

part of this study, all samples from malaria case-patients identified through clinical diagnosis were subject to a Paracheck-Pf immunoassay test (Orchid Biomedical Systems, Verna, Goa, India). Results indicated that, at the peak of the apparent malaria outbreak, the percentage of samples from clinically diagnosed cases that produced a positive diagnostic test was as low as 4% (Figure, panel B). These results are unlikely to reflect poor diagnostic performance of the testing (6); febrile illness other than malaria was likely the cause of the outbreak.

Recent experiences in Kabale also highlight the potentially unwieldy nature of indoor residual spraying campaigns in the absence of spatial targeting. In Kabale, a district-wide spraying campaign supported by the US President's Malaria Initiative (7) was planned for the 2006 transmission season. However, shortages of trained personnel and other institutional delays meant that spraying could not begin until the third week of June, by which time the epidemic had peaked (and densities of vector mosquitoes had presumably begun to fall). By July 17, <50% of the targeted structures had been sprayed. In the future, careful targeting of spraying to areas of highest epidemic risk might lead to more timely completion of spraying activities. It might also be beneficial to create special spray teams that can respond quickly to specific alerts.

Recent experiences in Kabale have underlined the potential value of simple monitoring tools for early detection of epidemics but have also shown potential barriers to effective epidemic control. Our findings highlight the need to build systems that improve routine collection of data on parasitologically confirmed cases of malaria and allow rapid investigation of anomalies in incoming clinical data. It is equally important to develop procedures that translate early warning information into timely decisions concerning which epidemic control

measures to use and how best to target them (8). Without these procedures, the value of early detection will be seriously undermined.

Funding for this research was provided by the Bill and Melinda Gates Foundation (through the Gates Malaria Partnership, London School of Hygiene and Tropical Medicine) and through the Department for International Development, UK.

**Jonathan Cox,*
Tarekegn Abeku,*
James Beard,*
James Turyeimuka,†
Enoch Tumwesigye,†
Michael Okia,‡
and John Rwakimari‡**

*London School of Hygiene and Tropical Medicine, London, UK; †Kabale District Health Management Team, Kabale, Uganda; and ‡Ministry of Health, Kampala, Uganda

References

- Nájera JA, Kouznetsov RL, Delacollette C. Malaria epidemics, detection and control, forecasting and prevention. Geneva: Division of Control of Tropical Diseases, World Health Organization; 1998.
- World Health Organization/Roll Back Malaria. Malaria early warning systems—concepts, indicators and partners. A framework for field research in Africa. Geneva: The Organization; 2001. WHO/CDS/RBM/2001.32.
- Abeku TA, Hay SI, Ochola S, Langi P, Beard B, de Vlas SJ, et al. Malaria epidemic early warning and detection in African highlands. *Trends Parasitol.* 2004;20:400–5.
- Lindblade KA, Walker ED, Onapa AW, Katungu J, Wilson ML. Highland malaria in Uganda: prospective analysis of an epidemic associated with El Niño. *Trans R Soc Trop Med Hyg.* 1999;93:480–7.
- Kilian AHD, Langi P, Talisuna A, Kabagambe G. Rainfall pattern, El Niño and malaria in Uganda. *Trans R Soc Trop Med Hyg.* 1999;93:22–3.
- Mboera LE, Fanello CI, Malima RC, Talbert A, Fogliati P, Bobbio F, et al. Comparison of the Paracheck-Pf test with microscopy, for the confirmation of *Plasmodium falciparum* malaria in Tanzania. *Ann Trop Med Parasitol.* 2006;100:115–22.
- The US President's Malaria Initiative. *Lancet.* 2006;368:1.
- Abeku TA. Response to malaria epidemics in Africa. *Emerg Infect Dis* [serial on the Internet]. 2007 May [4 Apr 2007]. Available from <http://www.cdc.gov/EID/content/13/5/681.htm>

Address for correspondence: Jonathan Cox, London School of Hygiene & Tropical Medicine, Department of Infectious and Tropical Diseases, Keppel Str, London WC1E 7HT, UK; email: jonathan.cox@lshtm.ac.uk

Extensively Drug-resistant Tuberculosis, Italy and Germany

To the Editor: Twenty-three countries have reported ≥ 1 case of extensively drug-resistant tuberculosis (XDR TB) (1); however, information about XDR TB is still incomplete. In particular, the response of XDR TB to treatment in countries with low incidence is not known. We compared mortality rates from XDR TB with those from multidrug-resistant (MDR) TB.

We analyzed data from all culture-confirmed TB cases diagnosed during 2003–2006 by the TB clinical reference centers in Italy (Sondalo, Milan, Rome) and Germany (Borstel, Grossshansdorf, Bad-Lippspringe) and reviewed original clinical records. Drug susceptibility testing for first- and second-line anti-TB drugs was performed according to World Health Organization (WHO) recommendations by quality-assured laboratories and retested at WHO Supranational Reference Laboratories (Rome/Milan; Borstel) (2–4).

XDR TB was defined as resistance to at least rifampin and isoniazid (MDR TB definition) in addition to

any fluoroquinolone and ≥ 1 of 3 injectable anti-TB drugs (capreomycin, kanamycin, amikacin) (3). Characteristics of MDR TB and XDR TB cases were compared by χ^2 test (categorical variables), Student *t* test (admission days), and Kaplan-Meier curve (sputum smear, culture conversion), where appropriate.

Of 2,888 culture-positive TB cases analyzed (Italy 2,140, Germany 748), 126 (4.4%) were MDR (Italy 83, Germany 43) and 11 (0.4%) were XDR (Italy 8, Germany 3). We estimate that the TB cases analyzed represent 24% of culture-positive cases reported in Italy (69.7% of MDR) and 4.2% of those reported in Germany (12.6% of MDR). XDR TB was diagnosed in each year of the study. All 11 XDR TB patients were receiving retreatment, and of the 126 MDR TB patients, 74 (58.7%) were receiving retreatment. All XDR TB patients were HIV seronegative; and of 109 MDR TB patients tested for HIV, 10 (9.2%) were HIV seropositive. Details about previous treatment regimens, drug resistance, and duration of treatment of XDR TB patients are summarized in the online Appendix Table (available from www.cdc.gov/EID/content/13/5/780_appT.htm). XDR TB patients were significantly more likely than MDR TB patients to be resistant to all first-line drugs (8/11 vs. 36/126, $p < 0.005$); 2 of these patients were resistant to all tested drugs (online Appendix Table).

In Germany, nonnationals accounted for 95.3% (41/43) of MDR TB cases and 100% (3 of 3) of XDR TB cases (all from the former Soviet Union); in Italy, they accounted for 72.3% (60/83) and 50% (4/8), respectively ($p < 0.001$). Of 126 patients with MDR, 8 (6.3%) died, 45 (35.7%) were treated successfully, 67 (53.2%) were still receiving treatment (after achieving bacteriologic conversion, radiologic and clinical improvement, or both), and 6 defaulted (4.8%). Of 11 patients with XDR, 4 (36.4%) died and 7 (63.6%) were still receiving

treatment. Compared with MDR TB patients, XDR TB patients had a 5-fold higher risk for death (relative risk 5.45; 95% confidence interval 1.95–15.27; $p < 0.01$) and required longer hospitalization (mean \pm SD 241.2 \pm 177.0 vs. 99.1 \pm 85.9 days; $p < 0.001$) and longer treatment durations (30.3 \pm 29.4 vs. 15.0 \pm 23.8 months; $p < 0.05$). Smear and culture conversions were observed for 4 XDR TB patients compared with 102 MDR TB patients (smear median 110 vs. 41 days; culture median 97.5 vs. 58 days, respectively); time to smear and culture conversion significantly differed between the 2 groups ($p < 0.01$). A higher percentage of XDR TB than MDR TB patients had received previous anti-TB treatment (100% [11/11] vs. 59% [74/126], respectively, $p < 0.01$) and were > 45 years of age (64% [7/11] and 23% [29/126], respectively, $p < 0.01$). Radiologic patterns of the thorax did not differ between XDR TB and MDR TB patients. In the overall sample, the only variable significantly associated with death (other than XDR TB status) was immigrant status ($p < 0.01$). The association between XDR TB status and risk for death remained significant after stratification by immigrant status ($p < 0.05$).

Our findings suggest that mismanagement of TB cases plays a major role in emergence of the problem in Europe (along with suboptimal infection control in congregate settings) (5), while in high HIV-prevalence settings (e.g., South Africa) XDR TB was mainly observed in patients never treated previously (6). Mortality rates among MDR TB patients treated in reference centers (6.3%) were lower than the rate observed in a previous study in general hospitals in Italy (8.7%) (5), although a proportion of our MDR TB patients are still completing treatment. This difference in rates is probably due to better management of MDR in the reference centers. Because of the high proportion of XDR TB patients still receiving treatment, further fol-

low-up is necessary to assess potential for cure. The clinical relevance of resistance to all first-line drugs or other factors (e.g., delayed or inadequate treatment, suboptimal observation of drug intake) as major determinants of death needs further evaluation. The appearance of XDR TB in western Europe confirms that poor management and poor infection control in congregate settings exist and that new rapid diagnostic tests and new drugs are urgently needed.

The study was in part funded by a grant from Istituto Superiore di Sanità-Centro Controllo Malattie, Ministry of Health, Rome.

**Giovanni Battista Migliori,*
Johannes Ortmann,†
Enrico Girardi,‡
Giorgio Besozzi,§
Christoph Lange,¶
Daniela M. Cirillo,#
M. Ferrarese,**
Giuseppina De Iaco,††
Andrea Gori,‡‡
Mario C. Raviglione,§§
and SMIRA/TBNET Study Group¹**

*Salvatore Maugeri Foundation, Tradate, Italy; †Bad Lippspringe Hospital, Germany; ‡Ospedale Lazzaro Spallanzani, Rome, Italy; §Eugenio Morelli Hospital, Sondalo, Italy; ¶Research Center Borstel, Borstel, Germany; #S. Raffaele Institute, Milan, Italy; **Niguarda Hospital, Milan, Italy; ††University of Brescia, Brescia, Italy; ‡‡University of Milan, Milan, Italy; §§World Health Organization, Geneva, Switzerland

¹Members of the SMIRA (Multicenter Italian Study on Resistance to Anti-tuberculosis Drugs)/TBNET (Tuberculosis Network in Europe Trials): Detlef Kirsten, Sabine Ruesch-Gerdes, Federica Piana, Luigi R. Codecasa, Carla Lacchini, Alberto Matteelli, Saverio De Lorenzo, Panaiota Troupioti, Gina Gualano, Patrizia De Mori, Lanfranco Fattorini, Elisabetta Iona, Giovanni Ferrara, and Rosella Centis

References

1. Migliori GB, Loddenkemper R, Blasi F, Raviglione MC. 125 years after Robert Koch's discovery of the tubercle bacillus: the new XDR-TB threat. Is "science" enough to tackle the epidemic? *Eur Respir J*. 2007;29:423-7.
2. Laszlo A, Rahman M, Espinal M, Raviglione M; WHO/IUATLD Network of Supranational Reference Laboratories. Quality assurance programme for drug susceptibility testing of *Mycobacterium tuberculosis* in the WHO/IUATLD Supranational Laboratory Network: five rounds of proficiency testing 1994-1998. *Int J Tuberc Lung Dis*. 2002;6:748-56.
3. World Health Organization. Extensively drug-resistant tuberculosis (XDR-TB): recommendations for prevention and control. *Wkly Epidemiol Rec*. 2006;81:430-2.
4. Shah NS, Wright A, Bai G-H, Barrera L, Boulahbal F, Martín-Casabona N, et al. Worldwide emergence of extensively drug-resistant tuberculosis. *Emerg Infect Dis*. 2007;13:380-7.
5. Ferrara G, Richeldi L, Bugiani M, Cirillo D, Besozzi G, Nutini S, et al. Management of multidrug-resistant tuberculosis in Italy. *Int J Tuberc Lung Dis*. 2005;9:507-13.
6. Gandhi NR, Moll A, Sturm AW, Pawinski R, Govender T, Lalloo U, et al. Extensively drug-resistant tuberculosis as a cause of death in patients co-infected with tuberculosis and HIV in a rural area of South Africa. *Lancet*. 2006;368:1575-80.

Address for correspondence: Giovanni Battista Migliori, WHO Collaborating Centre for TB and Lung Diseases, Fondazione S. Maugeri, Care and Research Institute/TBNET Secretariat/Stop TB Italy, via Roncaccio 16, 21049, Tradate, Italy; email: gbmigliori@fsm.it

Buruli Ulcer, Nigeria

To the Editor: Buruli ulcer (BU), a neglected tropical disease caused by *Mycobacterium ulcerans*, is characterized by necrosis of subcutaneous tissue, leading to chronic, painless, and progressive ulcers. Without proper treatment, BU results in severe and permanent disability in more than a quarter of patients. Most patients are children <15 years of age. BU has been reported in >30 countries (1). The World Health Organization (WHO) has described the epidemiology, clinical features, diagnosis, and treatment of BU (1-3).

In 1967, Gray et al. described 4 BU cases in the Benue River Valley in Nigeria (4). The authors also described unpublished reports of the disease in Banbur, Adamawa State, in the upper part of the Benue River Valley. In 1976, Oluwasanmi et al. described 24 BU cases in and around Ibadan (5). Since then, there has been no official report of BU in Nigeria. However, unofficial reports indicate that the disease is still present in the country. For example, between 1998 and 2000, BU cases from the Leprosy and Tuberculosis Hospital in Moniaya-Ogoja, Cross River State, were bacteriologically confirmed at the Institute of Tropical Medicine in Belgium (6). More recently, patients from Nigeria have been treated in the neighboring countries of Benin (7) and Cameroon (8).

To clarify the BU situation in Nigeria, the government, with technical assistance from WHO, carried out a rapid assessment in the southern and southeastern states of the country, where cases had been previously reported. Preassessment sensitization workshops for health workers within the selected states were held in June and July 2006. The assessment took place November 15-19, 2006. The team, which was made up of international experts and national and state

health officials, was divided into 2 groups. Group A visited Akwa Ibom and Cross Rivers States, and group B visited Anambra, Ebonyi, and Enugu States.

Based on the WHO case definitions (1), 14 of 37 patients examined were considered likely to have BU (9 active and 5 inactive cases); 9 were children ≤15 years of age. Eight patients were female, and 6 were male. One of the patients with active disease had the edematous form, 1 had osteomyelitis and ulcer, and the other 7 had ulcers (Figure). Ten of the patients had lesions on the lower limbs, 3 on the upper limbs, and 1 on the face. All cases were documented by registration on a modified version of the BU 02 form (1) and photography. Swab specimens were taken from all active ulcerative lesions. A fine-needle aspiration technique was used to obtain specimens from the edematous patient. In 4 (44%) of the 9 patients with active cases, the clinical diagnosis was confirmed by the IS2404 PCR at the Institute of Tropical Medicine.

The locations and number of cases identified in each are as follows: Ifite Ogwari village, Ayamelum Local Government Area (LGA), Anambra State (4 cases); Ndo Etok village, Ogoja LGA, Cross River State (3 cases); Nkpo Hamida village, Igbo-Eze North LGA, Enugu State (1 case); Iburu village, Ohaozora LGA, Ebonyi State (1 case); Akofu village, Ikwo LGA, Ebonyi State (1 case); Amagunze village, Nkanu East LGA, Enugu State (1 case); Okro Mbokho village, Eastern Obolo, Akwa Ibom State (1 case); Oron village, Oron LGA, Akwai Ibom State (1 case); and Ugwu Tank, Awka South LGA, Anambra State (1 case).

In conclusion, 30 years after the last publication (5) of cases in southwestern Nigeria, BU cases have been found in the southern and southeastern parts of the country. A similar phenomenon occurred in Cameroon, where a case search in 2001 in 2 districts where cases had last been reported 24

EID
Online
www.cdc.gov/eid