



The pathophysiology of HIV-associated cryptococcal meningitis

How does *Cryptococcus neoformans* infect humans?

Training module structure



- ▶ This training module is organised into 7 sections which can be accessed individually.
- ▶ This is section 2: **The pathophysiology of HIV-associated cryptococcal meningitis**
- ▶ It is recommended to complete all sections and access them sequentially from 1 to 7.
- ▶ All references and acknowledgments can be found in the notes section of each slide as well as more information and external links to resources.

Cryptococcus neoformans
ecology and
transmission

Note – there is
no inter human
transmission.
Disease occurs
from latent
infection in the
lung

Cryptococcal 'life cycle': an opportunistic pathogen

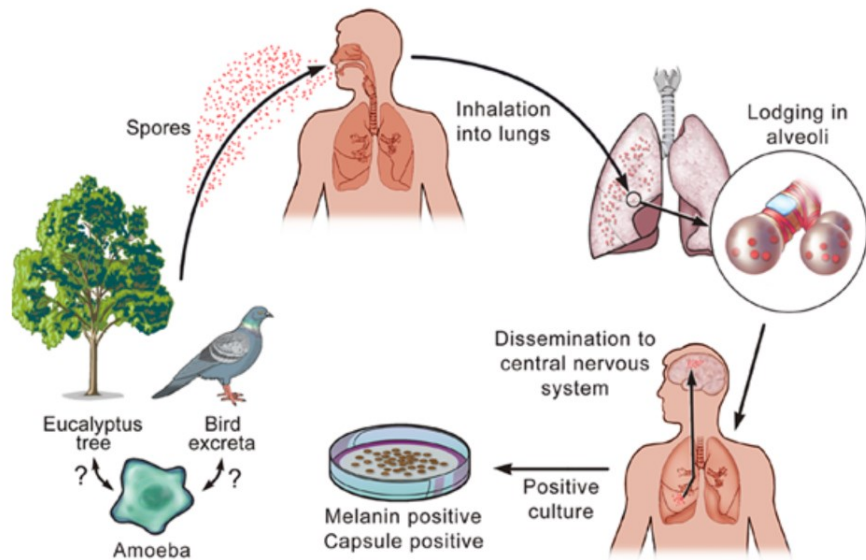
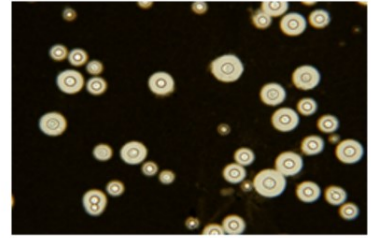
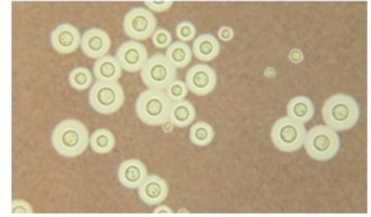


Figure from Raksha, Gurjeet & , Singh & Singh, Gurjeet. (2013). CRYPTOCOCCAL MENINGITIS: EPIDEMIOLOGY AND LABORATORY DIAGNOSIS. International Journal of Universal Pharmacy and Bio Sciences. 2. 234-241.



The “sugar-coated killer”

- ▶ Caused by an ubiquitous fungal pathogen found in soil.
- ▶ Reactivation of latent infection occurs among HIV-infected persons with severe immuno-suppression (usually CD4 count <200 Cells/ μ L).
- ▶ ‘Sugar-coated’ refers to the capsule which is a major virulence factor*.



The most common presentations in CD4 less than 100 Cells/ μ L.

Meningitis (inflammation of the tissue surrounding the brain) is the most common form of cryptococcal disease in HIV/AIDS patients.

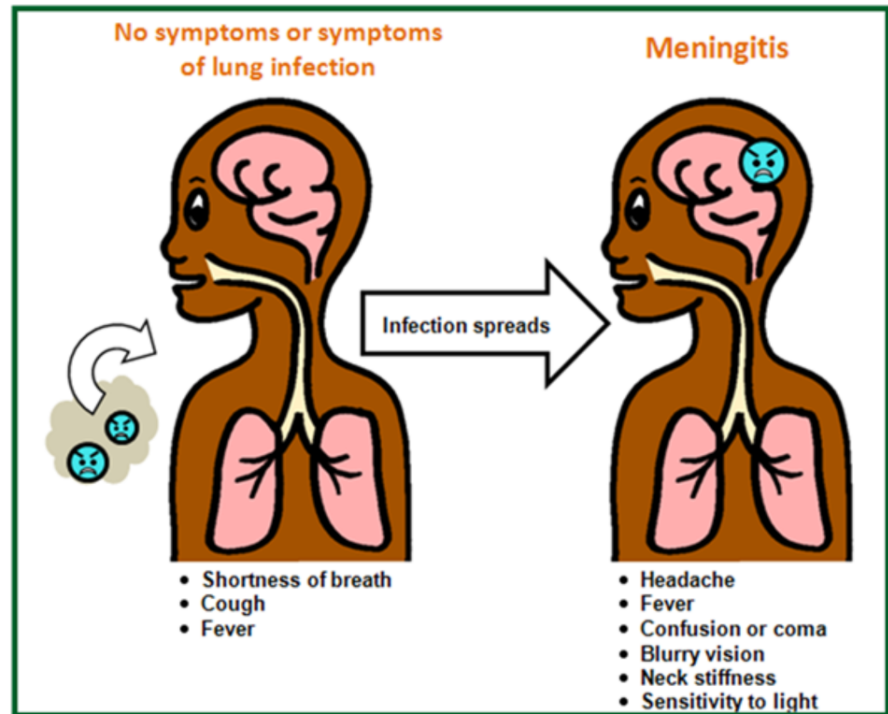
Encephalitis (infection of the brain itself) can also occur together with meningitis.

*Molecules produced by bacteria, viruses, fungi and protozoa that add to their pathogenicity.

This photomicrograph depicts *Cryptococcus neoformans* using a light India ink staining preparation. Photo from CDC/Dr. Leonor Haley CDC Public Health Library ID #3771

NO person-person transmission

NB
This is a 'time lapse' diagram showing infection spreading within the same patient.



Just like TB the primary infection also makes a granuloma, often in the lung. Once reactivated it can spread to other organs such as brain, joints, bone but has a particular affinity for the brain.

Once the fungus *Cryptococcus* has been reactivated has been activated it creates cryptococcal antigenaemia in the blood. Cryptococcal antigenaemia implies the presence of the organism in the blood and represents early dissemination from the lung. It predates the onset of CCM by an average of 3 weeks.

At first it is asymptomatic. This asymptomatic clinical phase can vary from 5 days to 200 days, but has an average of only 22.

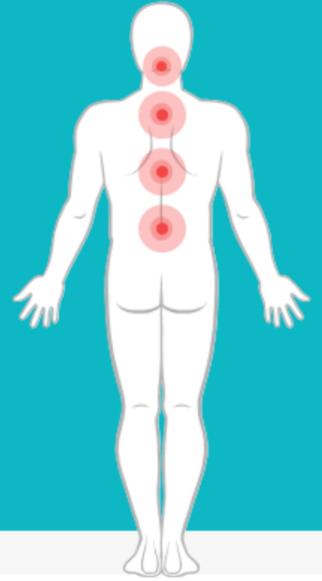
This is as opposed to asymptomatic infection in the lung which can last years/decades.

The majority of patients with a cryptococcal antigenaemia will progress to disseminated disease, it is just a matter of time, with the most common presentation being Cryptococcal meningitis.

Figure from South African NICD training Prevention, Diagnosis and Management of Cryptococcal Meningitis, August 2016.

DREAMM Clinical Training

HIV-associated cryptococcal meningitis





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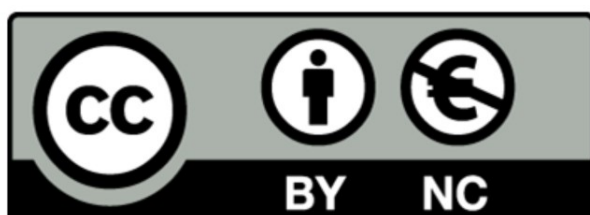
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Education programme topics

- ▷ General meningo-encephalitis patient management
- ▷ **Cryptococcal meningitis - CCM**
- ▷ Tuberculous meningitis – TBM
- ▷ Bacterial meningitis – BM
- ▷ Toxoplasmic encephalitis - Toxo
- ▷ Neurosyphilis – NS