

What is cryptococcosis?

- Cryptococcosis is the most common systemic fungal disease in cats worldwide.
- It is caused by the *C. neoformans*-*C. gattii* species complex which can also infect humans, domestic and wild mammals and birds.
- *C. neoformans* is considered an opportunistic pathogen in human urban populations, whereas *C. gattii* is a true pathogen, more prevalent in rural areas.
- Cryptococcosis is a rare non-contagious fungal disease, acquired from a contaminated environment.

Pathogenesis

- *Cryptococcus* is mainly an airborne pathogen, and basidiospores, which develop in the environment, penetrate the cat's respiratory system and induce primary infection.
- Cutaneous inoculation or spread from the respiratory to the central nervous system (CNS) is also possible.
- The yeast cell survives inside phagocytic cells such as macrophages, dendritic cells, and neutrophils, replicating both extracellularly and intracellularly.
- Host cells are also infected through host cell-to-cell transfer.

Clinical signs

- Infections caused by *C. neoformans* or *C. gattii* are indistinguishable clinically.
- Most common manifestations include:
 - Chronic nasal (serous, mucopurulent or haemorrhagic) discharge that can be monolateral or bilateral;
 - Naso-facial swelling followed by deep non-healing ulceration draining gelatinous exudate;
 - Nasopharyngeal granulomas presenting with stertor, inspiratory dyspnoea and open mouth-breathing;
 - Otitis media/interna with vestibular signs and proliferative or ulcerated lesions in the oral cavity or pharynx.

- Atypical forms are characterized by one or more skin nodules that are not painful but may be firm or fluctuant.
 - Solitary nodules are suggestive of direct inoculation.
 - Multiple nodules are suggestive of haematogenous spread from the primary site of infection.
- Haematogenous dissemination may lead to meningoencephalomyelitis, uveitis, chorioretinitis, osteomyelitis, polyarthritis, systemic lymphadenitis and multi-organ involvement.
- CNS involvement may occur following local dissemination through the cribriform plate, causing sudden blindness, seizures and/or behavioural changes.
- Apathy and cachexia appear in chronic cases with systemic dissemination.

Diagnosis

- **Cytology:** samples stained with Romanowsky-type stains demonstrate pink to violet, round or budding yeasts that vary in size (4-15 microns) and shape. They are typically surrounded by a clear, more or less thick halo corresponding to the unstained capsule.
- **Culture** is generally more sensitive than cytology for confirming infection. It should be performed from biopsied samples because mucous surfaces may be contaminated by *Cryptococcus*, leading to false positive results.
- **Histology** and **immunohistochemistry** can be used to confirm the invasion of tissues by *Cryptococcus* as well as for species differentiation.
- **PCR** has been developed for genetic identification in tissue and body fluids.
- **Antigen detection** is an easy and reliable test for cryptococcosis. Cryptococcal capsular antigen may be rapidly detected by latex cryptococcal antigen agglutination test (LCAT) on serum, cerebrospinal fluid or urine.

Prognosis

- Early diagnosis (before dissemination) is essential for a favourable prognosis.
- Owner compliance is crucial, because of the high costs and length of treatment.

Disease management

- Treatment guidelines have not been established and the choice of the appropriate antifungal drug depends on many factors, including owner compliance.
- Amphotericin B, fluconazole and itraconazole are most commonly used to treat cats.
- Surgical excision of any nodules located in the skin, nasal or oral mucosa is valuable in cats under medical therapy.
- In general, long-term treatment is recommended until the serum antigen test is negative. Renal (amphotericin B) and liver (fluconazole, itraconazole) toxicity have to be monitored.
- The presence of bird droppings, particularly pigeon droppings, and decaying vegetation substrates such as Eucalyptus leaves, may be considered a risk factor but efficient preventative measures have not been demonstrated.
- Vaccines are not available.

Table 1 Treatment of cryptococcosis

Drug	Dose and duration	Comments
Itraconazole	50–100 mg/cat q24h	Administration with food and acid pH required for good absorption, oral solution better than capsules, hepatotoxicity possible, monitor liver enzymes periodically/monthly
Amphotericin B	0.25 mg/kg EOD IV to a total dose of 4 mg/kg up to 16 mg/kg	Treatment of choice if CNS infection and/or systemic disease, significant nephrotoxicity, monitor renal function frequently/weekly
Flucytosine	25–50 mg/kg PO q6h	Synergic with amphotericin B, do not use as single treatment
Fluconazole	50 mg/cat q12h	Suggested treatment of choice, especially if CNS infection, good absorption without food, monitor liver enzymes
Surgical excision		Skin, oropharyngeal and nostril granulomas
Terbinafine	10 mg/kg q24h	Use terbinafine if resistance to azoles

EOD Every other day



Image courtesy of Maria Grazia Pennisi

- Cryptococcal disease: severe nasofacial swelling and deformity



Image courtesy of Maria Grazia Pennisi

- Cryptococcal disease: ulcerated skin nodules on the face