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Cryptococcus neoformans

Cryptococcus refers to a genus of encapsulated fungi belonging to the Division: *Basidiomycota* with more than 30 species ubiquitously distributed in the environment. There are two species complexes that cause disease in humans: the *Cryptococcus neoformans* complex (including *C. deneoformans*, formally *C. neoformans var. neoformans*) and the *Cryptococcus gattii* complex. Between species, differences exist in geographically distribution, environmental niches, host predilection and clinical manifestations. *Cryptococcus* was initially identified in 1894 but not recognised as major health threat until the AIDs pandemic in the 1980s, where *Cryptococcus* became increasingly common in patients with critically reduced T cell function. *Cryptococcus* is primarily a disease of the immunocompromised but is capable of causing disease in the immunocompetent.

Epidemiology:

Approximately 95% of all Cryptococcal infections are caused by *C. neoformans var. grubii* and 4-5% by *C. deneoformans* and *C. gattii. C. neoformans* is found worldwide and is strongly associated with excreta from birds such as pigeons in addition to environmental scavengers such as amoeba and soil nematodes, and a variety of tree species. Traditionally *C. gattii* was restricted to tropical and sub-tropical regions and associated with eucalyptus trees, however, there have since been outbreaks in British Columbia and the pacific northwest region of united states, associated with temperate trees such as firs and oaks. In comparison, *C. deneoformans* is more commonly found in European countries.

Pathogenesis:

Pathogenic *Cryptococcus sp*. primarily cause disease in the lungs and CNS, which commonly develops into Cryptococcal pneumonia and Cryptococcal meningitis, respectively. Following inhalation, the fungus is deposited in the pulmonary alveoli. In immunocompetent individuals' primary pulmonary infection is asymptomatic or minimally symptomatic. There are two outcomes: clearance by the host, or encounter with alveoli macrophages which can result in the establishment of a latent infection within phagolysosome. When local immunity is supressed, the yeasts re-activate, proliferate at the initial site of infection and can disseminate either within phagocytes or as free yeast cells. They are capable of crossing the blood-brain barrier in both forms leading to

infection of the central nervous system. Traumatic inoculation into tissue has also been described. Different species and/or strains may produce unique clinical manifestations. Immunocompromised patients are vulnerable to reactivation, as well as *de novo* infection. In such patients, cryptococcal pneumonia is usually symptomatic, progressing and disseminating more rapidly than in immunocompetent patients. Moreover, although *C. gattii* and *C. neoformans* have a predilection for the lungs and CNS, in severely immunocompromised patients it can widely disseminate and infect most organs.

Our assay:

At Micropathology Ltd, we use a qualitative single-round traditional PCR assay which targets the ITS and 5.8S rDNA gene for the detection of *C. neoformans.* Currently, UKAS accredited specimen types for this assay are whole blood and CSF. Turnaround times are stated in the user manual (http://www.micropathology.com/customer-downloads-handbooks.php) with results usually available in practice much sooner than the given time frame. Where there is a delay, we are usually confirming a result and addressing clinical data given with the specimen.