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# Cryptococcosis and One Health Perspective

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**Abstract**

***Cryptococcosis is a life-threatening systemic fungal disease caused mainly by Cryptococcus neoformans and Cryptococcus gattii. Both species of Cryptococcus occur in the environment as saprobes. The infection is observed in humans and in many animal species and carries high morbidity and mortality. Cryptococcal meningitis is currently responsible for approximately 180,000 deaths every year. The source of infection is exogenous, and the respiratory tract is recognized as the principal portal of entry for the pathogen. Humans and animals may acquire the infection from saprobic reservoirs in which the fungus grows. The clinical spectrum of the disease includes cutaneous, pulmonary, and meningeal forms. Laboratory testing is required to establish an unequivocal diagnosis. The pathogen can be readily isolated from clinical and environmental sources on Pal's sunflower seed medium. Several antifungal drugs, including amphotericin B, fluconazole, and itraconazole, are used for treatment. Cryptococcosis represents a major public health challenge, particularly among immunocompromised populations, including individuals with HIV/AIDS, transplant recipients, and patients receiving immunosuppressive therapy. From a One Health perspective, cryptococcosis exemplifies the complex interconnection between environmental sources, animal health, and human disease.***

*Keywords:* ***Cryptococcosis; Cryptococcus neoformans; Cryptococcus gattii; Fungal zoonosis; Immunocompromised patient, One Health; Pal's sunflower seed medium.***

## 1. Introduction

Cryptococcosis is a globally prevalent and enigmatic mycotic disease caused by basidiomycetous encapsulated yeasts of the genus Cryptococcus, primarily C. neoformans and C. gattii [1-3]. The disease most commonly presents as pulmonary infection or meningoencephalitis but may disseminate to involve the skin, bones, and other organs [3,4]. Despite advances in antifungal therapy, cryptococcosis remains associated with high morbidity and mortality worldwide. The burden of disease is particularly high among immunocompromised individuals, especially those with HIV/AIDS. Cryptococcal meningitis is a leading cause of AIDS-related mortality, accounting for more than 180,000 deaths annually [5]. In addition, infections caused by C. gattii increasingly affect immunocompetent individuals, posing new diagnostic and therapeutic challenges [6].



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Cryptococcosis is acquired through inhalation of airborne fungal propagules from environmental sources rather than through direct human-to-human or animal-to-human transmission [7]. The involvement of environmental niches, animal hosts, and human disease highlights the importance of understanding cryptococcosis through the One Health framework, which integrates human, animal, and environmental health. This communication reviews the ecology, animal and human health impact, and public health importance of cryptococcosis, and emphasizes the need for a unified One Health approach to its surveillance, prevention, and control.

## 2. Environmental Reservoirs and Ecology

The natural ecology of Cryptococcus species plays a central role in disease transmission. Emmons, an American mycologist, was the first to establish the ecological association of C. neoformans with pigeon droppings, in 1955 [8]. This finding was later substantiated by researchers throughout the world [7,9-12]. Cryptococcus neoformans is commonly isolated from soil enriched with pigeon and other bird droppings, whereas C. gattii is associated with decaying wood and tree species such as eucalyptus [1,3,6,7]. The accumulation of bird droppings in urban areas increases the risk of exposure to C. neoformans [1].

The pioneering work on C. neoformans and cryptococcosis over the last five decades was conducted by the author [3]. Pal was the first to report the prevalence of C. neoformans in pigeon droppings in Nepal [10] and Djibouti [11]. Pigeon excreta are now well documented as the chief reservoir of C. neoformans [1]. Cryptococcus neoformans was also isolated for the first time from air-conditioner dust in India, by Pal [13].

Environmental factors such as temperature, humidity, urbanization, deforestation, and climate change significantly influence the survival, growth, and dispersal of Cryptococcus species [14]. Environmental surveillance and ecological studies are therefore critical components of cryptococcosis control within the One Health paradigm, and veterinary observations can provide valuable early-warning signals that reinforce the role of veterinarians in the One Health framework.

## 3. Animal Health and Sentinel Importance

Cryptococcal infection has been diagnosed in a wide variety of animals, including cattle, buffalo, goats, cats, dogs, horses, sheep, monkeys, pigs, and wildlife [1,3,4,15-17]. Among these, cats and dogs are the most commonly affected. The etiologic significance of C. neoformans in mastitis of the goat and buffalo was elucidated by Pal in 1975 and 1980, respectively [3,4,17,18]. Clinical manifestations in animals may involve the respiratory, neurological, ocular, or cutaneous systems (Fig. 1). In dairy animals, C. neoformans causes a severe form of mastitis that poses a considerable challenge to treatment (Fig. 2).

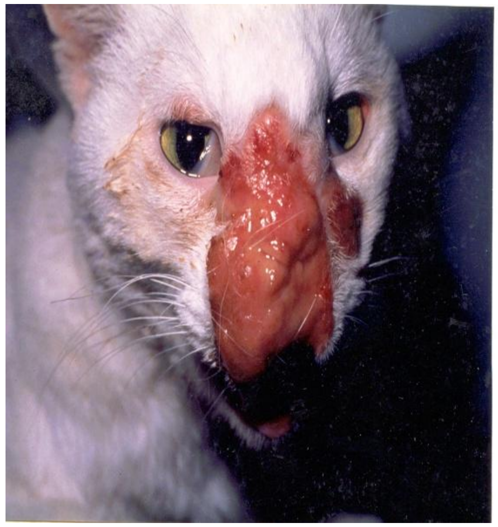

**Fig. 1.** A young female domestic cat showing a mucoid, chronic granulomatous mass on the nose due to *Cryptococcus neoformans*. The diagnosis was confirmed by direct microscopy of a skin-biopsy specimen in India ink, and by isolation of *Cryptococcus neoformans* on Pal's sunflower seed medium, in India.

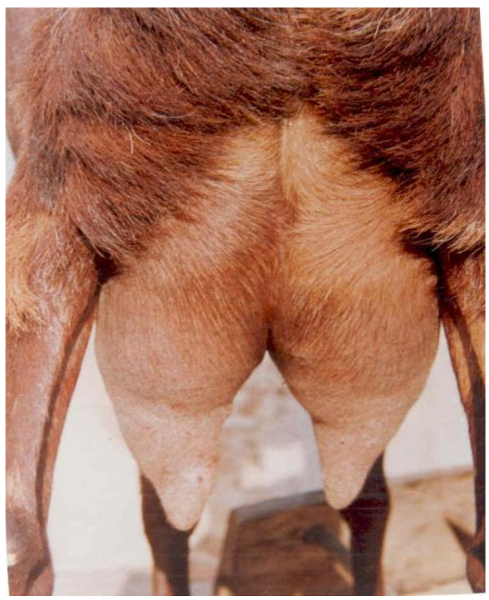

**Fig. 2.** A domestic goat with cryptococcal mastitis. *Cryptococcus neoformans* was isolated from the mastitic milk on Pal's sunflower seed medium.

It is important to note that animals are not considered a primary source of direct infection for humans, but they serve as sentinels of environmental exposure. In several instances, animal cases have preceded human infections, indicating increased environmental contamination [19]. Although cryptococcosis is not considered a classical zoonotic disease, the shared exposure of humans and animals to contaminated environments underscores the interdependence of animal and human health within the One Health framework [20].

## 4. Human Health Significance

In humans, cryptococcosis mostly affects individuals who are immunocompromised due to underlying conditions such as HIV/AIDS. Pigeon breeders, bird enthusiasts, pet-bird keepers, zoo attendants, and people involved in cleaning old monuments and historical buildings are considered more likely to acquire cryptococcal infection [1,3]. Cryptococcal meningitis is the most severe clinical manifestation of the disease and is often fatal if not diagnosed and treated promptly [1]. In this context, Dave and Pal [21] reported primary cutaneous cryptococcosis in a parrot handler who had sustained a minor hand injury while cleaning a wooden parrot cage; epidemiological investigation established the source of infection in the patient's immediate environment.

The symptoms of cryptococcosis are generally nonspecific, which leads to delayed diagnosis, especially in resource-limited settings. Although diagnostic methods such as cryptococcal antigen detection have improved case identification, access to these tools remains uneven across regions [2]. The emergence of C. gattii infections in apparently healthy individuals further complicates the clinical landscape and calls for heightened awareness among clinicians.

## 5. Environmental and Climatic Influences

Cryptococcus neoformans has been recovered from soil, parrot excreta, bat guano, munia bird droppings, pigeon feces, vegetables, fruits, air-conditioner dust, and empty wooden canary cages [1,3,4,9,12,13]. The related species C. gattii has been isolated from Eucalyptus trees [1]. Among avian species, pigeons in particular contribute significantly to the environmental dissemination of C. neoformans [1]. Interestingly, birds themselves rarely develop disease, likely because their higher body temperature inhibits growth of the pathogen [7]. Environmental factors including humidity, temperature, deforestation, urbanization, and climate change all influence the survival, growth, and dispersal of Cryptococcus species [14].

It is notable that C. neoformans can survive for more than two decades in old, dry pigeon excreta collected from sheltered sites not exposed to sunlight [3,16]. In our experience, environmental exposure in urban settings with heavy pigeon populations remains an important risk factor for C. neoformans infection. There is good evidence that both humans and animals can acquire the infection from the saprobic environment in which the fungus grows and multiplies [1,3,21].

Changing climatic conditions may further expand the ecological niche of Cryptococcus, potentially leading to new endemic regions [14]. Such environmental dynamics highlight the need to integrate ecological data into public health strategies.

## 6. Diagnosis

In the absence of characteristic clinical symptoms, the diagnosis of cryptococcosis relies on a combination of laboratory techniques, including direct microscopy of specimens (cerebrospinal fluid, sputum, bronchoalveolar lavage fluid, empyema fluid, and others) in India ink, cultural isolation, antigen detection, histopathological techniques, and molecular assays [1,3,16]. The cryptococcal antigen test is widely regarded as a reliable and rapid diagnostic tool.
The organism can be readily isolated from clinical specimens on Pal's sunflower seed medium, developed by Pal in 1980 [1]. The medium contains 45 g of pulverized sunflower seed, 20 g of agar, 100 mg of chloramphenicol, and 1000 mL of distilled water [22]. Both C. neoformans and C. gattii produce light-to-dark brown colonies on Pal's sunflower seed

medium (Fig. 3), which facilitates early identification of the pathogen; Candida species fail to produce brown pigment on this selective medium [3]. Pal's sunflower seed medium has also proved an effective tool for epidemiological investigations that helped establish the source of infection [21]. In addition, a modified version of the medium was used to study sexual reproduction in C. neoformans, revealing that the alpha mating type was more predominant among clinical and environmental isolates from Nepal, Belgium, India, and Japan [9,10,23,24]. Direct microscopy and isolation of the etiologic agent from clinical specimens remain the gold standard for diagnosis of this mycotic infection.

**Fig. 3.** Isolation of *Cryptococcus neoformans* from a clinical specimen of an immunocompromised patient on Pal's sunflower seed medium. *Cryptococcus neoformans* forms brown, smooth colonies on the medium, whereas *Candida tropicalis* grows as white colonies.

## 7. Treatment

Several antifungal agents, including amphotericin B, liposomal amphotericin B, flucytosine, ketoconazole, fluconazole, and itraconazole, are recommended for the management of cryptococcosis [1,3,16,17,21]. Primary cutaneous cryptococcosis in an immunocompetent parrot keeper was successfully treated with fluconazole by Dave and Pal [21]; the drug was well tolerated, and no adverse effects were reported by the patient. However, drug toxicity, cost, and limited availability continue to pose significant challenges, particularly in developing countries [5]. Treatment of immunocompromised patients is advised even in the absence of clinical signs, in order to prevent dissemination of infection. Because the prostate gland in male patients can serve as a reservoir for the fungus, a negative urine culture on Pal's sunflower seed medium is a useful indicator of effective treatment [1].

## 8. Prevention and Control

Persons working in pet-bird shops, historical buildings, zoological gardens, and old monuments are advised to use face masks to prevent inhalation of this highly infectious yeast [1,16]. Immunocompromised patients should avoid visiting avian habitats [1,16]. Pigeon droppings and avian habitats should be decontaminated with 5% formalin [1,16]. The public should be educated about the source of infection, mode of transmission, disease severity, and preventive measures against this potentially fatal mycozoonosis.

## 9. One Health Approach

Control of cryptococcosis requires a One Health approach involving coordinated efforts among physicians, veterinarians, microbiologists, and environmental scientists to develop effective surveillance and control strategies. Integration of animal health data with human epidemiological information can improve early detection and response, and environmental monitoring should be strengthened to identify high-risk areas. Policies aimed at improving urban sanitation and minimizing exposure to contaminated environments are equally important. Continued research is needed to better understand the ecology of Cryptococcus and its host-pathogen interactions. As cryptococcosis involves both humans and animals, the key role of veterinarians within the One Health programme should be recognized and supported.

## 10. Conclusion

Cryptococcosis remains a significant, yet often overlooked, mycotic disease with serious implications for human and animal health. Its strong association with environmental reservoirs makes it a classic example of a One Health issue. Implementation of a One Health approach, bringing together human, animal, and environmental health professionals, is strongly recommended for the control of this globally prevalent and potentially life-threatening mycosis. Early, accurate diagnosis and prompt treatment are advised to mitigate suffering and prevent complications, particularly among people with a compromised immune system. Further work on the ecology, epidemiology, diagnosis, chemotherapy, and vaccinology of cryptococcosis is warranted. Wider application of Pal's sunflower seed medium in public health and microbiology laboratories, for rapid diagnosis and epidemiological investigation of cryptococcosis, is suggested.

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## 12. Conflict of Authors

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