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Popular Article

## Aspergillosis in Dogs: A review

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### Abstract

Aspergillosis in dogs is caused by *Aspergillus fumigatus* and *Aspergillus terreus*. It is an aerobic fungus that is thermotolerant. It is found everywhere in the environment. The infection could be in two forms, one manifestation being sinonasal aspergillosis (SNA), and the other being disseminated canine aspergillosis (DCA). SNA destroys the nasal bone or the sinuses, whereas the DCA causes granulomas in various visceral organs. Various clinical signs like epistaxis, crusty nose, and granulomatous tissue growth is observed. Various radiological methods and sinuscopy can lead to a better diagnosis. The disease can be confirmed after the isolation of the fungi from the affected tissue. Various antifungal topical as well as systemic chemotherapy can be used for its treatment. In this article, we will emphasize aspergillosis in dogs, its causes, spread, pathogenesis, treatment etc.

**Keywords:** Aspergillosis, Sino-nasal aspergillosis (SNA), Disseminated canine aspergillosis (DCA)

### Introduction

*Aspergillus* species are ubiquitous saprophytic, filamentous fungi. It is an aerobic fungus that forms distinct colonies with different colours depending on its species. They are mostly found in soil where they thrive, but they also carry the potential to be infectious in plants and animals. The infection caused is generally termed Aspergillosis. The disease may also be the result of an allergic reaction due to inhaled conidia. There are more than 180 species of *Aspergillus* officially recognized throughout the world (Ward *et al.*, 2005). *Aspergillus fumigatus* is the most predominant species majorly causing tissue invasion, but the infection may also be caused by *Aspergillus niger*, *Aspergillus flavus*, *Aspergillus terreus*, *Aspergillus deflexus*, *Aspergillus nidulans* and *Aspergillus flavipes*. This

fungus grows on standard laboratory media like Sabouraud dextrose agar. Since there are many species of aspergillus, they could be differentiated based on the colour of the colonies formed. *Aspergillus fumigatus* will show a velvety bluish-green colony which will become stale grey with time. *Aspergillus terreus* show brown colonies whereas *Aspergillus niger* shows black colonies due to its large black sporing head. Aspergillosis is relatively uncommon in animals irrespective of various immunosuppressive reasons of viral diseases or chemotherapeutics. It causes canine sinonasal aspergillosis, equine guttural pouch mycosis, bovine mycotic abortion, etc (Seyedmousavi *et al.*, 2015).

The infection caused by aspergillus species of fungi in dogs is known as canine aspergillosis. They are characterized by sinonasal invasion of saprophytic fungi in the nasal passage. They may cause profuse mucoid to haemorrhagic chronic nasal discharge that may alternate with periods of epistaxis, ulceration of the external nares with crusting, and pain or discomfort in the facial region. The most common causative agent of sinonasal aspergillosis is *Aspergillus fumigatus* and *Aspergillus terreus*. This infection does not invade beneath the mucosal epithelium, but the commencement of a chronic inflammatory response destroys the nasal bone (Tell L. A., 2005).

### Genus *Aspergillus*

*Aspergillus* is the most widespread species of fungi worldwide. It is found in soil, trees, plants, dead organisms, etc. The asexual state is the dominant phase and is produced from the young somatic hyphae. It is mostly an opportunistic pathogenic fungus. *Aspergillus spp* secrete various enzymes that have the ability to degrade polymers for its nutritional requirement. One of them is amylases that degrade starch, others being pectinases and xylanases that can degrade pectin in plants and xylan respectively. The hyphae are septate and hyaline in nature and may be up to 8 µm in diameter. The conidiophores are unbranched and develop at right angles from a specialized type of hyphal cell known as foot cells. The tip of the conidiophores is modified enilconazole and gets enlarged which forms a vesicle that is partially or completely covered by flask-shaped phialides (Krijgsheld *et al.*, 2013). In order to stain *Aspergillus*, we can use Lactophenol blue staining method, or else we can also use Calcofluor mixed with 10% - 20% potassium hydroxide that will bind to the cell wall of the fungi thus enhancing its visibility under the microscope (Mehrotra and Aneja, 1990).

### Growth requirements

*Aspergillus* grows over a wide range of temperatures ranging from 6°C to 55°C, whereas they require relatively low humidity. Culture media generally used for growing aspergillus is Sabouraud dextrose agar, it is a general laboratory media for fungal growth that contains dextrose. This media can be supplemented with chloramphenicol which will help in reducing bacterial growth. Other media



like Malt extract agar and Potato dextrose agar are also recommended due to their rich nutritional content. In environmental sampling of xerophilic fungi like aspergillus, Dichloran glycerol agar is also used (Viegas *et al.*, 2021).

### **Transmission**

Aspergillus species are widespread in the environment and can be found on grains, compost, decaying carcasses or even vegetation, soil, streams etc. Due to their ubiquitous nature, they cause the most common mould infection in immune-compromised hosts. Airborne transmission is most seen but oral and sexual transmission is also recorded.

### **Pathogenesis**

In dogs, aspergillus causes Sino nasal aspergillosis (SNA) and systemic aspergillosis. Infection mostly occurs by inhalation of aspergillosis conidia. These conidia after inhalation get trapped in respiratory mucosa and interact with defensive molecules which are released from mucosal epithelial cells which are then phagocytosed by neutrophils and alveolar macrophages. Ligand-receptor interactions are responsible for the recognition, attachment and overall phagocytosis by phagocytes. If such infection occurs in the case of a healthy animal or a non-immunosuppressed dog, then the conidia are killed by macrophages and neutrophils. In the case of an immunosuppressed dog, these conidia germinate in the mucosa and mucus of nasal cavities and sinuses. Proteases, gliotoxin, fumagillin, verruculogen, and helvolic acid are secreted by conidia which cause slow detachment of cilia of mucociliary apparatus, which leads to loss of epithelial cells and thus exposed basement membrane which gets damaged subsequently as conidia germinate into hyphae. In the dogs that are immunocompetent and have SNA, lack of invasiveness is seen but still leads to the destruction of nasal turbinates and erosion of frontal bone in extreme cases (M.J. Day, 2009).

Disseminated Canine Aspergillosis (DCA) is caused by *Aspergillus terreus* and is characterised by granuloma formation in multiple organs. Kidneys, spleen, bone marrow and lymph nodes are commonly affected. DCA leads to necrosis and gangrene as infarct develops from thrombi caused due to vessel invasion. When the marrow of long bones is affected, it causes focal osteomyelitis and the infection usually spreads to the adjacent joint capsule and surrounding tissue (Bruchim *et al.*, 2006).

### **Clinical signs**

There are no such clinical findings of aspergillosis as this infection is opportunistic. They invade an animal's body during an immune-compromised state. Therefore, their body condition scores also drop.

In sinonasal aspergillosis in dogs, the nose appears dry and crusty. There may be a growth of



granular tissue or fungus that may block the nares of the dogs causing difficulty in breathing. Epistaxis is also one of the most common findings in sinonasal aspergillosis. It is more found in dolichocephalic dog breeds than brachycephalic dog breeds. In the case of disseminated canine aspergillosis, fever is observed. The CBC is seen to be abnormal. The animals show lethargy and circling behaviour if the fungus has affected the neuroanatomical structures.

### Lesions

- **Macroscopic**

Extensive erosion of nasal epithelium with destruction of nasal turbinates is seen in SNA, and erosion of frontal bone through periorbital soft tissue is seen. Erosion of cribriform plate and brain is seen in severe cases. Destruction of bones is not caused by the fungus itself but by the inflammatory response of the host to fungal toxins produced. Depigmentation of nares in the case of chronic SNA is usually seen. In DCA infarcts in the spleen, liver, and kidneys are seen, which may lead to necrosis and gangrene. Coalescing granulomas are seen in lymph nodes which disturb the normal histoarchitecture of. Focal osteomyelitis at the condyloid surface of bones is seen along with fungal arthritis if infection reaches to the bone.

- **Microscopic**

Inflammatory exudate of SNA shows Plasma cells, Lymphocytes and Neutrophils but not in all cases. Mast cells and Eosinophils are seen rarely. In the DCA Spleen, the myocardium, Kidneys, and Pancreas show granulomas with distinct fungal hyphae.

### Diagnosis

Observation of clinical signs and characteristic lesions like depigmentation of nose and skin in the surrounding area accompanied with purulent discharge, and periodic epistaxis from the same Nare, these are also known as hallmarks of canine aspergillosis. Radiological examination of nasal passage like X-ray imaging is helpful in visualizing granulomatous growth in nostrils and even bone erosions. Imaging techniques such as CT scan (Computed tomography) and MRI (magnetic resonance imaging) can be used to visualize granulomas in soft tissues seen primarily in DCA (Schultz *et al.*, 2008 and Taylor *et al.*, 2015). Rhinoscopy is known as the gold standard procedure in the diagnosis of SNA, however sinuscopy, biopsy and histological examination can also be used (Tell L. A., 2005). Culturing and isolation of the fungus from the sample can be used for definitive diagnosis (McClenny, N. 2005; Elad and Segal, 2018).

### Treatment

- Enilconazole is an imidazole that was first described in 1969. It has been significantly used for the treatment of dermatophytes earlier. They act by reducing the biosynthesis of ergosterol in



the fungal cell wall. Though the drug is considered to be safe when administered orally but its poor solubility confines it to be used topically. When the dose was as high as 620 mg/kg, emesis was observed as an acute side effect. Whereas if the drug was administered 20 mg/kg orally for 2 years, sporadic emesis and profuse salivation during administration along with inappetence and lowered weight gain was noted. The activity of alkaline phosphatase was also significantly increased, though there were minimal changes in the histopathology of the liver (Sharp *et al.*, 1993).

- In dogs suffering from aspergillosis showing rhinitis or sinusitis, treatment with 2-5 mg/kg of fluconazole was also proven to be beneficial by clinical trials (Sharp *et al.*, 1991).
- Surgical treatment along with antifungal chemotherapy has also proven to be beneficial based on clinical trials. Standard rhinotomy with the removal of the flap, combined with antifungals, like the infusion of 2 per cent enilconazole and oral itraconazole has shown positive results in dogs with severe or recurrent aspergillosis (Claeys *et al.*, 2006).

### Control & Prevention

The most important prevention is critical care in the case of immunocompromised animals due to varied reasons. Certain viral infections, chemotherapy in neoplastic conditions, corticosterone therapy and extreme stress make dogs immunocompromised. Dogs who are undergoing chemotherapy or who have recently undergone cancer treatment would need extra care in terms of sanitation and feeding. Mouldy feed should always be avoided.

### Conclusion

Aspergillosis though not a very common disease in dogs, is a matter of concern in immunocompromised dogs. Immunocompromised dogs are more prone to aspergillosis. Critical care of such dogs can help prevent this fungal infection. Even after the infection has occurred it is completely curable with appropriate treatments with antifungals and surgery if required.

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