Point-of-Care Urine Antigen Screening Tests for Tuberculosis and Cryptococcosis: Potential for Mortality Reduction in Antiretroviral Treatment Programs in Africa

To the Editor—Between 8% and 26% of patients enrolling in antiretroviral treatment (ART) services in sub-Saharan Africa die within the first year of therapy, and a majority of these deaths occur within the first few months [1]. Mortality risk is particularly high among those with the lowest baseline CD4 cell counts, and tuberculosis and cryptococcal meningitis are leading causes [1]. Packages of interventions to reduce mortality need to include specific measures to target these 2 diseases [2].

Previous studies have highlighted that much of the burden of undiagnosed prevalent cryptococcosis and tuberculosis among patients enrolling in ART services can be diagnosed by careful systematic screening of patients at baseline by testing serum samples for cryptococcal antigen and culturing sputum samples for *Mycobacterium tuberculosis* [3, 4]. However, screening using these methods requires laboratory-based processing of clinical samples remote from the site of care. Moreover, mycobacterial culture is slow. Thus, delays in availability of test results greatly undermine the potential for screening to rapidly direct appropriate clinical management and thereby improve prognosis. Simple, rapid, and low-cost point-of-care assays are needed.

We therefore read with great interest the findings of Jarvis and colleagues published in *Clinical Infectious Diseases* regarding the evaluation of a novel lateral-flow assay for cryptococcal antigen [5]. It was shown that this point-of-care screening test could be applied not only to serum and plasma, but also to urine samples, providing results within 10 minutes. Positive results might be used to direct further investigation or preemptive antifungal therapy. This publication coincided with our evaluation of a low-cost point-of-care assay for tuberculosis [6]; this detects the mycobacterial antigen lipoarabinomannan (LAM), which is present in the urine of a proportion of patients with human immunodeficiency virus (HIV)–associated tuberculosis. This simple, commercially available strip test (Determine TB-LAM Ag; Alere) had a diagnostic accuracy that was similar to that of the laboratory-based enzyme-linked immunosorbent assay version of the assay [7]. It provided a highly specific tuberculosis diagnosis in two-thirds of patients who had culture-confirmed tuberculosis and very low CD4 cell counts [6]. Similar to the cryptococcal antigen screening tool, the urine LAM test is a simple lateral-flow assay that requires no sample preparation, laboratory hardware, or power supply and provides results in just 25 minutes.

The development of these point-of-care diagnostic screening tests for cryptococcosis and tuberculosis potentially represents a major step forward for the clinical management of HIV-infected patients entering ART programs or requiring hospital admission in resource-limited settings. The assays might be used to systematically screen all new patients, regardless of symptoms, who have low CD4 cell counts (eg, <100 or <150 cells/μL). This patient subgroup has a high prevalence of both diseases, and rapid diagnosis and initiation of appropriate management are needed in view of high mortality risk. Simple urine antigen tests for other key pathologies, such as pneumococcal pneumonia [8], might also be useful in these clinical settings and should be evaluated. After development of these point-of-care assays, studies are now needed to determine how to best incorporate these new tools into clinical management and to assess their impact on patient outcomes.

Notes

Financial support. This work was supported by by the Wellcome Trust (to S. D. L.), the National Institutes of Health (grant numbers RO1 A1058736-01A1 and 5UO1A1069519-02 to R. W.) and the US Agency for International Development (grant number 3UO1A1069924-O2S to R. W.).

Potential conflicts of interest. All authors: No reported conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

Stephen D. Lawn[1,2] and Robin Wood[1]

[1]Desmond Tutu HIV Centre, Institute for Infectious Disease and Molecular Medicine, Faculty of Health Sciences, University of Cape Town, South Africa; and [2]Department of Clinical Research, Faculty of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, United Kingdom

References

1. Lawn SD, Harries AD, Anglaret X, Myer L, Wood R. Early mortality among adults accessing antiretroviral treatment programmes in sub-Saharan Africa. AIDS **2008**; 22:1897–908.
2. Lawn SD, Harries AD, Wood R. Strategies to reduce early morbidity and mortality in adults receiving antiretroviral therapy in resource-limited settings. Curr Opin HIV AIDS **2010**; 5:18–26.
3. Jarvis JN, Lawn SD, Vogt M, Bangani N, Wood R, Harrison TS. Screening for cryptococcal antigenemia in patients accessing an antiretroviral treatment program in South Africa. Clin Infect Dis **2009**; 48:856–62.
4. Lawn SD, Kranzer K, Edwards DJ, McNally M, Bekker LG, Wood R. Tuberculosis during the first year of antiretroviral therapy in a South African cohort using an intensive pretreatment screening strategy. AIDS **2010**; 24:1323–8.

5. Jarvis JN, Percival A, Bauman S, et al. Evaluation of a novel point-of-care cryptococcal antigen test on serum, plasma, and urine from patients with HIV-associated cryptococcal meningitis. Clin Infect Dis **2011**; 53:1019–23.
6. Lawn SD, Kerkhoff AD, Vogt M, Wood R. Diagnostic accuracy of a low-cost, urine antigen, point-of-care screening assay for HIV-associated pulmonary tuberculosis before antiretroviral therapy: a descriptive study. Lancet Infect Dis **2011;** e-pub ahead of print.
7. Lawn SD, Edwards DJ, Kranzer K, Vogt M, Bekker LG, Wood R. Urine lipoarabinomannan assay for tuberculosis screening before antiretroviral therapy diagnostic yield and association with immune reconstitution disease. AIDS **2009**; 23:1875–80.
8. Vernet G, Saha S, Satzke C, et al. Laboratory-based diagnosis of pneumococcal pneumonia: state of the art and unmet needs. Clin Microbiol Infect **2011**; 17(Suppl 3): 1–13.

Correspondence: Stephen D. Lawn, MRCP, MD, DTM&H, Desmond Tutu HIV Centre, Institute of Infectious Disease and Molecular Medicine, Faculty of Health Sciences, University of Cape Town, Anzio Rd, Observatory 7925, Cape Town, South Africa (stevelawn@yahoo.co.uk).

Clinical Infectious Diseases 2012;54(5):739–40

DOI: 10.1093/cid/cir908