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 cribiform 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.
Cryptococcosis in cats

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>
<thead>
<tr>
<th>Drug</th>
<th>Dose and duration</th>
<th>Comments</th>
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<tbody>
<tr>
<td>Itraconazole</td>
<td>50–100 mg/cat q24h</td>
<td>Administration with food and acid pH required for good absorption, oral solution better than capsules, hepatotoxicity possible, monitor liver enzymes periodically/monthly.</td>
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<tr>
<td>Amphotericin B</td>
<td>0.25 mg/kg EOD IV to a total dose of 4 mg/kg up to 16 mg/kg</td>
<td>Treatment of choice if CNS infection and/or systemic disease, significant nephrotoxicity, monitor renal function frequently/weekly.</td>
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<tr>
<td>Fluconazole</td>
<td>25–50 mg/kg PO q8h</td>
<td>Synergic with amphotericin B, do not use as single treatment.</td>
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<td>Surgical excision</td>
<td>Skin, oropharyngeal and nostril granulomas</td>
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<tr>
<td>Terbinafine</td>
<td>10 mg/kg q24h</td>
<td>Use terbinafine if resistance to azoles.</td>
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- Cryptococcal disease: severe nasofacial swelling and deformity
- Cryptococcal disease: ulcerated skin nodules on the face