



# WORLD HEALTH ORGANIZATION

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## Surveillance and control of *Mycobacterium ulcerans* disease (Buruli ulcer)

### Report by the Secretariat

1. Buruli ulcer is a devastating skin disease caused by *Mycobacterium ulcerans*, a pathogen belonging to the same family of organisms that cause tuberculosis and leprosy. Unlike these conditions, however, Buruli ulcer is a poorly understood disease that has emerged dramatically since the 1980s. The causative agent has unique features and its exact mode of transmission remains unknown. Rapid diagnostic tests are lacking, surveillance and reporting are poor, and antibiotics have little effect. Although Buruli ulcer has a low mortality rate, it frequently causes disabilities, and the costs of treatment and rehabilitation are prohibitive in the most severely affected areas. Despite these obstacles, solid progress is being made.

2. In early 1998, WHO responded to the growing spread and impact of the disease by launching the Global Buruli Ulcer Initiative, uniting multiple partners through common goals, technical strategies and agreed principles of action. Supported by a task force of experts, this Initiative has drawn together global expertise and led mobilization of resources. Also in 1998, WHO organized the first International Conference on Buruli Ulcer Control and Research in Côte d'Ivoire. The resulting Yamoussoukro Declaration on Buruli Ulcer drew attention to the severity of the disease as an emerging public health problem and expressed concern about its many poorly understood features. Participants at the conference recognized the value of multidisciplinary research, pledged to make all efforts to establish surveillance and to provide facilities for early treatment, and stressed the need for partnerships and health system development.

### PUBLIC HEALTH SIGNIFICANCE

3. Buruli ulcer is widespread in tropical and subtropical areas. Cases have been identified in more than 30 countries in Africa, Asia, Latin America, the western Pacific, and Australia, but west Africa is by far the worst affected area, with thousands of cases now being reported each year. In some African countries, Buruli ulcer has become the second most prevalent mycobacterial disease after tuberculosis. In Côte d'Ivoire, about 17 000 cases have been recorded since 1978, with up to 16% of the population affected in some villages; Benin has recorded 5700 cases since 1989; and a national survey in Ghana in 1999 identified 6000 cases, after which about 2800 new cases have been recorded. In Cameroon, the last notification was in 1977 when 47 cases were described in the Ayos and Akonolinga regions. No new information on the disease was reported since then and it was presumed that Buruli ulcer had vanished from Cameroon. Twenty-four years later in August 2001, a survey conducted in these same districts identified a total of 428 prevalent cases. In 2002 and 2003, 354 new cases were recorded in these two districts. A few cases have been reported in non-endemic areas in North America and

Europe as a sequel to international travel. Lack of familiarity with Buruli ulcer has frequently resulted in significant delays in the diagnosis and treatment of these cases.

4. The disease occurs most commonly in poor communities in remote rural areas. Around 70% of those infected are children under the age of 15 years. Cases often occur in geographical foci near water bodies, such as rivers, lakes, and swamps. Although the exact mode of transmission is unknown, recent findings suggest a role for some aquatic insects in the transmission cycle. No evidence indicates transmission from person to person. Risk factors identified to date include living close to foci where the disease is endemic, travelling to endemic areas, having regular contact with a contaminated aquatic environment, and local trauma to the skin.

5. Inadequate surveillance and probably gross underreporting raise the possibility that the number of cases may be much greater and their geographical distribution much wider than officially reported. Health workers' poor knowledge about the disease leads to considerable lack of recognition and underreporting of cases. Moreover, great stigmatization surrounds the disease, and cultural beliefs about its possible nonmedical cause keep people silent, hidden and reluctant to seek care.

6. The disease often starts as a painless nodule. When it is detected early, simple surgical excision of the nodule is curative. When left untreated, the disease progresses to massive destruction of skin and sometimes bone, breast, eyes and genitalia are destroyed, with permanent disabilities in an estimated 25% of cases. *M. ulcerans* is unique among mycobacteria in that, as they proliferate, the bacteria secrete a necrotizing toxin that destroys tissue and suppresses the immune system.<sup>1</sup> Because of this immunosuppression, the disease generally progresses with no warning signals, such as fever or pain, a fact which may also help explain why those affected fail to seek early treatment when the chances of cure are high.

7. Skin lesions characteristically occur most often on the extremities rather than on the trunk. The location and extent of skin and bone damage may restrict limb movement, hindering the performance of daily activities, or cause other and more severe permanent disabilities. Even when skin lesions heal, scarring can permanently restrict movement of limbs.

## COMPONENTS OF CONTROL

8. Early detection and treatment constitute the cornerstones of WHO's control strategy, which aims to reduce the suffering, disabilities, and socioeconomic damage caused by the disease. Other components include training of health workers to improve diagnosis, treatment and reporting, and intense public education campaigns in affected communities to reduce stigmatization and encourage early contact with health services. Control also requires provision of surgical equipment, drugs and medical supplies for essential patient care, and rehabilitative interventions to prevent or manage disabilities. Furthermore, as noted in the Yamoussoukro Declaration, better control requires surgical facilities at the peripheral level for the treatment of nodular and early ulcerative disease. All these activities need to be strengthened.

9. Diagnosis is mainly based on clinical assessment of symptoms. No simple diagnostic test for field use is presently available. Acid-fast bacilli can be revealed in smears from the necrotic base of ulcers by use of the Ziehl-Neelsen stain, but laboratories equipped to perform more complex

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<sup>1</sup> See also paragraph 16.

procedures, such as culture of *M. ulcerans*, polymerase chain reaction tests and histopathology, are often based in tertiary and research centres remote from affected areas.

10. The potential therapeutic value of antibiotics is in the early stages of investigation. At present, treatment relies on surgery, often involving extensive excision and skin grafting. To save lives, limbs have to be amputated in severe cases. Surgical treatment of nodular and early ulcerative disease costs an estimated US\$ 20 to US\$ 30, and requires only brief admission to hospital. The overwhelming majority of cases, however, are identified too late for simple cure, necessitating long stays in hospital, on average three months or more, which contribute to the disproportionately high cost of treatment and considerably disrupt schooling for children and work for adults. The average cost of treatment for a patient with advanced disease is estimated at US\$ 1200 in Côte d'Ivoire, US\$ 780 in Ghana and US\$ 962 in Togo. In addition to the cost of hospital-based treatment, in 2003, affected households in Ghana incurred average costs and lost output ranging from US\$ 34 for patients with a nodule to US\$ 312 for patients with an extensive ulcer.

11. In most cases, the prevention or minimization of contractures and disability requires basic physiotherapy, involving adequate positioning and early mobilization through exercise and activities that can be taught to families and carried out in the home. Rehabilitative interventions are also needed for established disabilities, including amputations.

12. Access to these interventions, both pre- and post-operatively, and an appropriate level of surgical skill are limited in most endemic areas. Moreover, effective treatment depends entirely on the availability of hospital beds, which are extremely scarce in rural areas. The rates of recurrence after surgical treatment range from 16% to 28% depending on the stage of disease at diagnosis and the experience of the doctor.

13. A single BCG vaccination given in infancy can induce protective immunity, which lasts for six months, or delay the onset of lesions. In addition, recent evidence suggests that BCG may confer some protection against disseminated *M. ulcerans* disease, including bone infection.

## RECENT ACHIEVEMENTS

14. Awareness of the disease has increased and the commitment of countries in which the disease is endemic is leading to some improvements in surgical facilities and laboratories. In some areas, surveillance is drawing on a system, set up for dracunculiasis eradication, that relies on trained village workers to detect cases at an early stage. In another approach, health-education strategies that helped to reduce the stigmatization associated with leprosy are being applied to Buruli ulcer in order to change attitudes and encourage patients to seek early care.

15. WHO has assessed the disease burden in selected countries, and provided technical and financial support to some of those hardest hit, including Benin, Burkina Faso, Cameroon, Congo, Côte d'Ivoire, Democratic Republic of the Congo, Gabon, Ghana, Guinea, Malawi, Papua New Guinea, Togo and Uganda, to strengthen national programmes and train local staff. Given the urgent need to improve treatment skills, international workshops on standardized procedures were held in 2002 and 2003 to train English- and French-speaking surgeons who would, in turn, pass on these skills to fellow surgeons and general physicians. To help to increase awareness within countries endemic for Buruli ulcer, WHO has distributed the first educational leaflets, in English and French, targeting community workers at district and village levels and comic books aimed at children, the most frequently affected group. Standardized case definitions and forms for the surveillance and clinical management of

patients have been issued together with illustrated step-by-step guides for standard diagnosis, management and patient referral.

16. In view of the urgent need for deeper knowledge and new control tools, the research arm of the Global Buruli Ulcer Initiative has been particularly important. The Ad Hoc Advisory Group on Buruli Ulcer, established in 1998, meets once each year to review the status of control and advise WHO on ways to intensify control activities and accelerate high-priority research. The *Mycobacterium ulcerans* genome sequencing project is scheduled for completion in mid-2004. Already, the project has uncovered the genetic blueprint for the production of mycolactone, the *M. ulcerans* polyketide toxin. Discoveries such as this are providing investigators worldwide with key insights into the pathogen and are providing a rich resource that is accelerating the development of therapeutic and diagnostic strategies. Research is being encouraged on identified priorities, and implementation of the proposals is expected to introduce new researchers and new ideas.

17. More than 40 nongovernmental organizations, research institutions, and foundations are now participating in the Global Buruli Ulcer Initiative. In collaboration with the Regional Office for Africa, a series of annual meetings of programme managers and other national experts was launched in 2000. A framework for control throughout Africa, formulated and adopted at the first meeting, has subsequently been elaborated with strategic plans for individual countries. Nonetheless, Buruli ulcer remains a neglected disease and much work, at all levels, needs to be done to improve prospects for control.

18. At the 113th session of the Executive Board members expressed concern about the inadequate control of a disease that has such a significant social and economic impact on poor communities. In particular, members requested WHO to explore coordination and support for research on Buruli ulcer through the Special Programme for Research and Training in Tropical Diseases. The Board adopted resolution EB113.R1.

## **ACTION BY THE HEALTH ASSEMBLY**

19. The Health Assembly is invited to consider the draft resolution contained in resolution EB113.R1.

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