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## **Screening for Cryptococcal Antigenemia in Patients Accessing an Antiretroviral Treatment Program in South Africa.**

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**BACKGROUND:** Cryptococcal meningitis is a leading cause of death in patients with acquired immunodeficiency syndrome and contributes substantially to the high early mortality in antiretroviral treatment (ART) programs in low-resource settings. Screening for cryptococcal antigen in patients who enroll in ART programs may identify those at risk of cryptococcal meningitis and permit targeted use of preemptive therapy.

**METHODS:** In this retrospective study, cryptococcal antigen was measured in stored plasma samples obtained from patients when they enrolled in a well-characterized ART cohort in South Africa. The predictive value of screening for cryptococcal antigen before initiation of ART for development of microbiologically confirmed cryptococcal meningitis or death during the first year of follow-up was determined.

**RESULTS:** Of 707 participants with a baseline median CD4 cell count of 97 cells/microL (interquartile range, 46-157 cells/microL), 46 (7%) were positive for cryptococcal antigen. Antigenemia was 100% sensitive for predicting development of cryptococcal meningitis during the first year of ART, and in multivariate analysis, it was an independent predictor of mortality (adjusted hazard ratio, 3.2; 95% confidence interval, 1.5-6.6). Most cases (92%) of cryptococcal meningitis developed in patients with a CD4 cell count  $\leq$  100 cells/microL. In this subset of patients, a cryptococcal antigen titer  $\geq$  1:8 was 100% sensitive and 96% specific for predicting incident cryptococcal meningitis during the first year of ART in those with no history of the disease.

**CONCLUSIONS:** Cryptococcal antigen screening before initiation of ART in patients with a CD4 cell count  $\leq$  100 cells/microL is highly effective for identifying those at risk of cryptococcal meningitis and death and might permit implementation of a targeted preemptive treatment strategy.

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