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Compliance with Antimicrobial Therapy for Buruli Ulcer

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We read with great interest the study by Philips et al. (1) reporting on successful outcomes of the combination of streptomycin and rifampin for 2 weeks, followed by clarithromycin and rifampin for 6 weeks, in the treatment of Buruli ulcer (BU). Currently, drug treatment for BU consists of 8 weeks of intramuscular streptomycin and oral rifampin. However, several recent studies, including the one by Philips et al., have described good outcomes with (partly) oral therapy using rifampin and clarithromycin (1–3), and a randomized controlled trial comparing the standard treatment with fully oral therapy is under way (4).

Oral therapy is highly desirable, as intramuscular injections are painful and administration is logistically complicated in a rural African setting, sometimes forcing patients to travel several hours daily for 8 weeks to the nearest health care facility. In addition, streptomycin carries a considerable risk of toxicity (5).

These factors might negatively affect treatment compliance. The current WHO-recommended strategy of early detection and decentralization of treatment favors community-based care over clinical admission. However, compared to hospital-based care, ensuring compliance might be challenging, although the adherence of BU patients under service conditions has never been studied. The WHO has issued a BU case record form that has been widely used in the context of national programs, with precise recording of the drug dosages administered. We reviewed these forms at the BU clinic of Nkawie-Toase Hospital in Ghana. Of the 286 BU patients treated between 2008 and 2012, only 46% completed the recommended 56 doses of streptomycin and rifampin. Noncompliance was significantly associated with self-referral, female gender, smaller lesions, and travel time.

We attempted to follow up on these noncompliers and were able to locate 57 former BU patients. When asked for their reasons for defaulting, 35% mentioned travel costs, 19% stopped coming when their ulcers were healed, and 14% defaulted because of the ototoxic adverse effects of streptomycin.

This large number of defaulters is perhaps not representative of BU drug treatment in Ghana. Yet, these findings indicate that noncompliance is in part related to streptomycin—because of both its toxicity and the cumbersome and costly daily travel to the health care facility for its administration. On the other hand, oral therapy might present inherent challenges in terms of compliance, as patients can be supplied with a full course of drugs to be taken at home and patients will not be regularly seen at the health care facility if no alternative form of directly observed treatment is provided.

The possible transition to an oral regimen has many apparent advantages but can pose a challenge to national programs and local services in terms of compliance. Studies that combine or compare oral and parenteral regimens, such as the one by Phillips et al., can potentially shed more light on this issue, and we therefore urge authors of these studies to comment on their experiences with compliance with both modes of treatment. In addition, should oral therapy be implemented outside a research setting, we suggest that compliance be systematically monitored.

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