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Pigeon Droppings as a *Cryptococcus* Reservoir: A Review

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Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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Review Article

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ABSTRACT

Cryptococcus neoformans are an encapsulated yeast and causative agent of cryptococcosis in man and animals. *C. neoformans* has worldwide distribution and infects immunosuppressed individuals, especially those suffering from AIDS. *Cryptococcus neoformans* and *Cryptococcus gattii* are the two species of *Cryptococcus* that are typically linked to human illnesses. It has been identified for its association with bird guano accumulations, particularly pigeon excrement, and has been isolated from various natural sources. The major environmental sources of *Cryptococcus neoformans* are soil contaminated with pigeon droppings or eucalyptus trees and decaying woods forming hollows in living trees. Pigeon droppings are a suitable environment for the growth of fungi and bacteria. Pigeon guano is a common source for infection propagules of *Cryptococcus neoformans* and is postulated to play a central role in transmission from the environment to humans. Pigeon dropping consists of nitrogen, phosphorus, potassium as well as other minerals. These constituents provide

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an excellent sanctuary that supports the growth of various microorganisms. The review emphasizes that pigeon droppings are a significant reservoir and spread site for the *Cryptococcus neoformans* fungus.

Keywords: Cryptococcus neoformans; cryptococcosis; pigeon droppings; epidemiology; fungi; public health.

1. INTRODUCTION

Fungus is a eukaryotic, heterophilic, and adaptable living group that can infect humans and animals (Pal, 2007a). They include molds, yeasts, and dimorphic fungus. Approximately 600 of the five million common fungal species have been linked to several clinical conditions in both people and animals (Pal, 2019a). Numerous sources, including soil, avian excrement, air, water, sewage, bat guano, fruits, vegetables, woodlands, grains, etc., are known to contain fungi (Pal, 2007b; Pal, 2017a; Pal, 2019b). Both humans and animals, including birds, are susceptible to fungal diseases, which are a major source of illness and mortality. The environment is the primary source of fungal infections, which can affect anyone because fungi are natural saprobes (Pal, 2007c). Pigeons are found throughout the world, although they originated in Africa. They are very adaptive and can withstand a wide variety of environmental factors (Gouge *et al*., 2022). Birds and their droppings can cause over 60 diseases, a majority of which are airborne and can be spread to humans simply by being close to them (Grisin, 2017). Humans and animals may become infected after being exposed to airborne particles carrying spores from bird droppings (Nyakudi, 2011). Avian droppings are known to contain a variety of pathogenic and opportunistic microorganisms. Bird droppings have been identified as a possible environmental source of yeasts that are harmful to humans. Pigeon guano, which is abundant in public areas, could especially be a potential carrier in the spread of pathogenic yeasts - into the environment and subsequently humans (Chee & Lee, 2005).

Humans and animals get the infection from an environment in which fungus thrives abundantly (Pal, 2007a). *Cryptococcus* is an invasive fungus that causes cryptococcosis, a disease that affects people with weak immune systems, but is rare in healthy people. Two *cryptococcus* species are commonly associated with human infections: *Cryptococcus neoformans* and *Cryptococcus gattii* (Lin *et al.,* 2015). The risk of acquiring cryptococcal infection is higher for zookeepers, pet bird keepers, pigeon breeders, and those who clean ancient structures (Pal, 2006).

2. CRYPTOCOCCOSIS

Cryptococcosis is an emerging, life-threatening, hidden fungal saprozoonosis of global importance (Pal, 2014). It is an acute, subacute, and chronic mycosis caused by the genus *Cryptococcus,* which consists of 37 species, of which *Cryptococcus neoformans* and *Cryptococcus gattii* are implicated in most cases. Cryptococcosis is a cosmopolitan infectious disease of humans and animals caused by an encapsulated basidiomycetous yeast-like fungus called *Cryptococcus neoformans* (Pal, 1985). Worldwide, Cryptococcosis is a potentially fatal opportunistic fungal infection. Acquired Immuno Deficiency Syndrome (AIDS), Malignancy, sarcoidosis, Hodgkin's lymphoma, Diabetes mellitus, and Organ transplantation are the risk factors for cryptococcosis (Chayakulkeeree et al., 2006). A fungal infection known as cryptococcosis is brought on by the encapsulated, basidiomycetous yeast *Cryptococcus neoformans*, which is among found in environments all over the world. It includes infections brought on by *C. neoformans var. neoformans and C. neoformans var. gattii*, two different forms of the fungus, While *C. neoformans var. gattii* primarily affects immunocompetent hosts. *C. neoformans var. neofromans* is frequently linked to infections in immunocompromised patients (Chayakulkeeree et al.,2006).

The encapsulated yeast of the genus *Cryptococcus* is the cause of the systemic mycosis known as cryptococcosis. *Cryptococcus* has a wide range of distribution. It is typically found in the waste surrounding pigeon nests, decaying wood, and soil polluted with pigeon or chicken droppings. Although pigeons are not afflicted, *C. neoformans* grow to high concentrations in their faeces. *Cryptococcus neoformans* and *Cryptococcus gatii* are the two most prevalent species. The infection enters the body primarily through the lungs. Clinical signs and symptoms include systemic spread and

silent lung colonization. Meningoencephalitis is the primary clinical sign (Tristano, 2010; Negroni, 2012). Cryptococcosis is most likely caused by inhaling the fungus, which causes a major focus in the lungs. Following hematogenous diffusion from the lungs, the CNS and skin are the two most prevalent sites of infection (Chayakulkeeree *et a*l., 2006). Human cryptococcosis and *Cryptococcus* infection are typically caused by inhaling environmental yeasts or spores of *Cryptococcus neoformans* and *Cryptococcus gattii. Cryptococcus neoformans* is the only known pathogenic species among the cryptococcal species (Maziarz et al., 2016; May et al., 2016).

3. CRYPTOCOCCUS NEOFORMANS

Generally single-budding, *Cryptococcus neoformans* is a spherical, yeast-like organism that ranges in size from 4 to 20µ in tissues and cultures. It is not dimorphic. Its primary feature is a thick, mucinous capsule, which is a pattern specific to pathogenic fungi but isn't always present in all strains and is often only observed in a small number of organisms. On existing culture media, it grows quickly at 37°C and room temperature (Baker *et al*.,1971). One significant environmental source of *C. neoformans* is avian guano. This bacterium may also mate and create infectious spores in pigeon droppings, where it thrives. Other bird droppings or cloacal swabs have occasionally been found to include both *C. neoformans* and *C. gattii* (Spickler,Anna Rovid. 2013). Systemic cryptococcosis in immunocompromised patients is primarily caused by *Cryptococcus neoformans* sensu stricto (formerly known as *C. neoformans variant grubii*). It is closely linked to bird droppings, particularly those of pigeons (Hagen *et a*l., 2015).

C. neoformans typically find its environmental reservoir in bird droppings, especially those of pigeons. But it has also been discovered in decomposing trees, wood and plant matter, soil, and waterways all of which are typically contaminated with bird droppings (Refai *et al*.,1983; Abo E l -Yazeed *et al*., 2006; Abou-EImagd *et al*., 2011; Saleh *et al*., 2011; El-Hariri *et al*., 2015). *Cryptococcus neoformans var. neoformans* is found globally and has been related to pigeons and other bird droppings, in addition to soils contaminated with these droppings (Speed & Dunt, 1995). F. Sanfelice identified *Cryptococcus* from peach juice samples for the first time in 1894(Sanfelice, 1894). *Cryptococcus neoformans* is primarily found in soil polluted by pigeon droppings, while *Cryptococcus gattii* is primarily found in eucalyptus trees and rotting tree hollows (Callejas et al., 1998; Chakrabarti *et al*., 1997; Lazera et al.,1998; Mahmoud, 1999). Two species, *C. neoformans* and *C. gattii* (Kwon-Chung, et al.,2002; Kwon-Chung, et al., 2006) with serotypes A, D, and AD for the former and B and C for the latter, comprise the species complex, according to the current taxonomy.

Two types of *Cryptococcus neoformans* are currently known to exist: Serotypes A (Franzot *et al*., 1999) and D are *C. neoformans variety grubii* and *C. neoformans variety neoformans*, respectively (Kwon-Chung *et al*., 2011). Based on capsular agglutination reactions, *C. neoformans* was first divided into four serotypes (A to D). The molecular study, however, has lately led to the classification of *C. gatti* (formerly known as *C. neoformans* serotypes B and C) as a separate species. Furthermore, two variants of *C. neoformans* have been identified: *C. neoformans var. grubii* (serotype A) and *C. neoformans var. neoformans* (serotype D). *C. neoformans* VNI, VNII, VNIII, and VNIV are the major molecular types into which the two species have been separated. *Cryptococcus neoformans* can be divided into four serotypes according to their polysaccharide capsule; serotype A and D are designated as variety *neoformans,* and serotypes B and C are categorized as variety *gattii* (Meyer *et al*., 1999; Ellis *et a*l.,2000; Sorrel *et a*l.,1996).

Cryptococcus neoformans is primarily associated with nests and soil that contain avian droppings, particularly those of pigeons (Chee & Lee, 2005). It is an encapsulated, round-to-oval-shaped yeast that reproduces via budding. Its surrounding polysaccharide capsule, when grown in a lab, ranges in size from 1 to more than 30 µm (Kwon-Chung, *et al*., 1992). *Cryptococcus neoformans* has been isolated from a variety of natural sources and is most generally associated with pigeon (order Columbiformes) droppings, but less frequently with the droppings of other birds, such as the order Psittaciformes and Passeriformes (Caicedo *et al*., 2000; Filiu *et al*., 2002). The primary saprobic reservoir of *C. neoformans* is pigeon droppings. It is important to mention that *C. neoformans* can survive for roughly 20 years in dry, ancient pigeon droppings (Pal, 2007b). Pigeon droppings have been identified as a primary source of *Cryptococcus neoformans* and other diseases in various countries (Dickx et al., 2010; Liu et al., 2012; Rad, 2013).

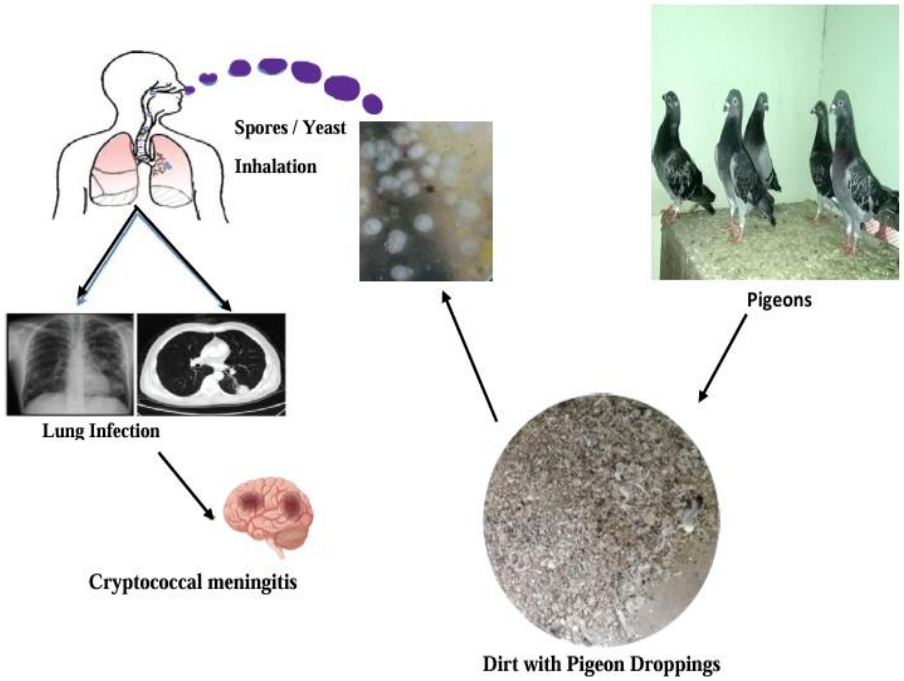

Fig. 1. Diagrammatic view of Pigeon droppings as a reservoir of *Cryptococcal* infection

4. PIGEON DROPPINGS

Pigeons are popular domestic birds and are often regarded as symbols of peace. Pigeon keeping is a primordial human interest. The Asian subcontinent has been known to be the pioneer of fancy pigeon farming from ancient times. Pigeons acclimatize quickly to a range of environments. Pigeons are common birds that may be found in almost every city and rural throughout the world. Pigeons live among humans as a source of food, hobby, and experimental purposes (Sari *et al*., 2008). Pigeons belong to the Columbidae family, which is distinguished by sturdy bodies, short necks, small heads, and thick, heavy plumage (Gifford, 1941). Approximately 800 domesticated pigeon breeds include messenger, flying/sporting, racing, fancy, and utility pigeons (https://en.wikipedia.org/wiki/List_of_pigeon_breeds).

Pigeons are the source of various diseases that are transmitted to humans, primarily through contact with dried bird droppings, feather dust, and mites (Kozdrun *et al*., 2015; Coudert *et al*., 2015). A recent rise in the number of pigeons has caused public health concerns. Pigeons spread harmful parasites, germs, fungi, and viruses that can harm both people and animals. Numerous literary works have examined how birds contribute to the spread of certain microorganisms. A lot of harmful germs, such as *Salmonella, Cryptococcus,* and *Chlamydia* species, may be found in pigeons (Haag-Wackernagel *et al*., 2004).

Pigeons have a rather high body temperature (approximately 40^0C), and yeasts cannot grow there. However, their dried excreta include low molecular weight nitrogenous compounds, that create favorable conditions for fungal growth (Naz, 2017). Certain microorganisms that have been isolated from pigeon droppings are known to be harmful to immunodeficient people, while infections from these organisms are also reported in immunodeficient individuals (Hamasha et al., 2004). Of all bird species, the pigeon has been most closely associated with *C. neoformans.* Some experimental work has documented that the alimentary tract of pigeons may be colonized by *C. neoformans* and that viable organisms are excreted in guano for many weeks (Littman *et al*., 1965 & 1968). Other findings suggest that pigeon droppings might enrich the soil and help the already-existing *C. neoformans* grow because guano probably contains a variety of chemical compounds, like

creatinine, that encourage this organism's growth (Denton *et al*., 1968).

Pigeon guano is a common source of infectious propagules of *C. neoformans* and is thought to serve a critical role in transmission from the environment to humans (Casadevall *et al*., 1998; Ensley *et al*., 1979; Sriburee *et al*., 2004; Swinne *et al*., 1989; Yamamoto *et al*., 1995). Pigeon droppings are becoming a significant environmental threat, as pigeon populations increase. Furthermore, pigeon excreta are a major public health problem because they are sources and carriers of opportunistic and pathogenic microorganisms such as fungi, bacteria, and viruses (Abulreesh *et al*., 2019; Santos *et a*l., 2020). Pigeon excrement is a significant problem for property owners and historical and archaeological buildings in various countries (Razani *et al*., 2018). Pigeon droppings contain nitrogen, phosphorous, potassium, and other minerals. The constituents produce an ideal environment that promotes the growth of numerous microorganisms (Nyakudi, 2011). Pigeon droppings are the primary saprobic reservoir of *C. neoformans*. It is vital to note that *C.neoformans* can survive for two decades in ancient and dry pigeon excreta that have been shielded from the ultraviolet rays of the sun (Pal, 2007c). 1g of dry pigeon droppings may contain 50 million viable cells of *C.neoformans* (Pal *et a*l., 2011). The uric acid in pigeon droppings also aids in the formation of a polysaccharide capsule, which resists phagocytosis and increases the pathogenicity of the organisms. This virulence factor has the potential to negatively impact a host's immune response during infection (Lee *et al*., 2011).

5. CONCLUSION

In conclusion, *Cryptococcus neoformans* is a pathogenic yeast commonly associated with environmental sources, particularly pigeon droppings. This microorganism thrives in the warm, moist environments created by bird feces, and it can pose a serious health risk to humans, especially those with weakened immune systems, such as individuals with HIV/AIDS. When people come into contact with contaminated pigeon droppings or inhale the fungal spores present in the droppings, they can become infected, leading to diseases like cryptococcosis. This infection primarily affects the lungs but can spread to the brain, causing meningitis in severe cases. As such, proper handling and cleanup of pigeon droppings, particularly in areas of high exposure, is crucial to prevent the transmission of *Cryptococcus neoformans* and protect public health. Further research and awareness about the risks associated with pigeon droppings and fungal infections are essential to minimize these threats.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declared that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of this manuscript.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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