic, demographic, disease-specific, resource use, and disease management characteristics. Households reported BU costs data by the year in which the costs were incurred. These household survey data and a cost-of illness approach were used to calculate the total annual costs per BU patient for BU-affected households. We then used multivariate regression analysis to examine the factors influencing the total costs per BU patient for affected households (hereafter referred to as the household model) from 2000 to 2003. The dependent variable for the household model was total costs per BU patient per household. The independent variables were based on selected disease stage, disease management, and socioeconomic characteristics for a reference BU patient. The reference patient for the household model had the following profile: male; had a nodule located on a lower limb; did not self-treat or seek treatment at a health facility; had an average age of 20.85 years (range: 0.83-88.00); had BU for an average of 3.33 years (range 0.08 to 15 years); had an occupation that was neither a student nor farmer, lived in Upper Denkyira district in 2003, lived in a household whose head had six years or less of formal education; was from a household with an annual reported earnings per capita of U.S. \$159.68 (range: 0.05-5,477); and had a caregiver at home or hospital who was not a farmer, trader, parent or sibling.

To examine the costs of BU for affected health care systems, we reviewed hospital medical records for 725 BU patients treated from 2000 to 2004 at the St. Martins Hospital, Agroyesum (in Amansie West district) and Dunkwa District Hospital (in Upper Denkyira district) to collect data on the patient demographics, disease stage, and cost. All personal identifiers were excluded from this study. The data from the health facilities were used to calculate the total annual costs per patient for a health facility.

To examine the factors influencing these costs, we used multivariate regression analysis to examine the factors influencing the total costs per BU patient for health treatment facilities (hereafter referred to as the health facility model) from 2000 to 2004. The dependent variable for the health facility model was total costs per BU patient for the health facility. The independent variables were based on a reference BU patient with the following profile: male; had a nodule; had an average age of 21.07 years (range: 0.5-90 years); and was hospitalized for an average of 76.82 days (range; 1-365 days) at St. Martin's hospital in 2004.

All calculations were converted from Cedis, the local currency, to 2003 U.S. dollars (U.S. \$). Costs incurred in 2003 were adjusted for time preference using a 3% discount rate. Data were entered into Microsoft Access and analyzed using STATA software.

## **Results**

For the household model, we enrolled and interviewed persons from 390 households in which 468 BU patients resided. Of these 468 BU patients, 57 were excluded from analysis due to incomplete survey responses and two were excluded based on outlying responses. Pooling 4 years of data for 409 patients provided 1,636 (4 X 409) potential observations of BU costs to consider for all BU patients. Of these 1,636 observations, 360 were excluded from the analysis because of missing data. For the health facility model, we had data from 725 BU patients: 415 from St. Martins Hospital and 310 from Dunkwa District Hospital from 2000 to 2004.

Results for the household model showed that the annual total BU cost per patient for a household with a reference patient was U.S. \$53.16 (95% CI: -\$44.42 - \$150.74) and showed a lot of variability depending on the patient's profile. Compared to the reference patient, the average annual total BU costs per patient ranged from -\$45.36 (95% CI: -\$174.16 - \$83.44) for a patient with an ulcer without joint involvement to \$407.65 (95% CI: \$245.23 - 570.06) for a patient with an amputation. BU costs per patient were much higher (>75%, compared to the reference patient) for patients with ulcers involving a joint, scar with a visible contracture, an amputation, lesion located above the neck region, who lived in Atwima district, sought treatment at a health facility, self-treated and sought treatment at a health facility, was a student, and had a caregiver who was a farmer.

Results for the health facility model showed that the average total BU cost per patient for a health facility treating a reference patient was U.S. \$154.25 (95% CI: \$149.39 - 159.11). Compared to the reference patient, the average total BU cost per patient showed some variability depending on the patient's profile, ranging from \$100.76 (95% CI: \$92.29 - 109.22) for a patient treated in 2002 to \$211.96 (95% CI: \$191.32 - 232.60) for patients with edema treated. Compared to the reference patient, BU costs were higher for patients who were female, were hospitalized for longer periods, had edema, plaque, or ulcers.

## **Conclusions**

The costs of BU per patient for affected households and health care systems are substantial. However, these costs vary greatly depending on the patient's profile. For planning purposes, BU program managers who make health care decisions for affected households and the health care system should consider the BU-patient profiles unique to their setting. For example, program managers who are planning on assisting households with BU costs per patient, for amputee patients who otherwise are similar to the reference patient, would use for budgeting purposes, \$407.65 per patient instead of \$53.16.

# **BURULI ULCER: AN ILLNESS OF EXCLUSION. LIVED EXPERIENCES AND SOCIAL ISOLATION OF BURULI PATIENTS IN CAMEROON**

*Dr Joan Muela Ribera*

Evidence gathered from preceding studies, and confirmed by the following, shows that Buruli Ulcer patients frequently prematurely abandon biomedical treatment even when effective. For a better understanding of possible contributing factors, socio-cultural and economic determinants of health seeking behaviour at the individual and household levels were investigated and analysed in the regions of Ayos and Akonolinga in Central Cameroon through a combination of quantitative and qualitative research methods and qualitative comparative analysis.

Data were gathered from 79 Buruli ulcer patients in Ayos and Akonolinga Hospitals, the only two institutions in the country with specialized Buruli ulcer programmes. In addition, in-depth information from 72 selected cases from adjacent local endemic communities was gathered. Patients' beliefs in witchcraft and their confidence in traditional healing have been cited as the probable motives leading to the interruption of biomedical treatment.

However, this study shows that, in fact, social isolation and high indirect costs are key factors in abandoning biomedical treatment. The high percentage of temporal and definite social isolation of patients, noted both during traditional healing and biomedical treatment, was expected to be the consequence of the belief that the illness is caused by sorcery or infractions of social rules and order.

However, social isolation was foremost a consequence of coping with the illness and its costs. On an individual level, the physical effects of the illness and the psychosocial effects caused by the uncertainty of the causes, the nature and the consequences of the illness have greater bearing on one's isolation. On a household level, the voluntary or involuntary, temporal or definite rupture of social relations between household members and patients due to the extremely high direct, indirect and occasional costs for coping with illness, seem to lead to inevitable isolation for a high percentage of patients, including children.

The results from this study challenge the common assumption that traditional interpretations of illness are key factors for social isolation and stigma.

# **THE SOCIO-ECONOMIC IMPACT OF BURULI ULCER ON HOUSEHOLDS AND COMMUNITIES IN CAMEROON**

*Dr Koen Peeters*

Buruli Ulcer is a devastating illness whose chronic course and frequent irreversible consequences pose a high burden on individuals, households and communities. Direct and indirect costs of the illness and household strategies for coping with Buruli ulcer were investigated. Results are based on field work with 79 Buruli Ulcer patients from Ayos and Akonolinga Hospitals and 72 cases from endemic communities in central Cameroon. Complete health-seeking itineraries were reconstructed for all Buruli patients at the hospital and the community levels. Direct and indirect financial costs of all biomedical and traditional treatments were recorded and analysed.

Treatment of Buruli Ulcer is often difficult and prolonged due to the advanced stage of the illness when patients arrive at a specialised hospital. Patients at Ayos and Akonolinga hospitals presented an average of 3 health encounters prior to hospital attendance at the specialised BU programmes. Noticeably, however, 56% of Buruli Ulcer hospital patients' first option for treatment was in the biomedical sector (though not in a specialised unit). Only 14% of these cases were properly diagnosed and initial treatment successful. Therefore, the advanced stage of the illness when arriving at Ayos and Akonolinga hospitals cannot solely be attributed to delayed treatment seeking or traditional healing.

On the other hand, however, at community level, extremely high direct and indirect costs and social isolation are avoided by looking for treatment locally or in the locality of a relative. Extra-local hospital treatment is therefore often avoided. From a socio-economic perspective, a decentralised system of treatment with minimal hospital stays would avoid chronic patient isolation, the disruption of social and economic activities and household impoverishment. A multidisciplinary study to evaluate a decentralised system of care and coordination with local traditional healers should be considered to improve access to the biomedical sector.

## **"CAB – COST ANALYSIS BURULI: DEVELOPMENT OF A SOFTWARE TO ASSESS THE CLINICAL TREATMENT COSTS OF BURULI ULCER"**

*Dr Manuel Stoecker*

CAB is the consecutive development of a software tool that helps management of organizations to calculate the cost of their BU projects. There are two main fields of usage for this tool. 1. Calculation of the treatment cost in an already existing BU hospital. 2. Generate scenarios for planned projects. Check what the cost would be if a project was realized. The tool is easy to handle and includes various written and graphical reports. CAB is based on free and open source software and can be downloaded on a site that will be announced during the congress.

The tool offers many interpretation features. The core is the various written and graphical reports. There can be shown the total cost for the whole hospital organization. Or, there can be displayed single indicators such as the treatment cost per patient, per clinical symptom, per single treatment step, per cost center etc. Management decides to what degree indirect cost (administration, fundraising, infrastructure etc.) shall be added to the direct treatment cost in order to complete the calculation. With its built-in currency converter the tool is able to display the results in one or several currencies at the same time. This facilitates the comparison of projects in different countries.

CAB has been developed due to the need of organizations to know more about the cost details of their BU hospitals. There can be discovered parts of a project, which use funds excessively, and others that work more economically and indicate the reasons for it. Furthermore CAB can deliver key figures such as the clinical treatment cost per patient or the treatment cost for all patients. These figures are important for the communication towards project partners, governments, policy makers and donors. Finally, if an organization would like to know how much a BU project would cost if it was realized, there can be created “virtual” projects. By introducing estimated data there can be defined different scenarios for which the cost then is calculated.

The insertion of data into CAB is organized in a “tree structure” in which every step of the treatment process and its assigned cost are entered. Users with a common knowledge of office-applications are able to understand the functions of the tool after a short learning period. Because the tool uses database functions, changes in prices for inputs can easily be adjusted as all data is linked. During the presentation the use of the software will be demonstrated by examples.

The CAB tool is the result of a cooperation between Lepira.ch, the company *softEnvironment* and Manuel Stöcker, a graduate of the University of Applied Sciences of Northwestern Switzerland. In 2004 the student spent 4 weeks in Cameroon to work on his diploma thesis in the degree course “International Management”. In Ayos, Central Province of Cameroon, he researched on the cost of the local BU hospital project of Lepira.ch. The findings, which were made during this research, consequently lead to the development of the CAB tool.

# **DISEASE AND WITCHCRAFT IN AYOS, CAMEROON: AN ILLUSTRATION OF THE COMPLEXITY OF THE DIFFERENT THOUGHT PATTERNS PRESENT AMONG THE POPULATION THROUGH AN ANALYSIS OF A DEBATE BETWEEN LOCAL ELITES**

*Mr António de Almeida*

The paper I propose to present to you today is an analysis of a debate witnessed by me in Cameroon in January 2004. Two priests, a philosopher and a doctor were debating the themes of witchcraft and development. The question of disease lay at the heart of this heated discussion.

Local beliefs are often seen as hindrances preventing patients from attending hospital. If these beliefs are to cease to be hindrances to the treatment of disease and to hospital treatment, every aspect of them needs to be taken into account by the medical establishment, NGOs and «development activists» if a genuine and effective solution is to be found.

My aim in this presentation is to show that belief in a biomedical system may occasionally serve the believer's own ends and support their own thought pattern if it does not go hand in hand with a willingness to accommodate other systems of care and thought patterns. By analysing the physician's position and setting it against those of the two other participants, I hope to clarify this problem.

## **By way of an introduction**

I intend to analyse passages from positions adopted at a specific place, at a precise time and before a particular audience. In no way is it my intention to judge what is being said, I merely wish to draw attention to it in order to illustrate exactly what the biomedical system wishes to and is capable of representing; « the voice of science », in contrast to two other systems of belief: the traditional one (upheld by the philosopher) and the religious one (by the two priests).

The biomedical system asserts, frequently with arrogance, the superiority of science, progress and technology. Wouldn't it be preferable for us, in our effort to control Buruli ulcer, to open up our minds to other health systems, to put into perspective the efficacy of our scientific model? Are we capable of accepting a medically pluralistic universe, in other words of accepting that several systems of health care and treatment are effective and of allowing them to coexist ?

Having said this, an analysis of this debate offers us a glimpse of the direction in which our system of values may be heading by failing to take account of the issues raised : poor perception by indigenous populations of the implementation of prevention and case-detection campaigns; less than optimum case management of patients; hugely problematic treatment within the hospital establishment; cure and unsatisfactory «reinsertion» of patients within society, etc. This, in short is the purpose of my analysis.

The aim of this paper is to enable each of us to recognize ourselves as part of this scientific pattern of thought and to examine our own day-to-day practice, how we present and define our system of values, our medicine and our worldview to people who do not share the same system of thought.



## **BASIC RESEARCH**



# **MOLECULAR CHARACTERIZATION OF *MYCOBACTERIUM ULCERANS* STRAINS FROM DIFFERENT GEOGRAPHICAL LOCATIONS IN AUSTRALIA AND SOUTH EAST ASIA**

*Janet Fyfe<sup>1</sup>, Maria Globan<sup>1</sup>, Caroline Lavender<sup>1</sup>, Paul Johnson<sup>2</sup> and Tim Stinear<sup>3</sup>*

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Outbreaks of *Mycobacterium ulcerans* infection have been recognized in coastal areas of Victoria since the 1940s, with sporadic cases detected in humans and also native wildlife. Cases are also reported from areas of Far North Queensland and the Northern Territory with a single case recently in north Western Australia. We have used a combination of four genotyping methods (2426 PCR, VNTR, pTBN12-RFLP and MLST) to define the characteristics of isolates from all these geographical areas. A phylogeny was then inferred from the combined data. Unlike the situation with African strains, which are genotypically very similar, there is considerable genetic diversity amongst the Australian isolates. Some of the genotypes identified in Australian isolates have also been identified in strains from Papua New Guinea and Malaysia. Of the four methods we have used, VNTR typing, which can be performed on DNA extracted from *M. ulcerans* lesions has provided the most discriminative and timely means of linking new cases to known outbreaks.

## GENETIC DIVERSITY OF *MYCOBACTERIUM ULCERANS*

*Gerd Pluschke, Diana Diaz, Markus Hilty, Michael Käser, Simona Rondini, Dorothy Yeboah-Manu*

Swiss Tropical Institute, Basel, Switzerland

Molecular typing methods such as multi-locus sequence typing, 16S rRNA sequencing, restriction fragment length polymorphism and sequence analysis of genes of immunodominant antigens have revealed a remarkable lack of genetic diversity of *M. ulcerans* and a clonal population structure within given geographical regions. The discriminatory power of all these methods is particularly insufficient to differentiate between African isolates.

Variable number of tandem repeat (VNTR) typing, a PCR-based technique identifying alleles of defined regions of DNA that contain a variable number of copies of short sequence stretches, is showing a higher discriminatory power. Typing of a collection of isolates from Ghana with this technique allowed us to demonstrate the presence of three different genotypes within this country. Results were indicative for an ongoing microevolution of *M. ulcerans* and for the spreading of new variants (1). However, the level of resolution obtained by VNTR typing was still insufficient for local epidemiological studies aiming to reveal transmission pathways and environmental reservoirs of *M. ulcerans*. Innovative molecular genetic fingerprinting methods are thus required for this purpose.

Our comparative genomic analysis of *M. ulcerans* clinical isolates with a novel plasmid-based microarray technology revealed extensive large sequence polymorphisms indicative for progressing genome shrinking. Categorization of the deleted genes according to their biological functions indicates that *M. ulcerans* is adapting to a more stable environment. The significant insertional/deletional diversity revealed by analysis with a prototype microarray covering <10% of the genome suggests, that a genome-wide array may make a genetic fingerprinting method for micro-epidemiological studies available.

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# STRAIN DIVERSITY AND EVOLUTION OF *MYCOBACTERIUM ULCERANS* UNCOVERED BY DNA MICROARRAY TECHNOLOGY

Michael Käser, Simona Rondini, Timothy Stinear, and Gerd Pluschke

Swiss Tropical Institute

## Background

*Mycobacterium ulcerans*, the etiologic agent of Buruli ulcer, is characterized by a remarkable lack of genetic diversity. Standard strain genotyping methods do not have sufficiently high resolution for micro-epidemiological studies, thus better fingerprinting methods are needed to unravel transmission and spreading of this emerging pathogen.

## Methods

We conducted comparative genomic hybridization of 30 *M. ulcerans* strains of world-wide origin with a newly developed plasmid-based microarray technology, suitable for organisms lacking genome sequence information. Identified genomic differences were analyzed by PCR and sequencing and subjected to *in silico* sequence comparison with *M. marinum*.

## Results

The microarray based comparative genomic analysis revealed extensive large sequence polymorphisms among the *M. ulcerans* clinical isolates. These insertional/deletional genome rearrangements depict progressing genome shrinkage similar to that observed for the emergence of *M. ulcerans* from its progenitor, the environmental mycobacterium *M. marinum*. Categorization of the deleted genes revealed biological functions possibly no longer required for the pathogen. In depth analysis showed evidence that the Asian and Southern American strains are closer to *M. marinum* than isolates from African and Australian countries, further substantiating a draft evolutionary scenario for *M. ulcerans*.

## Conclusions

Comparative analysis of the genomes of *M. ulcerans* isolates suggests that this emerging pathogen is adapting to a more stable environment. The significant genomic diversity revealed by analysis with a prototype microchip suggests that a microarray covering many more sequence stretches may lead to a genomic fingerprinting method urgently needed for micro-epidemiological studies and aiming to characterize transmission pathways and environmental reservoirs of *M. ulcerans*. A whole genome microarray, based on spotting of PCR products, is currently under development.

## HETEROGENEITY AMONG *M. ULCERANS* FROM AFRICA

*Mr Pieter Stragier*

Buruli ulcer (BU), the third most common mycobacterial disease after tuberculosis and leprosy, is a major health problem in several West and Central African countries. Mode(s) of transmission, natural reservoir(s) and other key aspects of the epidemiology of BU are not fully understood, partly due to an apparent lack of genetic diversity of *M. ulcerans* as revealed by several independent genetic markers (2-5). Conventional and molecular data suggest that *M. ulcerans* is an environmental pathogen because of the selective association of BU endemic foci with wetlands, overflowed river banks and the detection of *M. ulcerans* specific sequences in water, mud, aquatic insects and plants. Specific reservoir(s) of the etiologic agent cannot be definitively assigned; however, we have cultivated *M. ulcerans* from a single aquatic insect from Benin.

Noteworthy is the striking geographical and temporal homogeneity established by current typing methods in African isolates from Angola, Benin, Democratic Republic of Congo (DRC), Ghana, Ivory Coast, and Togo (2-5). The development of more discriminating typing methods is essential for unravelling the source and mode of transmission of *M. ulcerans* and other epidemiological aspects of BU.

Here we report the first evidence of genetic diversity in *M. ulcerans* isolates from DRC, Sudan and Uganda. Previously, we identified tandem repeat loci (2, 5) in the genome of *M. ulcerans*. A selection of these MIRUs and VNTRs were used in this study to analyse *M. ulcerans* extracts from tissue specimens from Benin, Togo, Gabon, Uganda, and Sudan and on previous isolates from patients from Cameroon, DRC, and Congo Brazzaville.

Comparison of MIRU-VNTR copy numbers using 4 loci revealed 11 different profiles. *M. ulcerans* isolates from DRC and tissue extracts from patients from Sudan (Nzara) and Uganda (Nakasongola) showed distinct profiles, different from the originally homogeneous African genotype (Table 1). In DRC there are now 3 different genotypes according to 3 different regions, i.e. Bas-Congo, Maniema (Kasongo), and Orientale (Bunia). Isolates from Gabon, Congo Brazzaville, and Cameroon had the typical African genotype, now designated the Atlantic African genotype.

It is obvious that *M. ulcerans* isolates from Africa are very homogeneous. All isolates from West Africa (Ivory Coast, Ghana, Togo, Benin) and Central Africa (Cameroon, Gabon, Congo Brazzaville, DRC Bas-Congo, Angola) have the identical MIRU-VNTR profile and all originate from regions (i.e. Bas-Congo) or countries that border the Atlantic Ocean. The isolates that come from regions or countries in the Nile River basin (i.e. Orientale in DRC, Sudan, and Uganda) or the Congo River basin (i.e. Maniema) have distinct profiles.

These results are significant because: (i) This is the first demonstration of heterogeneity among *M. ulcerans* from different African countries. (ii) This is the first detection of MIRUs and VNTRs in clinical specimens, even in smear negative specimens (6).

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# NERVE DAMAGE INDUCED BY *MYCOBACTERIUM ULCERANS* - ROLE OF MYCOLACTONE

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## Purpose

Buruli ulcer is a chronic painless skin disease caused by *Mycobacterium ulcerans*. We reported that in mice inoculated with *M. ulcerans*, nerve bundles are invaded and damaged by the bacilli (Goto M *et al.*, *Am J Pathol*, *in press*). *M. ulcerans* produces toxic lipid mycolactone, and mycolactone induces apoptosis to guinea-pig lesion. In this study, we examined whether mycolactone can induce nerve damage.

## Methods

Mycolactone A/B was isolated from *M. ulcerans* 1615. It was dissolved by small amount of ethanol, diluted by 7H9 broth, and inoculated to left footpad of female BALB/c mice aged 6 weeks old. On day 4 and 7, footpad sensory disturbance was examined by von Frey microfilaments. On day 7, perfusion fixation was done by 4% paraformaldehyde (PFA) or 4% PFA + 1% glutaraldehyde. Footpad, spleen, thymus, lung, liver, small intestine and kidney were examined by H&E staining. Epon sections of footpads were also examined.

## Results

1, 3 and 10 ug of mycolactone did not induce significant gross and histological changes (each n=3). 30, 100 and 200 ug of mycolactone induced local swelling (on day 7, control, 2.2mm; 30 ug, 2.8mm; 100 ug, 3.7mm; 200 ug, 3.7mm), redness and erosion at the injected site (each n=5). Sensory test showed no significant changes on day 4, but hyperesthesia was noted on day 7 ( $P=0.02$ ). Histological examination of the footpads revealed focal epidermal erosion, moderate stromal edema, and mild infiltration of neutrophils. Blood vessels showed high endothelial venule, and focal hemorrhage was observed. Nerve bundles showed loss of Schwann cell nuclei and/or intraneural hemorrhage beneath the erosion. Some Schwann cells showed nonspecific degeneration, but intracytoplasmic vacuoles observed in *M. ulcerans* inoculation was not yet identified. Spleens of 100 and 200 ug inoculation showed mild swelling, but thymus, lung, liver, small intestine and kidneys showed no significant changes.

## Discussion

Our study clarified that lesions similar to Buruli ulcer can be induced by mycolactone, associated with nerve degeneration. However, von Frey sensory test did not show paralysis of the lesion, instead, hyperesthesia was observed. This result was not consistent with our previous study of *M. ulcerans* inoculation to mice, where loss of sensation was evident by the same sensory test (Goto *et al. in press*). Further study to evaluate the long-term neurotoxic effects of mycolactone is required.

## TOWARDS THE DEVELOPMENT OF A DIAGNOSTIC TEST FOR BURULI ULCER

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Buruli ulcer is a severe disease that has reached epidemic proportions in many parts of Western and Central Africa. Early case detection is a key strategy to prevent serious disease and the development of a field-based diagnostic test for detection of pre-ulcerative disease is a World Health Organisation research priority in the fight against Buruli ulcer. In this study we have used a reverse genetics approach to try and identify *Mycobacterium ulcerans*-specific antigens that could be used to develop a simple to use, rapid diagnostic test for Buruli ulcer, such as a strip test using a small sample of patient blood. Using the recently completed genome sequence of *Mycobacterium ulcerans*, 33 gene sequences specific to *M. ulcerans* were identified. These genes were expressed as recombinant proteins in *Escherichia coli* and are now being tested against sera from convalescent Buruli ulcer patients, household contacts and uninfected controls to try and identify a patient-specific antibody response (i.e. a B-cell response). So far, 16 of the 33 recombinant proteins have been tested but none were specifically recognised by sera from Buruli ulcer patients. Antigen screening is ongoing and will be augmented in a second phase to the project that will explore the ability of the 33 candidate antigens to stimulate a specific T-cell response from Buruli ulcer patients. Antigens that show either a consistent B-cell or T-cell response will be used in the development of a diagnostic test.

## **USING THE COMPLETE GENOME SEQUENCE OF *MYCOBACTERIUM ULCERANS* TO ADDRESS RESEARCH PRIORITIES FOR THE CONTROL OF BURULI ULCER**

*Dr Tim Stinear*

Genomics has been instrumental in the fight against *Mycobacterium tuberculosis*. Since the publication of the first *M. tuberculosis* genome in 1998 there have been significant advances towards effective treatment options such as the entry of the first new TB vaccines and a dramatic expansion of our understanding of its pathogenesis. One of the most recent and promising advances in this field has been the discovery of new effective therapeutic agents against TB. So how is knowledge of the complete genome sequence of *Mycobacterium ulcerans* helping to control Buruli ulcer? Already, studies of its genome by different research teams have produced new tools for improved diagnostics and molecular epidemiology, uncovered the basis for the synthesis of the toxin mycolactone and revealed shared biochemical pathways with *M. tuberculosis*. Some these pathways are targets for the new anti-tuberculous drugs and their presence in *M. ulcerans* suggest that these new agents may also find applications in treating Buruli ulcer. Other insights from the *M. ulcerans* genome include predictions that the bacterium will produce some unique, potentially antigenic proteins and these are being investigated to develop a field-based blood test for Buruli ulcer. Following the example of post-genomic tuberculosis research, the knowledge extracted from the *M. ulcerans* genome will translate into improved health outcomes for those at risk of contracting or afflicted with Buruli ulcer.

## **MYCOBACTERIUM ULCERANS COMPARATIVE GENOMICS PROVIDES CLUES TO ENVIRONMENTAL HABITAT AND NEW TOOLS FOR DIAGNOSIS**

*Dr Tim Stinear (on behalf of the M. ulcerans genome project team)*

Ongoing comparative genomics between *M. ulcerans* and the closely related *Mycobacterium marinum* has revealed metabolic streamlining as a key theme in the evolution of *M. ulcerans*. Pseudogene formation and DNA deletion of critical genes in anabolic pathways such as those for isoprenoid biosynthesis suggest that the bacterium has evolved to grow slowly. *In silico* reconstruction of metabolic pathways suggests that exogenous lipids are an important carbon and energy source for the bacterium. Analysis of electron transport chains implies that *M. ulcerans* maybe defective for growth under microaerophilic and anaerobic conditions. From these data, together with previous observations such as production of mycolactone, preservation of phthiodiolones, and a significantly reduced antigenic repertoire (e.g. PE/PPE and ESX family proteins), one could speculate that the bacterium survives as a slow-growing, relatively inert entity, perhaps in an aerobic, intracellular niche. Comparative genomics has also revealed DNA sequences that are unique to *M. ulcerans* (i.e sequences other than IS2404, IS2606 and the mycolactone plasmid pMUM that are absent from *M. marinum*). Examination of the distribution of these sequences among different strains of *M. ulcerans* indicates that some of them maybe useful as new molecular markers for detecting *M. ulcerans* in the environment.

**EPIDEMIOLOGY AND TRANSMISSION**



# **APPLICATION OF VNTR TYPING TO *MYCOBACTERIUM ULCERANS* PCR-POSITIVE ENVIRONMENTAL SAMPLES FROM VICTORIA, AUSTRALIA**

*Caroline Lavender*<sup>1</sup>, *Maria Globan*<sup>1</sup>, *Paul Johnson*<sup>2</sup>, *Tim Stinear*<sup>3</sup> and *Janet Fyfe*<sup>1</sup>

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Variable number tandem repeat (VNTR) typing, where regions of tandem repeat (TR) DNA sequences are PCR-amplified and the number of repeat DNA sequences at each locus determined, has become a useful tool for determining the epidemiological relationship and geographic origin of *Mycobacterium ulcerans* isolates.

We have recently detected *M. ulcerans* by real-time PCR in soil from a storm water drainage system, an ornamental lake and from a small proportion (0.33%) of mosquitoes trapped during 2004-5 in an area in Victoria, Australia, where *M. ulcerans* is endemic.

Our aim was to use VNTR typing to: 1) confirm that the DNA extracted from the environmental samples was *M. ulcerans* and 2) show that the *M. ulcerans* from these environmental samples was the same genotype as that of patients with *M. ulcerans* infection from this region.

A nested PCR was developed for locus 9 to increase the sensitivity of the reaction (as our environmental extracts contained low concentrations of DNA compared to isolates). The rationale for using locus 9 was that it discriminates between the various genotypes of *M. ulcerans* circulating in Australia.

We obtained PCR products for three environmental samples: two different soil extracts from a soak pit and an earthworm from the same site. All three PCR products were identical in sequence to the reference patient strain from this region.

We plan to continue this work by expanding the number of loci examined and to further increase the sensitivity of the PCRs in order to genotype a larger number of environmental samples.

# INVESTIGATION OF EPIDEMIOLOGICAL AND ENTOMOLOGICAL ASPECTS OF *MYCOBACTERIUM ULCERANS* TRANSMISSION TO HUMANS IN CAMEROON: PRELIMINARY RESULTS

*Dr Sara Eyangoh*

## Case-control study

We conducted a retrospective case-control study to determine risk factors for clinical expression of Buruli ulcer and the risk factors of exposure to *M. ulcerans* among 100 cases and 100 control patients. The initial analyses revealed no significant risk factor for the development of Buruli ulcer.

## Prevalence de *M. ulcerans* in the environment

Insects were collected at water points (marshes of the Nyong or of other rivers) in the vicinity of the locations where patients and control cases were interviewed for the epidemiological survey. Analyses using PCR showed *M. ulcerans* to be present in the water scorpions, naucoridae, belostomatidae and the larvae of dragonflies, dytiscidae and nepidae.

## Phenotyping and genotyping of the isolates

We isolated and identified 5 mycobacterial strains from the cultures of ground material and salivary glands of the aquatic insects using analysis of hsp65 gene polymorphism and 16S RNA sequencing (*M. arupense* (2), *M. terrae*, *M. houstonense*, *M. perigrinum*,).

Genome analysis of the *M. ulcerans* isolates was performed using VNTR and RFLP IS2404 markers which showed considerable homogeneity.

## Entomological Aspects

We drew up an inventory of different aquatic insects : *Nepidae*, *Ranatrinae*, *Belostomatidae*, *Naucoridae*, *Notonectidae*, *Corixidae* , mayflies, trichoptera, two types of aquatic coleopteran of the Hydrophilidae family and larvae of Dytiscidae and Gyrinidae.

## RESULTS FROM A CASE-CONTROL STUDY ON RISK FACTORS IN AUSTRALIA

*Ms Tricia Quek*

In Australia, cases of Buruli ulcer (BU) have been largely confined to the eastern region in the state of Victoria. However, in the last seven years there have been several outbreaks of BU on the Bellarine Peninsula, in south-eastern Australia; the entire Bellarine Peninsula is now considered endemic for *M. ulcerans*. In order to better understand the cause and treatment for this infection, we conducted a case-control study to establish factors for disease acquisition.

We devised a questionnaire that addressed factors such as outdoor-related lifestyle, general behaviour, soil, freshwater, and insect exposure; this was mailed to our case and control subjects. Sixty-one adult cases were identified through the Department of Human Services in Victoria and treating physicians affiliated with our study; 49 of these cases responded to our study (80% response rate). Of the 810 Bellarine Peninsula residents who were randomly selected from the Commonwealth Electoral Roll, 608 people responded to our study (78% response rate). Thus, a total of 657 individuals provided us with questionnaire data for the study.

There were 24 male and 25 female case patients who participated in the study (median age 70 yr, IQR 58 – 82). Our analysis determined odds ratios for developing BU, and was adjusted for age and town of residence. Lifestyle patterns supported the current notion that a direct route of inoculation is required for transmission. Initial results suggest that protective measures against environmental exposure reduce the odds of developing BU; these factors include applying insect repellent (OR: 0.38; 95% CI: 0.20 – 0.71), wearing clothes that cover the lower limbs (0.51; 0.27 – 0.97), and wearing shoes that totally encase the feet during the summer (0.31; 0.11 – 0.88). Our data did not support use of immunosuppressive medication or exposure to wildlife or domesticated animals as risk factors for disease development. Further multivariate analysis is currently underway.

The modifiable factors that we identified in reducing the risk of BU may be effective in preventing further cases from occurring; they are relatively simple public health messages and so warrant further investigation.

## ***M. ULCERANS* AND ENVIRONMENTAL RESERVOIRS**

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*Mycobacteria ulcerans* is an environmental pathogen associated with slow moving water. Evidence from IS2404 PCR suggests that *M. ulcerans* DNA is present in aquatic insects of at least 5 different genera, snails, tadpoles, small fish, aquatic vegetation, detritus and many other aquatic sources. The possibility that insects might serve as a reservoir for *M. ulcerans* was first proposed by Francoise Portaels in 1999 based on detection of IS2404 DNA in water bugs (Naucoridae and Belostomatidae) collected in West Africa. Subsequently elegant laboratory work from Laurent Marsollier has shown that *M. ulcerans* can colonize predacious water bugs (Naucoridae) collected from swamps in France. In order to investigate the association between *M. ulcerans* and aquatic insects in West Africa we have conducted studies on insects and other aquatic material collected in endemic and non-endemic regions Ghana to determine the presence of *M. ulcerans* in environmental samples.. In addition we have established laboratory models using wild caught predacious water insects from Ghana and investigated whether these insects can be colonized by *M. ulcerans*. Preliminary results from these studies suggest that *M. ulcerans* cannot establish a productive infection in Belostomatidae collected from Ghana.

PCR analysis of a large number of aquatic samples for *M. ulcerans* DNA suggests that the presence of IS2404 DNA cannot be used as sole criteria for the presence of *M. ulcerans* DNA. Although the addition of mycolactone-specific probes improves specificity, we have recently discovered a novel plasmid encoded mycolactone, Mycolactone F, in 9 isolates of *M. marinum* isolated from diseased fish in Israel and Greece, as well as from 5 isolates of *M. pseudoshottsii* isolated from diseased fish in US. These isolates also contain multiple copies of IS2404. Results from these studies suggest that mycolactone producing mycobacterial species are far more widely distributed than previously thought and that more work must be done to develop specific probes for detection of *M. ulcerans* in the environment.

## TRANSLOCATION OF *MYCOBACTERIUM ULCERANS* WITHIN THE CEPHALIC CAPSULE OF WATER BUGS

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*M. ulcerans* is the only mycobacterium capable of multiplying in the salivary glands of water bugs (*Naucoridae*). Colonization takes place after ingestion of prey contaminated by the bacillus. The bug grasps its prey with its forelegs, which are covered with piercing silk hairs and at the same time thrusts into the prey its four stylets formed by the mandibles and maxillae, which channel the digestive juices; these are retractable parts of the rostrum which, after a meal during which they become infected, are housed in a capsule located in the insect's head. Translocation of the bacilli into the main cavity occurs when they adhere to the capsule's basal membrane through a still unidentified process. At this stage, the role played by mycolactone, a toxin produced by *M. ulcerans*, is not important as identical results have been obtained with a mutant incapable of synthesizing toxin. Regardless of the strain, the bacilli are then phagocytosed by the plasmatocytes, which act as shuttle cells to the salivary glands. However, it is only at this intermediate stage that mycolactone plays an essential role in colonizing the salivary glands. As a mutant produces no toxin, it is not possible to detect it in the salivary glands.

(Research supported by the French Raoul Follereau Association)

# **SPATIAL RELATION BETWEEN ARTISANAL MINING AND *MYCOBACTERIUM ULCERANS* INFECTION IN THE AMANSIE WEST DISTRICT, GHANA**

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Since the introduction in 1989 of Ghana's Small Scale Mining Law, which registered and legalized artisanal mining, there has been a sharp increase in outbreaks of Buruli ulcer, a skin disease caused by *Mycobacterium ulcerans*. The Amansie West District, in the gold-rich Ashanti region, is worst affected. Ghana's gold occurs in association with sulphide minerals, particularly arsenopyrites and it is hypothesized that BU incidence is related to the environmental consequences of artisanal gold mining. Proximity analysis reveals an inverse association between BU incidence and distance to artisanal minesites. It is argued that the exposure of neighbouring communities to increased levels of arsenic, mobilized by mining disturbance and oxidation of arsenopyrite, increases risk of infection

**Keywords:** Buruli ulcer, minesites, artisanal mining, spatial association, arsenic, Offin River.

# LANDSCAPE FEATURES AND AQUATIC HABITATS ASSOCIATED WITH PATTERNS OF *M. ULCERANS* INCIDENCE IN GHANA, AFRICA

*Authors: M. Eric Benbow, Richard W. Merritt, Jiaguo Qi, Ryan Kimbirauskas, Daniel Boakye, Pam Small*

It is commonly accepted that high prevalence of *Mycobacterium ulcerans* Infection is often coupled with standing aquatic habitats where adjacent landscape features have been disturbed through human activity. However, this relationship has not been quantitatively investigated. An initial step for understanding the transmission of this disease is to test this first assumption, providing valuable insight into the broad geographic patterns of infection and associated ecological factors that may be important for environmental reservoirs and/or vectors.

We used LandSat ETM+ images of Ghana, Africa to define landuse-landcover (LULC) relationships at different scales of infection resolution (i.e., region, district, community level) to explore broad patterns of geographic variation associated with disease incidence. At the regional scale, higher incidence in southern Ghana is most associated with mosaic forest/cropland with scattered patches of mosaic forest/savanna. The northern regions of Ghana that have lower incidence are primarily deciduous woodland and shrubland with sparse trees, and less human-mediated disturbance. However, at the district and community scales there is high variation among LULC and disease burden, and these analyses are ongoing.

In studies focused on understanding the ecology of aquatic habitats within and between regions with both endemic and non-endemic districts, we sampled water quality, macroinvertebrates and *M. ulcerans* from 20 sites. From these analyses, it is evident that there are substantial ecological differences between districts that appear to be unrelated to broad district-level disease reporting data, but may be important from community-to-community. Therefore, we propose that future research efforts into understanding Buruli ucler ecology carefully consider disease burden within the context of LULC relationships. Aquatic and microbial ecology, at discretely defined geographic and demographic scales, should be included with these analyses.



## **ANNEXES**



## ANNEX 1: LIST OF PARTICIPANTS

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