



### What is cryptococcosis?

- Cryptococcosis is a rare non-contagious fungal (yeast) disease, acquired from a contaminated environment.
- It is caused by the *C. neoformans*-*C. gattii* species complex which can also infect humans, domestic and wild mammals and birds.
- Various genotypes with different epidemiology and virulence exist, but they are not commonly identified in practice.
- Despite being rare, cryptococcosis is the most common systemic fungal disease in cats worldwide.

### Pathogenesis

- Cryptococcus is an airborne pathogen but skin inoculation of fungal basidiospores that develop in the environment can also occur.
- Primary site of infection is the upper respiratory tract followed by local invasion and dissemination in any tissues.
- 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

- Disease caused by different genotypes or species 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 ulcerations 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.
- Disease of the central nervous system (CNS) occurring after local invasion through the cribriform plate manifests with sudden blindness, seizure and/or behavioural changes.
- In case of haematogenous dissemination various progressive monofocal or multifocal signs are seen.
- 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, quite 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 a first line, easy and reliable test for cryptococcosis. Quantitative detection of capsular antigen can be rapidly obtained by latex cryptococcal antigen agglutination tests (LCAT) on serum, urine, and other fluids.

### Prognosis

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

## FACT SHEET

## Disease management and prevention

- 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 and masses must be considered in affected tissues as a valuable aid in cats under medical therapy.
- In general, long-term treatment is recommended until the LCAT 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.

## Common antimicrobial treatments for cryptococcosis in cats

Drug	Dose and administration	Notes
Amphotericin B (50 mg vial; stock solution 5 mg/ml)	0.25 mg/kg q48h IV (cumulative dose: 4-8 mg/kg) 0.5 mg/kg q48h SC in 350 ml/cat of hypotonic solution* (cumulative dose: 7-23 mg/kg)	First choice in CNS, eye and systemic disease in combination with flucytosine (if available) or fluconazole. Nephrotoxic drug: monitor renal function and avoid if renal disease present.
Flucytosine (250-500 mg oral formulations)	25-50 mg/kg q8h PO	Always in combination with amphotericin B (synergistic activity). Lower dose in cases of renal disease. Gastrointestinal adverse signs.
Fluconazole (50 mg capsule or 10 mg/ml oral suspension)	50 mg/cat (or 10 mg/kg) q12-24h PO	Teratogenic drug. Gastrointestinal adverse signs. First choice monotherapy in localized forms of disease.
Itraconazole (10 mg/ml oral solution)	5 mg/kg q24h PO	Teratogenic and hepatotoxic drug.
Terbinafine (250 mg tablet)	30-40 mg/kg q24h PO	In combination with azole drugs or as monotherapy in azole-refractory cases. Gastrointestinal adverse effects.

\* 0.45% NaCl + 2.5% dextrose (obtained by combining 0.9% NaCl and 5% dextrose 1:1)



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.