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NEWSLETTER

The TB LAM antigen test

A tool for diagnosing HIV-associated tuberculosis

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Introduction

Approximately one third of the world's population have been infected with *Mycobacterium tuberculosis* (MTB), and new infections occur at a rate of one per second.

- Worldwide, 10.4 million people are estimated to have contracted tuberculosis (TB) in 2015, of which 11% were HIV-positive.
- An estimated 1.8 million people died worldwide in 2015 due to TB.
- South Africa had the sixth largest absolute number of incident TB cases in 2015, but ranked first globally regarding incidence rate (834 per 100 000 population).
- In 2015, an estimated 57% of TB patients in South Africa were also HIV-positive, of which 85% received antiretroviral therapy.
- In South Africa the mortality rate due to TB in 2015 was 46 per 100 000 population in patients who were not co-infected with HIV, but the mortality rate was significantly higher amongst HIV co-infected people (133 per 100 000 people).

Worldwide, TB is the most common opportunistic infection affecting HIV-positive individuals, and it remains the most common cause of death in patients with AIDS. Frequently, the diagnosis of TB is not made timeously. This is because immunodeficient individuals are more likely to be smear negative due to low sputum bacillary load, may have atypical clinical and radiological presentations, and are often unable to produce sputum for testing. Unfortunately, these severely ill patients may die while awaiting the results of TB culture. Rapid assays that can detect TB can therefore be of considerable benefit.

TB LAM antigen test

Lipoarabinomannan (LAM) is a glycolipid found in the outer cell wall of mycobacteria. LAM antigen is released from metabolically active or degrading bacterial cells during active TB infection and passes via the kidneys into the urine. A lateral flow assay is available for the detection of LAM antigen in urine.

The advantage of testing a urine sample is that it may be positive for LAM irrespective of the anatomical site of infection, is readily available, doesn't produce hazardous aerosols and poses a lower biohazard and infection risk to healthcare workers, laboratory staff and other patients.

In a recent systematic review by the World Health Organisation (WHO) the pooled sensitivity and specificity for urinary LAM antigen testing in symptomatic HIV-infected inpatients with a CD4 cell count $\leqslant$ 100 cells/μL was 56% and 90%, respectively. In symptomatic patients with a CD4 cell count > 100 cells/μL the sensitivity decreased significantly to only 26%. When urinary LAM antigen testing was combined with sputum microscopy to diagnose active TB in HIV-infected patients the pooled sensitivity was 62%, which is higher than either test alone (37% and 47%, respectively). In comparison, the combination of urinary LAM antigen testing and sputum Xpert MTB/RIF increased the sensitivity to 83%, with a sensitivity of 77% for sputum Xpert MTB/RIF alone. The pooled specificity of both combinations was 91%.

It is therefore recommended that the urinary LAM antigen test should be used in conjunction with TB culture and molecular testing to detect TB in symptomatic HIV-infected patients with CD4 cell counts < 100 cells/μL (or in critically ill patients regardless of CD4 cell count), especially if disseminated TB is suspected.

Please keep in mind:

- A negative LAM antigen test does not exclude TB.
- Since LAM is found in all mycobacteria, a positive LAM antigen result in patients with a low CD4 cell count does not distinguish between infection with MTB complex and other mycobacteria e.g. *Mycobacterium avium*. Therefore a specimen should always be submitted for molecular testing and culture to confirm the identity of the species responsible for the positive LAM antigen result.
- A positive LAM antigen result should prompt the initiation of TB therapy while awaiting the TB culture result.
- If a patient with a positive LAM antigen result does not respond to TB therapy, drug resistance or infection with another mycobacterium should be suspected.

Lancet Laboratories offers TB LAM antigen testing performed on urine samples to assist in rapidly diagnosing active mycobacterial infections in severely immunosuppressed HIV-infected patients. A minimum of 1 mL of a first void urine specimen is required for testing.

References

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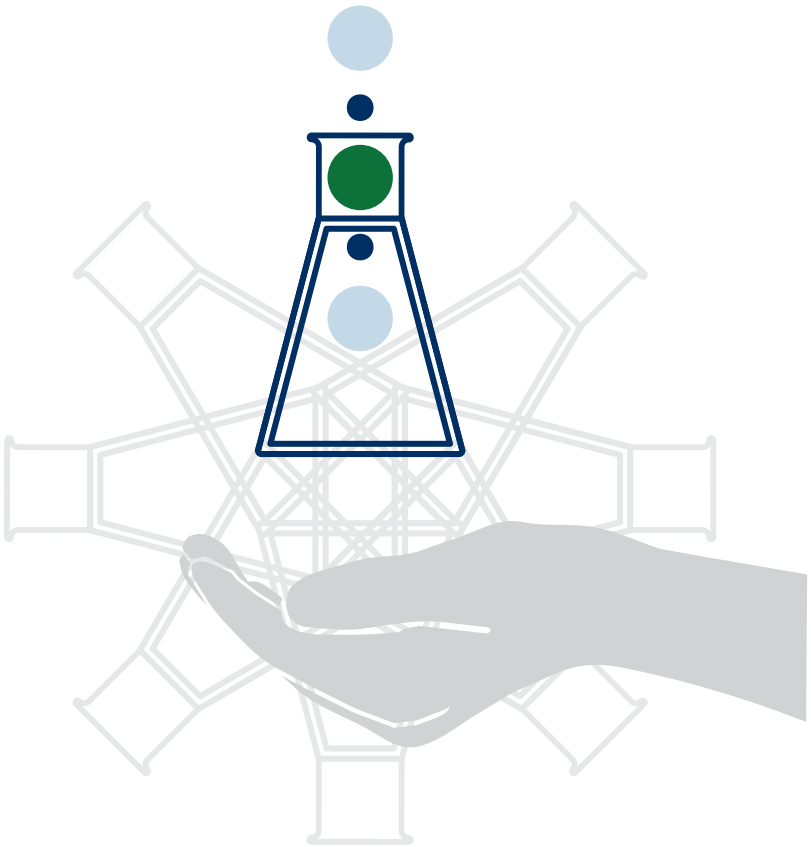
2. World Health Organisation. The use of lateral flow urine lipoarabinomannan assay (LF-LAM) for the diagnosis and screening of active tuberculosis in people living with HIV: Policy guidance. Available at: http://apps.who.int/iris/bitstream/10665/193633/1/9789241509633_eng.pdf?ua=1&ua=1.



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