THE PATHCARE NEWS

PREVENTING INVASIVE CRYPTOCOCCAL DISEASE THROUGH ACTIVE SCREENING FOR CRYPTOCOCCAL ANTIGENEMIA IN PEOPLE LIVING WITH ADVANCED HIV

Cryptococcal meningitis remains a significant cause of morbidity and mortality among people living with HIV (PLHIV), particularly in resource-limited settings. In South Africa, it is estimated that cryptococcal meningitis accounts for approximately 15% of AIDS-related deaths, underscoring its significant health burden. Despite advances in antiretroviral therapy (ART), individuals with CD4 counts below 200 cells/mm^3 remain at elevated risk for opportunistic infections, including cryptococcal disease caused by *Cryptococcus neoformans* (and rarely, *Cryptococcus gattii*). Cryptococcal fungi are found worldwide in soil, bird droppings, associated with trees and found in decaying organic matter. Cryptococcal disease mostly occurs in people with defective T-cell mediated immunity, with HIV infection, the major risk factor. Other risk factors include solid organ transplant recipients, and individuals taking immunosuppressive drugs.

Cryptococcal antigenaemia precedes the development of cryptococcal meningitis by weeks to months. Early identification of cryptococcal antigenaemia and intervention are thus critical to improving patient outcomes. Reflex cryptococcal antigen (CrAg) testing for people living with HIV with low CD4 cell counts (CD4 <200 cells/mm^3) has proven to be an effective strategy in reducing the burden of cryptococcal meningitis through early detection and preemptive treatment. Reflex CrAg testing is the standard of care in the public health sector and is recommended in both national guidelines (SA HIV Clinicians Society), and international guidelines like the global 2022 WHO and 2024 European Confederation of Medical Myology, American Society of Microbiology, International Society for Human and Animal Mycology guidelines, to name a few.

Studies conducted in South Africa have demonstrated that early CrAg testing and treatment are beneficial. It significantly reduces the mortality rate and preemptive fluconazole therapy is cost-saving compared to the high costs associated with hospitalization and treatment during the management of patients with established cryptococcal meningitis. Modeling studies have demonstrated that reflex testing is highly cost-effective, particularly in regions with a high prevalence of cryptococcal disease. PathCare's CrAg testing statistics demonstrates a cryptococcal antigenaemia prevalence in people with HIV and CD4 <100 cells/mm^3 of between 6-8%, and a 1-2% prevalence in those with CD4 <200 cells/mm^3 – nearly identical to those of patients accessing the public health sector.

Everyone testing positive for serum or plasma (or whole blood) CrAg during screening should be carefully evaluated for signs and symptoms of meningitis. Those with signs or symptoms of meningitis should have a lumbar puncture and, where feasible, those without signs or symptoms of meningitis should also have a lumbar puncture, with CSF examination and CSF CrAg testing to exclude active cryptococcal disease.

In keeping with local and global recommendations, PathCare will be performing REFLEX CRYPTOCOCCAL ANTIGEN TESTING IN ALL PEOPLE WITH ADVANCED HIV WITH CD4 CELL COUNTS <100 cells/ mm^3 in order to:

- Enable early identification of cryptococcal antigenaemia.
- Enable rapid clinical follow-up, performance of routine lumbar puncture and exclusion of cryptococcal meningitis.
- Early initiation of appropriate antifungal therapy in those with cryptococcal antigenaemia with/ without meningitis.
    - Serum CrAg screen (+) positive, CSF CrAg negative: Fluconazole 1200mg po daily as induction treatment
    - Serum CrAg screen (+) positive, CSF CrAg positive: initial induction therapy of 2 weeks:
        - **Preferred: IV liposomal Amphotericin B 3-4mg/kg/day + Flucytosine 100mg/kg in 4 divided doses preferred.**
        - **Alternative: IV liposomal amphotericin B + fluconazole 800 - 1200mg po daily**
    - Induction therapy is followed by the consolidation phase with Fluconazole 800 mg daily for 8 weeks then maintenance therapy with fluconazole 200 mg daily for a minimum of 1 year in total.
    - Fluconazole maintenance therapy can be discontinued when a patient has had at least one CD4 count > 200 cells/ mm^3 and confirmed HIV virologic suppression.
- Reduce overall cryptococcal disease-associated morbidity and mortality

Please click/scan the QR link to update your special instruction to include reflex CrAg testing in people living with HIV when the CD4 cell count is <200 cells/mm3.

References are available upon request.

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