



World Health
Organization



GUIDELINES FOR
**DIAGNOSING, PREVENTING AND
MANAGING CRYPTOCOCCAL
DISEASE AMONG ADULTS,
ADOLESCENTS AND CHILDREN
LIVING WITH HIV**

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Guidelines for diagnosing, preventing and managing cryptococcal disease among adults, adolescents and children living with HIV

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DEFINITION OF KEY TERMS

Age groups	<p>The following definitions for adults, adolescents, children and infants are used in these guidelines for the purpose of implementing recommendations for specific age groups. Countries may have other definitions under national laws.</p> <ul style="list-style-type: none"> • An adult is a person older than 19 years of age. • An adolescent is a person 10–19 years of age inclusive. • A child is a person one year to younger than 10 years of age. • An infant is a child younger than one year of age.
Advanced HIV disease	For adults, adolescents and children five years or older, advanced HIV disease is defined as a CD4 cell count <200 cells/mm ³ or a WHO clinical stage 3 or 4 event at presentation for care (1). At presentation, all children living with HIV younger than five years should be considered as having advanced HIV disease.
Cryptococcal antigen positivity	Positive serum, plasma or cerebrospinal fluid cryptococcal antigen. A positive cerebrospinal fluid antigen test indicates cryptococcal meningitis.
Cryptococcal disease	Infection with <i>Cryptococcus</i> species that impair normal body function, detected by abnormal clinical symptoms or signs.
Cryptococcal infection	Growth of <i>Cryptococcus</i> species in the body is documented by direct growth of the organism (culture) or indirect detection (positive antigen test in a person without prior cryptococcal disease or India ink stain). A positive culture or first positive antigen test usually implies active disease.
Cryptococcoma	Localized, solid, tumour-like mass caused by growth of the cryptococcal organism and associated inflammatory response; can be intracranial or extracranial.
Cryptococcus species	The most common species causing human disease in the context of HIV-infection is <i>Cryptococcus neoformans</i> . <i>Cryptococcus gattii</i> also occurs in the context of HIV, and the resulting disease is indistinguishable from that caused by <i>C. neoformans</i> .
Meningeal disease	A disease presenting with nervous system signs or symptoms, specifically involving the meningeal layer surrounding the brain.
Microbiological culture-positive relapse	A new episode of active disease following resolution of the previous episode.
Non-meningeal disease	Disease that does not involve the brain but involves either only a single site in the body (localized) or involves two non-contiguous sites in the body (disseminated).
Persistent symptoms	Symptoms consistent with cryptococcal disease that fail to resolve after two weeks of initial antifungal induction treatment.
Raised intracranial pressure	Cerebrospinal fluid opening pressure ≥ 25 cm H ₂ O.
Recurrent symptoms	Symptoms consistent with cryptococcal disease that reappear after full resolution following treatment for the initial episode of cryptococcal meningitis.
Suboptimal treatment	Treatment with inadequate drug regimen, dose or duration of induction, consolidation or maintenance therapy; may also result from drug interactions or drug resistance.
Sustained clinical response	Resolution of clinical symptoms and signs of cryptococcal disease for at least two continuous weeks.
Treatment failure	Lack of clinical or mycological response among people who received suboptimal treatment or who received optimal treatment but failed to respond clinically.

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