

Cryptococcosis in Animals and Birds: A Review

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Abstract: Cryptococcus infections in bovines was mostly reported in association with mastitis, mainly in cattle. *Cryptococcus neoformans* was recognized as the cause of severe outbreaks of mastitis in cattle and also in sporadic cases in buffaloes. Bovine systemic cryptococcosis was rarely diagnosed. In camels, cryptococcosis is very rare. It has been reported in South American camelids (llamas, alpacas and vicunas). In equines, cryptococcosis is uncommon. The nasal cavity is the most common site of infection. Sporadic cases have been associated with granulomatous pneumonia, nasal granuloma, endometritis and placentitis with neonatal cryptococcal pneumonia, abortion and mesenteric lymph node abscesses. Cryptococcal meningitis in equines is almost associated with pneumonia and disseminated infection. Cryptococcus species were reported in sheep and goats as causes of mastitis. Experimental mastitis in goats was induced by unilateral intramammary inoculation of *Cryptococcus neoformans*. Nasal cryptococcosis is frequently seen as clinical signs in cats and dogs. With time, infections involving the nasal cavity can spread to adjacent structures and disseminate to the brain and other organ and even the skin. Cryptococcal pneumonia and meningitis due to *Cryptococcus gattii* was reported also in goats. In wild animals, cryptococcosis occurs in different animals and Cryptococcus species. can affect the gastrointestinal and respiratory systems, nasal cavity and eyes.

Keywords: Cryptococcosis, *Cryptococcus neoformans*, *Cryptococcus gattii*, bovines, equines, camels, sheep and goats, cats and dogs, wild animals, birds.

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1. Introduction

Cryptococcosis in animals is a systemic fungal infection of worldwide significance that usually initially infects the nasal cavity, paranasal tissues, or lungs. It can then disseminate, most commonly to the skin, eyes, or central nervous system. Cryptococcosis is a fungal disease caused by *C. neoformans* and *C. gattii*, which are ubiquitous, saprophytic, round, basidiomycetous yeasts (5 to 10 µm) with a large heteropolysaccharide capsule (1 to 30 µm) that does not take up common cytologic stains.

According to the current classification, the species complex comprises two species, namely *C. neoformans* and *C. gattii* [1 & 2] with serotypes A, D and AD for the former, and B and C for the latter species. *Cryptococcus neoformans* currently consists of two varieties: *C. neoformans* variety *grubii* (serotype A) [3] and *C. neoformans* variety *neoformans* (serotype D) [4]

Recently, Hagen *et al.* [5] proposed the genus *Cryptococcus* to include 3 separate species, *C.*

neoformans (*Cryptococcus neoformans* var. *grubii*) represented by genotypes VNI and VNII, *C. deneoformans* (*Cryptococcus neoformans* var. *neoformans*) represented by genotypes VNIII and VNIV, and *Cryptococcus gattii* (represented by genotypes VGI, VGII, VGIII, and VGIV).

The environmental reservoir of *C. neoformans* is usually related to bird faeces, particularly pigeon droppings. However, this yeast has also been found in decaying trees, wood and plant debris, waterways and soil, all usually contaminated with bird excrement [6, 7, 8, 9, 10, 11, 12]. The epidemiology of clinical disease depends largely on the species of infecting organism. *Cryptococcus neoformans* var. *grubii* (serotype A) and *C. neoformans* var. *neoformans* (serotype D) are globally distributed and infect predominantly immunocompromised hosts. *Cryptococcus gattii* (serotypes B and C) has recently been recognized as a species distinct from *C. neoformans* based on molecular and mating type characteristics.

2. Cryptococcosis in domestic animals

2.1. Cryptococcosis in bovines:

Cryptococcus infections in bovines was mostly reported in association with mastitis, mainly in bovines. Klein [13] was the first to isolate a yeast from a case of mastitis, which he reported to be identical with strains of *Cryptococcus neoformans* of human and plant origin. Almost 50 years later, *Cryptococcus neoformans* was recognized as the cause of severe outbreaks of mastitis in cattle [14, 15, 16, 17].

Pounden *et al.* [18] reported the clinical aspects of an outbreak in which 106 cows were affected in a 235 cow-herd. They stated that during the outbreak, *Cryptococcus* has been isolated from samples where no visible changes were noted in either the gland or milk, and the cases with visible signs varied from mild and transient swelling of one or more quarters of the udder to severe swelling and distention of the affected glands

Cryptococcal mastitis was detected also in sporadic cases by Abdel Ghani *et al.* [19], Rahman *et al.*, [20], Moawad, [21], Hassan *et al.* [22], mostly, following treatment with antibiotics [23, 24, 25, 26]. On the other hand, Rippon [27] emphasized that *cryptococcal* mastitis in dairy cows is worldwide in distribution.

Cryptococcus neoformans was the most commonly recorded species in cows [28, 29, 8]. *Cr .neoformans* was also recorded as a cause of mastitis in buffaloes [30, 31]. Other species like *C. albidus*, *C. laurentii*, *C. flavus*, *C. lactativorus*, *C. luteolos*, *C. terreus*, *C. uniguttulatus* and *Cryptococcus species* were also reported in few reports [28, 32, 33, 34, 35, 36, 37, 38, Table 1].

Cryptococcal pneumonia was infrequently reported in bovines [39, 22]. On the other hand, bovine systemic cryptococcosis was rarely diagnosed. Only two reports could be found in the available literature [40, 41]. Similar findings were obtained in case of abortion caused by *Cryptococcus species* [40, 41].

Table 1: Cryptococcosis in bovines

Cryptococcus	References
Cryptococcal mastitis	
<i>C. neoformans</i>	8,9,13,14,15,16,17,18,19,20,21,22,23,24,25,26,27,28,29,30,31,34,116,117,118,119,120,121,122,123,124,125
<i>C. albidus</i>	28, 32
<i>C. laurentii</i>	32,33, 34 , 35,37
<i>C. flavus</i>	32
<i>C. luteolos</i>	32
<i>C.uniguttulatus</i>	36
<i>C. lactativorus</i>	12 129,130,1316
<i>C. terreus</i>	38
<i>Cryptococcus species</i>	30, 32, 127.128
Cryptococcal pneumonia	
<i>C. neoformans</i>	22,39,
<i>C. laurentii</i>	39
Cryptococcal abortion	
<i>C. neoformans</i>	22,39
<i>C. laurentii</i>	39
Systemic cryptococcosis	
<i>C. neoformans</i>	40
<i>C. species</i>	41

2.2. Cryptococcosis in equines

In equines, cryptococcosis is uncommon and sporadic cases have been reported, however it is relatively common in Western Australia, and there is an epidemiologic relationship between *C. gattii* and the Australian river red gum tree (*Eucalyptus camaldulensis*) and between *C. neoformans var neoformans* and bird (particularly pigeon) excreta. From the literature it appears that the nasal cavity is the most common site of equine cryptococcosis. Sporadic cases have been associated with granulomatous pneumonia, nasal granuloma, endometritis and placentitis with neonatal cryptococcal pneumonia, abortion, mesenteric lymph node abscesses , intestinal polypoid granulomas, osteomyelitis and meningitis [Table 2] .

Cryptococcal nasal infections in equines involved also the frontal and maxillary sinuses and the corresponding lymph

nodes and in most cases a polyp or granuloma that almost completely occupied the nasal cavity was reported. **Zoppa et al. [42]** reported a case of nasal obstruction caused by fungal granuloma in a 9-year-old horse with serosanguineous nasal discharge, absence of breath out through the right nostril, and respiratory noise. Endoscopic and radiographic examinations revealed a six centimeter diameter mass, covered by yellowish mucosa, which was obstructing the entire right nasal cavity and part of the left one. The mass was excised through a right frontal sinusotomy. The microscopic examination and the culture revealed a cryptococcal granuloma.

Equine cryptococcal pneumonia was reported mostly in single cases characterized by diffuse, severe interstitial

pneumonia [43], often as granulomatous pneumonia [44, 45].

Ryan and Wyand [43] reported neonatal cryptococcal pneumonia in a foal, followed by placentitis and abortion in the mare at her next pregnancy. Histologic examination of lung sections showed diffuse, severe interstitial pneumonia, while **Blanchard and Filkins [46]** reported *Cryptococcal* pneumonia in a 9-month-old equine foetus aborted by a healthy American Paint mare. Endometritis was diagnosed on biopsy, and vaginal specimens obtained for culture were *Cryptococcus*-positive.

The clinical, radiographic and post-mortem findings in 6 horses with cryptococcal pneumonia were described by **Riley et al. [47]** and **Begg et al. [48]**. The infected animals were reported to suffer from chronic cough, fever, weight loss that developed later into dyspnoea, tachypnoea and exercise intolerance. The diagnosis in most cases was established using lateral thoracic radiography and transthoracic ultrasonography and confirmed by the detection of encapsulated, budding yeasts in smears made from transtracheal washings and needle aspirates of the pulmonary lesions, demonstrated in Wright's-stained preparations.

Cryptococcal meningitis in equines is almost associated with pneumonia and disseminated infection [49, 50, 51, 52, 53, 54, 55, 45].

Cho et al. [55] presented extensive gross and microscopic cavitory lesions of cerebral cryptococcosis in a 5-year-old, quarter horse mare. The mare was dehydrated, became markedly depressed and ataxic, and violently resisted any

attempt of restraint. **Hart et al. [54]** reported a 4-year-old Tennessee Walking Horse with episodic fever and acute bilateral blindness of approximately 7 days' duration and **Del Fava et al. [45]** described a case of cryptococcal granulomatous pneumonia and meningitis in a mature Thoroughbred horse stabled at an equine racing center located in an urban area of Brazil.

The diagnosis in cryptococcal meningitis was achieved by cytologic evaluation of the CSF for detection of encapsulated *Cryptococcus neoformans* or serology by serum latex agglutination test and by histological sections of the brain that showed granulomatous encephalitis with the classic "soap-bubble" appearance associated with the characteristic encapsulated yeast cells [54, 45].

Disseminated cryptococcosis was diagnosed by **Lenard et al. [56]** in a 4-year-old Arab mare, including osteomyelitis of the proximal phalanx of the left hind limb, osteomyelitis with associated soft tissue granuloma of a rib and disseminated, large cryptococcal nodules in the lungs. The mare presented had a large swelling over the right caudodorsal thorax and a marked swelling of the left hind fetlock. The mass was hypoechoic and round, with the 17th rib visible as an echogenic structure that casts an acoustic shadow in the centre of the mass. The lesion in the dorsoproximal aspect of the proximal phalanx had a large area of cortical lysis with speculated periosteal new bone and extensive soft tissue swelling. The affected rib had a pathological fracture. Multiple, well circumscribed, soft

tissue opacity nodules (1 to 8 cm diameter) are present in the lung.

Table 2 Cryptococcosis in equines

Cryptococcus	References
Cryptococcal nasal infections	
<i>C. neoformans</i>	15,42,83,132,133,134
Cryptococcal pneumonia	
<i>C. neoformans</i>	43, 44,45,46,47,48,135,136
Cryptococcal meningitis	
<i>C. neoformans</i>	45,49,50,51,52,53,54,55
Cutaneous cryptococcosis	
<i>C. species</i>	127,138
Cryptococcal endometritis and placentitis	
<i>C. neoformans</i>	46,139
Abdominal cryptococcosis	
<i>C. neoformans</i>	47
Disseminated cryptococcosis	
<i>C. species</i>	56

2.3. Cryptococcosis in camels

The only case of cryptococcosis in camels found in the available literature was reported by **Ramadan et al. [57]** in a camel (*Camelus dromedarius*) in Saudi Arabia. The tissue reaction in cryptococcosis varied depending on the organ affected. Two basic histological patterns were described: gelatinous and granulomatous. The granulomatous lesion consisted of histiocytes, giant cells and lymphocytes. The pathology in this camel was modified by the secondary bacterial infection. All other cases were reported in vicuna [58], alpaca [59, 60] and llama [61]. Most of these cases suffered from meningitis caused by *Cryptococcus gattii*.

The case described by **Bildfell et al. [61]** was in a pastured 17-year-old male llama, which was found in lateral recumbency, was undergoing continuous tonic clonic convulsions of all limbs with periodic spasms of the head and neck. The animal was hypothermic and unresponsive to stimuli. A complete neurologic examination could not be

performed due to the clinical status of the animal. The llama was in good body condition with no history of serious health problems and no known exposure to toxins. The owners had noted this llama to be mildly anorexic during the preceding 3 days but had not attempted any therapy. A health program for the 16 animals on the premises included periodic deworming, vaccination, and health checks. Differential diagnoses at the time of presentation included various neurologic diseases such as trauma, organophosphate toxicity, hypomagnesemia, visceral larval migrans, equine herpes virus type 1 (EHV1) encephalomyelitis, rabies, and bacterial infections of the CNS such as listeriosis or brain abscessation. After considering the prognosis, the owner requested that the llama be euthanatized without further clinical work-up. Tissues affected included the brain, spinal cord, lung, and kidney. The character of the leukocytic response varied from minimal to pyogranulomatous

meningitis with intralesional yeast that were bordered by a

2.4. Cryptococcosis in sheep and goats

Cryptococcus species were reported in sheep and goats as causes of mastitis, pneumonia, meningitis and abortion [Table 3].

Experimental mastitis in goats was reported by unilateral intramammary inoculation of 10 goats with 2×10^6 cells of *Cryptococcus neoformans* [62]. The infection resulted in the development of mastitis, with gross and microscopic lesions being restricted to the infected udder halves only and there was no dissemination of infection to the opposite uninfected udder halves as well as to other organs of the body. The experiment was continued for 40 days, with 2 animals, each from the infected and control groups being killed on 5th, 10th, 20th, 30th and 40th day post-inoculation (DPI). Initial enlargement of the infected udder halves was followed by marked decrease in size leading to very small, firm and nodular udder halves. After infection, there was also sharp fall in the milk yield. Cryptococcal organisms were demonstrated in the mastitic milk and udder impression smears with special stains. *C. neoformans* was re isolated from the milk of the only infected udder halves up to 25th DPI. Microscopically, there was initially acute diffuse purulent mastitis which later on became chronic, characterized by marked infiltration of lymphocytes, macrophages, extensive fibrosis and development of multiple granulomas. The cryptococcal organisms could be demonstrated in the udder sections only up to 30th DPI.

non-staining halo.

Mycotic pneumonia in goats due to *Cryptococcus gattii* was reported in Spain by **Baro et al.** [63]. The strains were isolated from lung (10 samples), liver (1 sample), and brain (2 samples) tissue specimens from six goats suffering from predominantly severe pulmonary disease that were autopsied. Biotyping was performed by culturing the isolates on L-canavanine-glycine-bromothymol blue medium and testing them for the assimilation of D-proline and D-tryptophan. Serotyping by agglutination tests confirmed the characterization of all strains as *C. gattii*.

C. gattii was reported to cause 5 epidemic outbreaks of cryptococcosis in goats grazing freely in west Spain grasslands [64]. The goats belonged to various milking breeds and were grazing with variable status of health and husbandry. Goats affected by cryptococcosis showed similar respiratory symptoms, consisting of mucopurulent nasal discharge, cough, dyspnea and progressive cachexia, causing death in a period of 2 to 4 weeks. In three outbreaks many animals also showed ataxia, midriasis, blindness and progressive paralysis. Clinical prevalence varied from 2 to 12% in the different outbreaks.

On the other hand, **Gutiérrez and García Marin** [65] presented an adult Blanca-Celtibérica doe originating from a goat herd with a high prevalence of tuberculosis with respiratory signs. At necropsy, this goat had a diffuse and severe mycotic pneumonia associated with the presence of *Cryptococcus neoformans* concomitant with pulmonary focal caseous nodules from which *Mycobacterium bovis* was

isolated. Microscopically, the mycotic lesion was a granulomatous pneumonia with many large foamy macrophages containing intracellular yeast bodies. The extensive mycotic changes, their granulomatous nature, and the lack of positive response to different immunologic tests for mycobacterial infection suggested an impaired immune status in this animal.

Cryptococcal meningitis in goats was described by **Luvizotto et al. [66]**, who euthanized four-year-old male goat with a history of neurological disorder. It presented uncommon nodules in the brain and lungs associated with multiple abscesses, predominantly in the spleen and liver. Histological examination of brain and lung sections revealed yeast forms confirmed to be *Cryptococcus gattii*. On the other hand, **Stilwell and Pissarra [67]** described a case of a five year old buck showing severe neurological signs, including paraplegia and strong pain reaction to touch of the hindquarters region. Postmortem examination revealed lumbar meningitis, lung nodules and caseous lymphadenitis lesions. Encapsulated *Cryptococcus neoformans* were identified from the lungs and meninges, showing that cryptococcal meningitis should be included in the

differential diagnosis of goats showing paresis and hyperesthesia. Both *Cryptococcus gattii* genotype AFLP4/VGI and *Cryptococcus neoformans var. neoformans* genotype AFLP2/VNIV were incriminated as causes of meningoencephalitis in goats by **Maestrale et al. [68]**.

Cryptococcal meningitis in goats was described by **da Silva et al. [69]**, who performed a study aimed to report a 5-year-old goat showing intermittent dry cough, ruminal tympany, anorexia, fever, tachycardia and tachypnea in State of São Paulo, Brazil. Postmortem examination revealed numerous 2.0-6.0 cm diameter yellow gelatinous pulmonary masses. Tissues were evaluated by a combination of pathological, mycological, and molecular diagnostic techniques. Microscopically, pneumonia granulomatous, multifocal to coalescing, moderate, with many intralesional carminophilic yeasts was observed. The immunohistochemistry and mycological culture confirmed *Cryptococcus* spp. Internal transcribed spacers and orotidine monophosphate pyrophosphorylase nucleotide differentiation demonstrated that the isolate corresponds to the *C. gattii* VGII molecular subtype.

Table 3: Cryptococcosis in sheep and goats

Cryptococcus	Animal	References
Cryptococcal mastitis		
C. neoformans	goats	62,140
Cryptococcal pneumonia		
C. neoformans	goats	22,63,65
	sheep	22,141
C. gattii	goats	69,142,143,144
Cryptococcal meningitis		
C. neoformans	goats	67,68
	sheep	68
C. gattii	goats	66,68
	sheep	68
Cryptococcal abortion		
C. gattii	goats	144

2.5. Cryptococcosis in cats and dogs

In cats and dogs, cryptococcosis can be either focal or disseminated, affecting a single organ system or many [Table 4]. It can begin insidiously, and may gradually become more severe over weeks or months. Fever may be absent, and if present, is often mild. Other nonspecific signs can include lethargy, anorexia and weight loss. The most common site of localized infections is the nasal cavity. Nasal cryptococcosis is frequently seen clinical signs including sneezing, snoring or snorting, dyspnea, nasal deformities and/ or a mucopurulent, serous or sero-sanguineous nasal discharge. Polyp-like masses sometimes protrude from one or both nostrils. Cutaneous or subcutaneous swellings and nodules may be seen on the face, particularly the bridge of the nose, side of the face, upper lip or nostril. Some of these lesions may ulcerate. In addition, the submandibular lymph nodes are often enlarged. Rhinitis in cats was reported to be caused by *C. neoformans var. neoformans* [70, 71, 72, 73].

With time, infections involving the nasal cavity can spread to adjacent structures and disseminate to other organs [74, 75, 76, 77, 78], including the brain [79, 80] and eyes [79, 81] and even the skin [82]. Cutaneous involvement usually appears as fluctuant or firm papules and nodules. Some skin lesions may ulcerate, but there is little or no pruritus. Direct inoculation of organisms into the skin can occasionally cause solitary lesions.

Cryptococcus gattii has emerged since 1999 as an important pathogen of humans and animals in southwestern British Columbia. Historically thought to be restricted to the tropics and subtropics, *C. gattii* has posed new diagnostic and

treatment challenges to veterinary practitioners working within the recently identified endemic region. Clinical reports of canine and feline cryptococcosis caused by *C. gattii* diagnosed between January 1999 and December 2003 were reported. The most common manifestations of disease were respiratory and central nervous system signs. Multivariate survival analysis revealed that the only significant predictor of mortality was the presence of central nervous system signs upon presentation or during therapy. Case fatality rates in both species were high. [70, 73, 83, 84].

Trivedi *et al.* [85] mentioned that Cryptococcosis, principally caused by *Cryptococcus neoformans* and *Cryptococcus gattii*, is the most common systemic mycosis of cats worldwide. Cats may be infected following inhalation of spores from the environment, with the nasal cavity suspected as being the initial site of colonization and subsequent infection. Other sites of infection in cats are the skin, lungs, lymph nodes, central nervous system (CNS), eyes and, occasionally, periarticular connective tissue. Cryptococcosis can be diagnosed using serology (antigen testing), cytologic examination of smears, histopathology or culture. Treatment of localized disease is generally successful using azole antifungal drugs; however, cats with CNS involvement or disseminated disease require additional treatment with amphotericin B, with or without flucytosine. The prognosis is variable, depending on host and pathogen factors. Some cats require long-term (>1 year) treatment or indefinite therapy. Cats of any breed, gender and age may be

affected. Retroviral status does not appear to be a risk factor for developing cryptococcosis and indoor cats are not protected from disease.

Feline cryptococcosis occurs worldwide, but is most frequently reported in Australia, western Canada and the western United States. Species and molecular type vary in different geographical regions and may affect clinical presentation and antifungal susceptibility patterns. Serologic tests that detect cryptococcal antigen in serum are sensitive and specific, but false negatives can occur in cats with localized disease. Long-term drug therapy can be expensive and has the potential for toxicity.

Pennisi et al. [86] mentioned that Cryptococcosis is worldwide the most common systemic fungal disease in cats; it is caused by the *Cryptococcus neoformans*–*Cryptococcus gattii* species complex, which includes eight genotypes and some subtypes (strains) with varying geographical distribution, pathogenicity and antimicrobial susceptibility. Cats acquire the infection from a contaminated environment. The prognosis is favourable in most cases, provided a diagnosis is obtained sufficiently early and prolonged treatment is maintained. Basidiospores are the infectious propagules of *Cryptococcus* species as they penetrate the respiratory system and induce primary infection. Asymptomatic colonisation of the respiratory tract is more common than clinical disease.

Cryptococcosis caused by *C. neoformans* or *C. gattii* is indistinguishable clinically. The disease can present in nasal, central nervous system (which can derive from the nasal form or occur independently), cutaneous and systemic

forms. An easy and reliable test for cryptococcosis diagnosis is antigen detection in body fluids. Only isolation and polymerase chain reaction allow identification of the species genotype. Amphotericin B, ketoconazole, fluconazole and itraconazole have all been used to treat cats. Surgical excision of any nodules in the skin, nasal or oral mucosa assists recovery. Continued treatment is recommended until the antigen test is negative. Efficient preventive measures have not been demonstrated. Vaccines are not available.

Cryptococcus species other than *C. neoformans*/*C. gattii* complex were reported in cats by **Danesi et al. [87]**, who sampled cats from 162 urban and rural feral cat colonies over 3 years. Of 766 cats from which nasal swabs were obtained, *Cryptococcus* spp. were recovered from 95 (12.6%), including 37 *C. magnus* (4.8%), 16 *C. albidus* (2.0%), 15 *C. carnescens* (1.9%), 12 *C. neoformans* (1.6%), as well as *C. oeirensis* ($n = 3$), *C. victoriae* ($n = 3$), *C. albidosimilis* ($n = 2$), *Filobasidium globisporum* ($n = 2$), *C. adeliensis* ($n = 1$), *C. flavescens* ($n = 1$), *C. dimnae* ($n = 1$), *C. satoi* ($n = 1$), and *C. wieringae* ($n = 1$) with prevalence <1%. Thirteen *Cryptococcus* species were identified by polymerase chain reaction and sequencing of internal transcribed spacer amplicons. Statistical analysis did not identify any predisposing factors that contributed to nasal colonization (eg, sex, age, season, or habitat). Results suggested that asymptomatic feral cats may carry *C. neoformans* and other *Cryptococcus* species in their sinonasal cavity. Genotyping of the specific cryptococcal isolates provides a better understanding of the epidemiology of these yeasts.

Table 4: Cryptococcosis in cats and dogs

Cryptococcus	Animal	References
Cryptococcal rhinitis		
<i>C. neoformans var. neoformans</i>	cats	70,71,72,73
	dogs	71,145
<i>C. gattii</i>	cats	70,73,83, 146,147,148
	dogs	83,145
<i>C. species</i>	Cats	149
Disseminated cryptococcosis		
<i>C. neoformans var. neoformans</i>	dogs	74
<i>C. gattii</i>	cats	78
	dogs	76
<i>C. albidus</i>	cats	75
<i>C. magnus</i>		77
Cryptococcal meningitis		
<i>C. neoformans var. grubii</i>	cats	80
	dogs	80
<i>C. gattii</i>	cats	80
	dogs	80
<i>C. species</i>	cats	79, 150
Cryptococcal skin infection		
<i>C. species</i>	cats	82
Cryptococcal ophthalmitis		
<i>C. neoformans var. neoformans</i>	cats	81
<i>C. species</i>		79
Cryptococcal urinary tract infection		
<i>C. species</i>	cats	150.

3. Cryptococcosis in wild animals

In wild animals, cryptococcosis occurs in different animals and *Cryptococcus* spp. can affect the gastrointestinal and respiratory systems and eyes [Table 5]. The koala often have primary infection of the upper or lower respiratory tract as the first disease feature. Among captive wild animals, cryptococcosis has been documented in Marmoset monkey [88], Rhesus monkey [89], Squirrel monkey [90], Short-eared elephant shrews, Large tree shrews Lesser tree shrews [91], Common marmoset [92] Eastern gray squirrels [93], wild rabbit [94], *Bandicota indica* [95], Common Toad [96], Cheetah [97], Spinner dolphin [98], Harbor Porpoise [99],

Koala [100, 101, 102], Ferret [103], California sea lion [104], Gorilla gorilla [105].

Krockenberger et al. [106] mentioned that *Cryptococcus gattii* has been shown to have a strong association with eucalypts frequently used by koalas and, not surprisingly, it has been shown to colonize the nasal cavities of koalas. The progression from nasal colonization to tissue invasion is critical for understanding the pathogenesis of cryptococcosis in this species and provides a model for pathogenesis of cryptococcosis in other species. **Krockenberger et al. [107]** studied the relationship among *Cryptococcus gattii*, koala and the environment. The koala

was used as a natural biological sampler in an attempt to understand the dynamics of *Cryptococcus gattii* in Australian environments. Evidence of asymptomatic nasal and skin colonization for extended periods by large numbers of *Cryptococcus gattii* was obtained and geographical factors assessed. The key finding was the ability of koalas to amplify numbers of *Cryptococcus gattii* in certain environments. Koalas were not found to be obligatory for

the survival of the organism in all environments. Geographical factors alone could not explain differing rates of nasal and skin colonization in koalas in different environments. A strong association between healthy koalas and *Cryptococcus gattii* was confirmed and *Cryptococcus gattii* was isolated from novel sources, including the turpentine gum tree (*Syncarpia glomulifera*), tallowwood (*Eucalyptus microcorys*) and flooded gum (*E. grandis*).

Table 5. Cryptococcosis in wild animals

<i>Cryptococcus species</i>	Animals	References
<i>C. neoformans</i> var. <i>neoformans</i>	Koalas	102,151
	monkeys	89
	Shrews	91
	common toad	96
<i>C. neoformans</i> var. <i>grubii</i>	Ferrets	80,106
	bandicoot	95
	Gorilla	105
<i>C. gattii</i>	Cheetah	97,152,155
	Koalas	101,106,107,154
	Ferrets	80,103,106
	Dolphins	156,157
	Porpoises	99,158
<i>C. albidus</i>	Sea lion	104
<i>C. yokohamensis</i>	Koalas	100
<i>C. species</i>	Ferrets	103
	Monkeys	88,90
	Koalas	153
	Marmosets	92

4. Cryptococcosis in birds

Cryptococcus neoformans is known to inhabit natural environments such as soil and grows in bird excreta, especially that of pigeons [108, 109, 110]. Infections in birds are rare. *C. neoformans* has been isolated from the faeces of canaries (26%), carrier pigeons (18%), budgerigars (2%) and psittacine birds (1%), apart from domestic poultry [111, 112]. *Cryptococcus* species have been reported to be

associated with the trachea of fowls, isolated from broilers of a poultry-processing plant [113].

Cryptococcus laurentii was reported to be associated with feather loss in a glossy starling (*Lamprolaima chalybaeus*). The bird exhibited patchy feather loss, especially around the back and beak area, and greyish crusts sticking quite firmly

to the underlying skin. The feathers had a greasy appearance and disseminated a musty odour.

Malik et al. [114] analyzed clinical and laboratory findings in 15 unreported cases of avian cryptococcosis from Australia contrasted with 11 cases recorded in the literature. *Cryptococcus* species produced localized invasive disease of the upper respiratory tract of captive parrots living in Australia. This resulted in signs referable to mycotic rhinitis or to involvement of structures contiguous with the nasal cavity, such as the beak, sinuses, choana, retrobulbar space and palate. *Cryptococcus* appeared to behave as a primary pathogen of immunocompetent hosts. One tissue specimen was available from an Australian racing pigeon with minimally invasive subcutaneous disease; immunohistology demonstrated a *Cryptococcus* infection, presumably subsequent to traumatic inoculation of yeast cells into the subcutis.

Cryptococcus neoformans var. *grubii* was isolated from a tissue specimen from an Australian racing pigeon with

minimally invasive subcutaneous disease; and was demonstrated immunohistologically in the subcutis tissues [114].

Cryptococcus gattii produced localized invasive disease of the upper respiratory tract of captive parrots living in Australia. This resulted in signs referable to mycotic rhinitis or to involvement of structures contiguous with the nasal cavity, such as the beak, sinuses, choana, retrobulbar space and palate. *Cryptococcus* appeared to behave as a primary pathogen of immunocompetent hosts [114]. *Cryptococcus gattii* was reported in a 14-yr-old female Pesquet's parrot (*Psittichas fulgidus*) with lethargy and decreased ability to fly. Radiographs revealed an irregular osteolytic lesion isolated to the distal right humerus. Bone biopsy of the lesion, cytology, and histopathology were diagnostic for osteomyelitis with intralesional yeasts confirmed to be on fungal culture [115]. Most of the studies on *Cryptococcus* in avian species are concerned with bird droppings as seen in [Table 6].

Table 6: *Cryptococcus* species isolated from avian droppings

<i>Cryptococcus</i> species	References
<i>C. neoformans</i> var <i>neoformans</i>	6,7,8,11,110,159,160,161,162,163,164,165,166,167,168,169,170,171,172,173,174,175,176
<i>C. neoformans</i> var. <i>grubii</i>	177,178,179,180
<i>Cryptococcus gattii</i>	159,170,174
<i>Cryptococcus laurentii</i>	6,162,165,166,174,181
<i>Cryptococcus luteolus</i>	174
<i>Cryptococcus ater</i>	174
<i>Cryptococcus species</i>	182

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