

## Confirmed Case of Buruli Ulcer, Senegal, 2018

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Buruli ulcer is a necrotizing skin disease caused by *Mycobacterium ulcerans* and is usually associated with tropical climates and exposure to slow-moving or stagnant water. We report a case of Buruli ulcer that may have originated in an urban semiarid area of Senegal.

In January 2018, a 14-year-old boy came to an urban clinic in Dakar, the capital of Senegal, with a 2-week history of skin lesions. He had a 1 × 1 cm ulcerous erosion over a 6 × 16 cm painful edematous lesion on his right calf; he was febrile, with a temperature of 38.5°C. He was initially treated for cellulitis with amoxicillin and clavulanate acid, along with wound care. Two days later, the lesion had evolved. Debridement revealed considerable necrotic subcutaneous tissue extending 1–3 cm under the epidermal edge. The most proximal of the 3 ulcers had a diameter of 1 cm, the next measured 5 × 6 cm, and the last was an L-shaped lesion measuring 6 × 28 cm, running from midcalf to toes. Infection with *Mycobacterium ulcerans* was suspected because of rapid tissue necrosis, classic undermining edges, patient age, location of the lesions, and failure of standard care (Appendix Figure 1, <http://wwwnc.cdc.gov/EID/article/25/3/18-0707-App1.pdf>).

The patient was admitted to the hospital and treated with parenteral gentamicin, oral metronidazole, and wound care. The wound bed was swabbed; culture revealed *Acinetobacter* and *Pseudomonas*. Antimicrobial drug therapy was changed to parenteral gentamicin and oral ciprofloxacin. Four swab specimens were obtained from the wound, and quantitative real-time PCR assay targeting the IS2404 putative transposase gene and the mycolactone polyketide synthase gene confirmed the presence of *M. ulcerans*. Targeting IS2404 is considered the diagnostic standard for Buruli ulcer (1). Targeting IS2404 PCR analysis for

*M. tuberculosis* and negative controls were both negative (Appendix). A skin graft was performed, and the patient was discharged and given rifampin/isoniazid, ciprofloxacin, and wound care.

The patient had been born in rural Guinea-Conakry and moved to Senegal 3 years before his illness. His mother reported that he had been fully vaccinated, although no records remain. He moved to Senegal in 2015 and lived in Dakar for 18 months, then moved east to the semiarid area of Diourbel to attend Koranic school for another 18 months. He denied engaging in any agricultural or mining activities or bathing, washing, or swimming in bodies of fresh water during his 3 years in Senegal. He also denied returning to Guinea-Conakry or other travel since his arrival in Senegal. In Guinea-Conakry, he had been involved in agricultural activities, including rice farming. The family does not use mosquito nets, and he reported occasional insect bites.

Worldwide, Buruli ulcer is the third most common mycobacterial infection, inflicting debilitating cost and social stigma on patients and their families (2,3). The highest incidence of Buruli ulcer is found in tropical or subtropical sub-Saharan Africa, but 2 cases have been reported in Mali, a semiarid country not usually associated with Buruli ulcer (3–5). The only other known case of Buruli ulcer in Senegal was in a traveler from Europe who had been building canoes in fresh water along the tropical Senegal–Guinea border (6).

The mode of transmission of *M. ulcerans* is poorly understood and may vary by region. The bacterium has been found in aquatic environments, animals, and insects. Animal reservoirs and insect vectors have been proposed, but no definitive vector has been identified (7). A systematic review found that poor wound care, living or working near aquatic environments, and failure to wear protective clothing (long pants and long-sleeved shirts) were risk factors associated with *M. ulcerans* infection. Results among other researchers searching for risk factors have been contradictory (8). The reported incubation period ranges between 34 and 264 days, with a mean of 4.5 months (9). A multicenter study in West Africa demonstrated no significant evidence of protection from *M. ulcerans* infection after bacillus Calmette-Guérin vaccination (10).

This case of Buruli ulcer is noteworthy because it is a confirmed case originating in a semiarid region of West Africa, suggesting that the endemic area of this disease is poorly defined or changing. The patient appears to have contracted the disease in Senegal without the usual water-related risk factors, although he was exposed to insect bites. It is possible but unlikely that he contracted the disease in Guinea-Conakry 3 years earlier, which would mean that he had an incubation period 2 years longer than any previously reported cases. There is no evidence to suggest his possible bacillus Calmette-Guérin vaccination delayed wound development.

This case illustrates the need to better define the geographic extent and modes of transmission of this debilitating disease so that primary control measures can be identified. In addition, health workers must be provided with the training and tools to diagnose and treat *M. ulcerans*. Research into a point-of-care diagnostic test is needed so that timely treatment can minimize disability and costs to the family.

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### About the Author

Ms. Turner is a family nurse practitioner living and working in Dakar, Senegal. Her background includes trauma and pediatric primary care in high-income and low-income countries.

### References

1. Sakyi SA, Aboagye SY, Otchere ID, Yeboah-Manu D. Clinical and laboratory diagnosis of Buruli ulcer disease: a systematic review. *Canadian J Infect Dis Med Microbiol*. 2016;2016:5310718. <http://dx.doi.org/10.1155/2016/5310718>
2. Guarnier J. Buruli ulcer. Review of a neglected skin mycobacterial disease. *J Clin Microbiol*. 2018;56:01507–17.
3. World Health Organization. Treatment of *Mycobacterium ulcerans* disease (Buruli ulcer). Guidance for health workers. Geneva: The Organization; 2010. p. 1–3.
4. Ezzedine K, Pistone T, Guir V, Malvy D. Painful Buruli ulcer in a Malian visitor to France. *Acta Derm Venereol*. 2010;90:424. <http://dx.doi.org/10.2340/00015555-0862>
5. Bessis D, Kempf M, Marsollier L. *Mycobacterium ulcerans* disease (Buruli ulcer) in Mali: a new potential African endemic country. *Acta Derm Venereol*. 2015;95:489–90. <http://dx.doi.org/10.2340/00015555-1942>
6. Ezzedine K, Pistone T, Cottin J, Marsollier L, Guir V, Malvy D. Buruli ulcer in long-term traveler to Senegal. *Emerg Infect Dis*. 2009;15:118–9. <http://dx.doi.org/10.3201/eid1501.080123>
7. Merritt RW, Walker ED, Small PLC, Wallace JR, Johnson PDR, Benbow ME, et al. Ecology and transmission of Buruli ulcer disease: a systematic review. *PLoS Negl Trop Dis*. 2010;4:e911. <http://dx.doi.org/10.1371/journal.pntd.0000911>
8. Jacobsen KH, Padgett JJ. Risk factors for *Mycobacterium ulcerans* infection. *Int J Infect Dis*. 2010;14:e677–81. <http://dx.doi.org/10.1016/j.ijid.2009.11.013>
9. Trubiano JA, Lavender CJ, Fyfe JAM, Bittmann S, Johnson PDR. The incubation period of Buruli ulcer (*Mycobacterium ulcerans* infection). *PLoS Negl Trop Dis*. 2013;7:e2463. <http://dx.doi.org/10.1371/journal.pntd.0002463>
10. Phillips RO, Phanuz DM, Beissner M, Badziklou K, Luzolo EK, Sarfo FS, et al. Effectiveness of routine BCG vaccination on Buruli ulcer disease: a case-control study in the Democratic Republic of Congo, Ghana and Togo. *PLoS Negl Trop Dis*. 2015;9:e3457. <http://dx.doi.org/10.1371/journal.pntd.0003457>

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## Management of Patients with *Candida auris* Fungemia at Community Hospital, Brooklyn, New York, USA, 2016–2018<sup>1</sup>

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*Candida auris* is an emerging fungus that can cause invasive infections. It is associated with high mortality rates and resistance to multiple classes of antifungal drugs and is difficult to identify with standard laboratory methods. We describe the management and outcomes of 9 patients with *C. auris* fungemia in Brooklyn, New York, USA.

*Candida auris* is an emerging fungus that can cause invasive infections associated with high mortality rates and is often resistant to multiple classes of antifungal drugs. Risk factors for infection include nursing home exposure; invasive devices, such as tracheostomy tubes or percutaneous endoscopic gastrostomy tubes; immunocompromised status; and use of broad-spectrum antimicrobial drugs (1). On the basis of limited data available, echinocandins are recommended as initial therapy for *C. auris* infection (2). We review the management of 9 case-patients who had *C. auris* fungemia at a 300-bed community hospital, attached to a 450-bed nursing home, in Brooklyn, NY, USA. There have been 9 occurrences of *C. auris* fungemia at this institution since 2016.

Our case series demonstrates the complex patient population at risk for invasive infection with *C. auris*. Patients infected were generally >70 years of age and had multiple chronic concurrent conditions (Appendix Table, <https://wwwnc.cdc.gov/EID/article/25/3/18-0927-App1.pdf>). Most patients came from nursing homes, and more than half had invasive devices, such as tracheostomies or

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## Appendix

### Details of PCR Analysis

#### Materials and Methods

We took a total of 12 swabs, as well as a small piece of biopsied tissue, and homogenized them in sterile water. We divided the swabs into groups of 4 (named “swab 1” to “swab 3”); the small piece of biopsy was named “swab 4.” For DNA extraction, we washed 400  $\mu\text{L}$  of the sample 3 times with sterile water then centrifuged it at  $15.000 \times g$  for 15 min. We resuspended the pellet in 50  $\mu\text{L}$  of NaOH 50 mM and heated it at  $95^\circ\text{C}$  for  $\geq 15$  min. We then purified the DNA using the QIAquick PCR purification kit (QIAGEN, <https://www.qiagen.com/>) after adjusting the pH by adding 10  $\mu\text{L}$  of 3 M sodium acetate pH 5.2, following the manufacturer’s recommendations.

We determined the presence of *Mycobacterium ulcerans* by quantitative real-time PCR assay targeting the IS2404 putative transposase gene using the primers MuF1: 5'-TTGGTGCCGATCGAGTTG-3', MuR1: 5'-CGCTTTGGCGCGTAAA-3' with the dye MuFT1: FAM-CACCACGCAGCATTCTTGCCGT-BHQ1 (1), and the mycolactone polyketide synthase gene, using the primers KRTF: 5'-TCACGGCCTGCGATATCA-3', KRTR 5'-TTGTGTGGGCACTGAATTGAC-3' and the dye FAM-ACCCCGAAGCACTGGCCGC-BHQ1 (2). We performed the amplifications using thermocycler conditions as follows: an initial denaturation step at  $95^\circ\text{C}$  for 3 min followed by 40 cycles of denaturation at  $95^\circ\text{C}$  for 15 sec and extension at  $60^\circ\text{C}$  for 1 min.

We determined the presence of *Mycobacterium tuberculosis* complex by quantitative real-time PCR assay targeting the IS6110 insertion element using the primers Tb762F: 5'-CCTGCGAGCGTAGGCGT-3', Tb762R: 5'-CTCGTCCAGCGCCGCTT-3' and the dye

S762FB: FAM- GACAAAGGCCACGTAGGCGAACCCCT -BHQ1. We performed the amplification using the following thermocycler conditions: an initial denaturation step at 95°C for 3 min followed by 45 cycles of denaturation at 95°C for 15 sec and extension at 60°C for 20 sec.

For quantification of DNA, we used 10-fold dilutions of known concentration of *M. ulcerans* or *M. tuberculosis* complex positive control. We also included a negative control in each assay.

## Results

We observed amplification for the *M. ulcerans* IS2404 gene in the 4 samples, with a quantity of DNA detected ranging from  $6.3 \times 10^2$  to  $4.6 \times 10^3$  genome units (GU) per mL (Appendix Table 1 and Appendix Figure 2), and for the mycolactone polyketide synthase gene, with a quantity of DNA detected ranging from  $4.3 \times 10^2$  to  $1.6 \times 10^4$  GU per mL (Appendix Table 2). No DNA amplification was observed for the *M. tuberculosis* complex IS6110 gene or for the negative controls.

## References

1. Rondini S, Mensah-Quainoo E, Troll H, Bodmer T, Pluschke G. Development and application of real-time PCR assay for quantification of *Mycobacterium ulcerans* DNA. J Clin Microbiol. 2003;41:4231–7. <http://dx.doi.org/10.1128/JCM.41.9.4231-4237.2003>
2. Fyfe JA, Lavender CJ, Johnson PD, Globan M, Sievers A, Azuolas J, et al. Development and application of two multiplex real-time PCR assays for the detection of *Mycobacterium ulcerans* in clinical and environmental samples. Appl Environ Microbiol. 2007;73:4733–40. <http://dx.doi.org/10.1128/AEM.02971-06>

**Appendix Table 1.** Cycle threshold ( $C_t$ ) value of PCR targeting *M. ulcerans* IS2404 and mean quantity of genome unit per mL obtained for each swab.

Sample	$C_t$ value of PCR targeting IS2404 (2 points performed)	Mean quantity of genome unit per mL
Positive control dilution $10^{-1}$	30.09, 20.08	$3.50 \times 10^6$
Positive control dilution $10^{-2}$	23.55, 23.55	$3.50 \times 10^5$
Positive control dilution $10^{-3}$	26.99, 26.74	$3.50 \times 10^4$
Positive control dilution $10^{-4}$	29.97, 30.12	$3.50 \times 10^3$
Positive control dilution $10^{-5}$	34.11, 34.02	$3.50 \times 10^2$
Negative control	No $C_t$	0
Swab 1	29.98, 29.96	$4.56 \times 10^3$
Swab 2	30.13, 29.91	$4.43 \times 10^3$
Swab 3	32.94, 32.45	$7.49 \times 10^2$
Swab 4	32.19, 32.30	$1.00 \times 10^3$

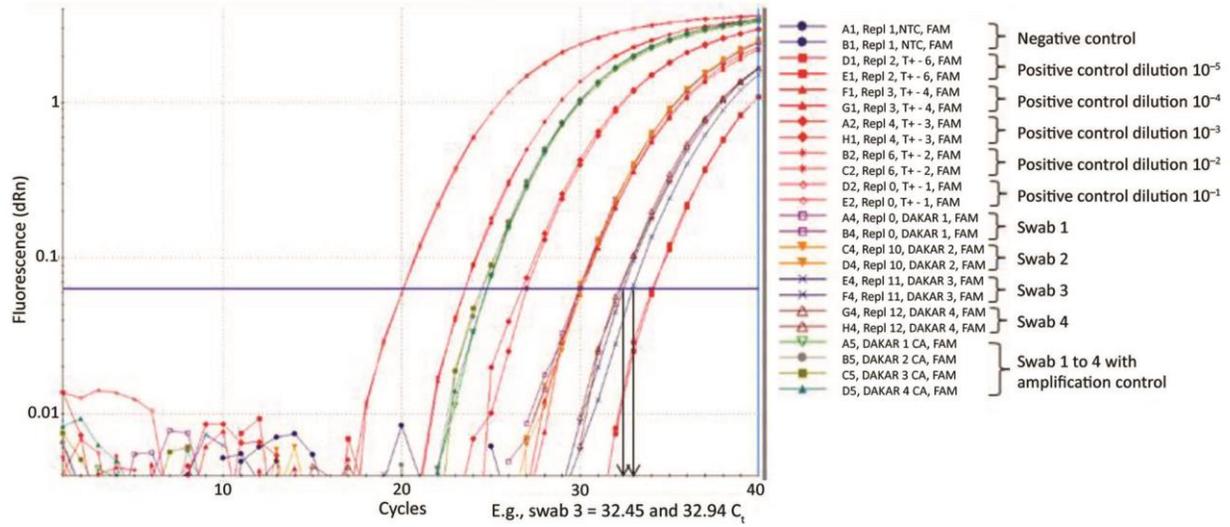
**Appendix Table 2.** Cycle threshold ( $C_t$ ) value of PCR targeting mycolactone polyketide synthase gene obtained for each swab\*

Sample	$C_t$ value of PCR targeting mycolactone polyketide synthase gene (2 points performed for controls and 6 for clinical samples)
Positive control dilution $10^{-1}$	23.61, 23.42
Positive control dilution $10^{-2}$	27.32, 27.16
Positive control dilution $10^{-3}$	30.60, 30.71
Positive control dilution $10^{-4}$	35.01, 33.62
Positive control dilution $10^{-5}$	36.61, 37.65
Negative control	No $C_t$ , No $C_t$
Swab 1	No $C_t$ ( $\times 5$ ), 37.14
Swab 2	No $C_t$ ( $\times 3$ ), 35.54, 35.57, 35.68
Swab 3	No $C_t$ ( $\times 3$ ) 34.62, 33.33, 34.03
Swab 4	32.06, 31.53, 31.92, 31.29, 31.71, 32.26

\*For quantification of DNA, 10-fold dilutions of known concentration of *M. ulcerans* were tested (positive control dilution  $10^{-1}$  to  $10^{-5}$ ). The negative control corresponds to water rather than DNA extract.



**Appendix Figure 1.** Leg infected with *Mycobacterium ulcerans* (Buruli ulcer) with undermining edges.



**Appendix Figure 2.** Amplification plots of *Mycobacterium ulcerans* IS2404 gene.