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## **Fungal Airway Diseases** ( 19-Mar-2002 )

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#### **Etiology and Pathogenesis**

Fungal airway disease is fortunately rare in horses but whenever it develops it is invariably significant. Fungal infections of any sort within the airways are almost unheard of in feral populations of wild horses and so they can rightly perhaps be termed a disease of domestication.

Fungal spores are almost an inevitable contaminant of the airway of horses. The challenge is increased by modern management practices that use preserved fodder as major source of nutrition at time when grazing is sparse or when the horses cannot easily or practicably be turned out.

Significant fungal infections are known to affect:

- the nasal cavity
- paranasal sinuses
- guttural pouches
- the lungs

Fungal infections within the nasal cavity, paranasal sinuses and guttural pouches have particular importance for their secondary effects that arise from tissue destruction.

Fungal-related lung disease can be the result of direct lung infection (fungal pneumonia/"Farmers Lung") but by far the most common implication of fungal spores is the disease known as Recurrent Airway Obstruction (Chronic Obstructive Small Airway Disease/Small Airway Disease/Equine COPD). In this case the affected animal is believed to show a hypersensitivity response to certain species of fungal spores; the fungus is acting as an allergen and not an infectious pathogen. This disease is not considered in this section. Focal fungal granuloma sometimes occur in the lung parenchyma and these may be single or multiple. The clinical consequences vary with location, numbers, severity and, of course, with the pulmonary demand of the individual horse.

The large majority of these infections are due to *Aspergillus* spp. Infections but opportunistic infection with *Mucor* spp., *Candida* spp. ... may rarely occur. Almost all recorded cases of pulmonary fungal infection are secondary to local or systemic immunocompromise. In the latter case severe immunocompromising disease such as the Severe Combined Immunodeficiency Syndrome of Arabian foals or the Fell Pony Immunocompromise Syndrome in young horses, or Cushing's Disease in older horses, may be accompanied by infection with *Coccidiomycosis immitis*, *Histoplasma capsulatum* and *H. farciminosium* or *Cryptococcus neoformans* [1]. In these cases the underlying disorder may be obscured by the overwhelming fungal infection. Where these organisms are identified, the immune status of the patient must be carefully assessed because, although in theory at least, the infection may be treatable it is a great disappointment when there is a recurrence. This is the more likely because clearing/treating fungal infections of the airway is always difficult and can be prolonged.

*Aspergillus* spp. infections of the airway fall into three basic categories:

1. Destructive lesions of the nasal cavity, paranasal sinuses and guttural pouch

2. Proliferative lesions of the nasal cavity, paranasal sinuses and guttural pouches
3. Fibrosing alveolitis/pneumonia

The same etiological circumstances are present at all the sites- the consensus is that some mucosal damage needs to be present before fungal infection can develop but this is far from established. Indeed in some of the more serious nasal and sinus fungal infections such as rhinophycomycosis (*Pythium* spp.) or coccidiobolomycosis (*Coccidioides immitis*) primary infections have been suggested. *Aspergillus* spp. (or other fungal) infection of the upper airway will inevitably contaminate the lower airway and it is very surprising therefore to find that pulmonary fungal infection is extremely rare.

There is no evidence of direct transmission of respiratory fungal infection between horses and it is important to appreciate that fungal organisms can be identified in many normal horses, thus implying that pathological lesions are the result of opportunist infection at sites of mucosal damage.

### Occurrence

Clinical signs of fungal airway disease are most common in housed horses and more particularly those that have an immunocompromising disease [2] or other underlying primary lung pathology (including viral or bacterial infections) [3]. A few cases may develop following prolonged antibiotic treatments where it is presumed that the symbiotic and commensal bacteria are destroyed leaving "an open field" for the fungal proliferation. Focal fungal infections can develop in areas of damaged tissue and especially necrotic tissue and so pulmonary abscesses can be the primary source. The pathogenesis of nasal cavity, paranasal sinus and guttural pouch mycoses is very uncertain. The distribution of the lesions within the nasal cavities suggest that the lesions develop spontaneously - there is no defined locus that is more often affected than others. The same cannot be said for the guttural pouch in which the lesions occur more commonly over the dorsal region of the exposed section of the internal carotid artery. Another locus is the maxillary artery on the lateral wall. In some cases however the entire upper portion of the pouch can be severely affected. The lesions in the guttural pouch are usually destructive and so arterial perforations can occur. This is usually catastrophic unless the early hemorrhages can be detected and the condition treated surgically. Lesions that develop on the mucosa of the upper hemisphere of the guttural pouch can also cause destruction or damage of the nerves. Nevertheless, healthy horses may succumb to the infections given a suitable challenge. For the most part, fungal infections are therefore best regarded as opportunistic and these are usually *Aspergillus*, *Candida* and *Mucor*. spp.

### Clinical Features

**a) Fungal Infection of the Nasal Cavity and Paranasal Sinuses** - This is a relatively common event in stabled horses in Europe and USA. The specific type of lesion varies with the various etiological agents. Thus *Aspergillus* spp. infection is usually highly destructive and is only rarely proliferative (Fig. 1) while *Coccidioides* spp. cause chronic, focal lesions that may persist for long periods without dramatic changes (Fig. 2). The progression of the condition also varies with the species and location.



Figure 1. A destructive conchal lesion as a result of *Aspergillus fumigatus* infection. - To view this image in full size go to the IVIS website at [www.ivis.org](http://www.ivis.org) . -



Figure 2. Fungal rhinitis with focal destructive lesions due to *Conidiobolus coronata*. - To view this image in full size go to the IVIS website at [www.ivis.org](http://www.ivis.org) . -

Early infections are usually asymptomatic. An astute owner may notice a vague "musty" odour on the breath and a slight serous nasal discharge may be detected.

Usually there is a long standing honey coloured nasal discharge with most of the fungal infections of the nasal cavity or paranasal sinuses and in some more advanced cases the characteristic musty smell is replaced by a distinctive fetid odour of bone necrosis. In the development stages, but more prominently in the later stages of development the discharge can have flecks of blood and occasionally small pieces of bone (the result of conchal destruction) may be identified in the discharges.

Note: Suspect cases of nasal or respiratory tract aspergillosis in particular should be treated with considerable caution because of the possibility of zoonotic infections. In particular it may be unwise to repeatedly inhale the breath of a suspect case. Usually diagnosis will be established simply by nasal and sinus endoscopy. Some of the conditions are serious threats to human health and so in areas where these occur veterinarians should be extra circumspect and should warn owners of the possibility of human infection.

**b) Guttural Pouch Mycosis** - Guttural pouch mycosis is possibly the most common and certainly the most dramatic fungal infection of the respiratory tract of horses. The clinical features vary according to the location and extent of the fungal growth. The large majority affect the roof of the pouch and at this site can cause damage to the internal carotid artery (resulting in mild or later to catastrophic bleeding), or the common trunk of cranial nerves IX, X and XII (Fig. 3). The latter results in neurological compromise in laryngeal and pharyngeal function; dysphagia and or laryngeal and pharyngeal paralysis are common signs in this case. In addition the post ganglionic sympathetic trunk runs in the same region and affected horses can have obvious Horner's Syndrome (mild ptosis and facial sweating). Deeper penetration of the mucosa of the pouch in the dorsal regions can cause damage to the other cranial nerves in the vicinity - most notably the Facial nerve (XII) and the Trigeminal nerve (V). The former results in facial paralysis (usually involving the ipsilateral ear and upper eyelid as well as the muzzle) while the latter results in loss of cutaneous sensation over the head.



Figure 3. Guttural pouch mycosis affecting a very small locus (arrow) over the root of CNIX, X and XII. The horse was markedly dysphagic with left sided pharyngeal and laryngeal paralysis. - To view this image in full size go to the IVIS website at [www.ivis.org](http://www.ivis.org) . -

Vascular damage to the internal carotid artery causes a dramatic and well-recognised extreme epistaxis (Fig. 4 and Fig. 5). However, the history of the horse will usually confirm that the characteristic honey coloured nasal discharge (sometimes with a few flecks of blood) has been present. Quite often also there are one or two more obvious episodes of bleeding although these are often dark in colour and markedly postural. It is likely that this arises because there is a mild bleed that accumulates in the pouch prior to the catastrophic disruption of either the internal carotid or the external maxillary artery.



Figure 4. A large destructive *Aspergillus* lesion over the internal carotid artery causing the bleed seen in the adjacent photograph. - To view this image in full size go to the IVIS website at [www.ivis.org](http://www.ivis.org) . -



Figure 5. Severe epistaxis derived from a carotid rupture in the left guttural pouch. Severe bleeding can be seen to issue from the ostium. - To view this image in full size go to the IVIS website at [www.ivis.org](http://www.ivis.org) . -

**c) Pulmonary Fungal Infection** - The signs are usually vague and by no means pathognomonic. General signs of malaise and depression may be all that is seen. Auscultation may reveal areas of lung consolidation but coughing is not a prominent feature. Some cases do cough and show hemoptysis. In most cases however, general signs of pulmonary disease are obvious; a high resting respiratory rate with harsh sounds on auscultation (suggestive of high speed turbulent air flow) and a very poor exercise tolerance.

### Diagnosis

The diagnosis of upper airway fungal infection is usually relatively straightforward but diagnosis of lower airway fungal infection can be much more difficult.

Endoscopy and endoscopic biopsy (with or without fungal culture) and culture form the mainstays of diagnosis of upper airway fungal infections (Fig. 6). Endoscopic examination must include detailed examination of the upper airway (a reasonable proportion have fungal infection elsewhere).

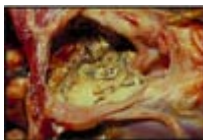


Figure 6. *Post mortem* picture of a fungal plaque on the roof of the guttural pouch. - To view this image in full size go to the IVIS website at [www.ivis.org](http://www.ivis.org) . -

Sinuscopy may be needed if the infection is within the sinuses because there are difficult (but not impossible) to access *per nasum* with an endoscope.

Lower airway fungal infection is often much more difficult to diagnose because of the lack of specificity for the methods used. Even identification of fungal elements in the trachea may not indicate pathological pulmonary infection. A non-specific accumulation of muco-pus in the trachea is frequently present. This can sometimes have a brown, mucinous appearance. The color may be due to changes in blood that is shed into the airway during coughing. The presence of significant amounts of blood may be associated with the destructive forms of *Aspergillus* in particular and it is important to differentiate blood that originates from the upper airway from that derived from pulmonary damage (either fungal or otherwise). The results of tracheal and lung washes may be grossly misleading because relatively high proportion of normal animals have fungal species within the airway (as commensals or opportunistic pathogens).

Radiographic features are also not pathognomonic. Frequently there is radiographic evidence of focal or generalised pulmonary solidification but again the changes may be subtle and the difficulties of interpretation of pulmonary radiographs add difficulty. While large areas of consolidation may be detected usually the lesions have a more milliary nature and a presumptive radiographic diagnosis of patchy bronchopneumonia is usually made. Where extensive fungal granuloma occur in the lung tissue radiography can be helpful (Fig. 7). However, the radiographic appearance of diffuse fungal pulmonary infection can simply show a diffuse radiodensity with a prominent alveolar or fibrosing pattern, focal lesions may be mistaken for neoplastic disease (usually multiple secondary metastatic tumours).



Figure 7. Fungal granulomata in the lungs of a 9 year old gelding presented with severe progressive dyspnea and a hemorrhagic nasal discharge. *Aspergillus fumigatus* was cultured from both tracheal aspirates and from the lesions *post mortem*. - To view this image in full size go to the IVIS website at [www.ivis.org](http://www.ivis.org) . -

A diagnosis of fungal pulmonary disease is only achieved by combined diagnostic investigations.

Biochemical estimations and hematology may be helpful in confirming the chronic nature of the disorder but is seldom indicative of fungal infection specifically.

Lung biopsy also may be misleading because a negative biopsy may be obtained because the lesions tend to be small and focal and may easily be missed by the biopsy instrument. The accuracy can be improved significantly by the use of ultrasound-guided biopsy.

Laboratory examinations (direct and cultural) will usually establish the nature of the infection. There remains the caveat, however, that many cases have some fungal elements in the airway normally.

There are no serological tests that provide any definitive diagnostic information.

The diagnosis is frequently only reached on post mortem examination [4].

### **Treatment**

Management of the underlying pathology in cases in which the fungal infection is secondary, has to take some priority. The high incidence of critical underlying primary disease means that treatment of the fungal infection is seldom undertaken except where the lesions can be managed by direct application of an antifungal drug. Thus the treatment is effectively limited to superficial nasal, paranasal sinus and guttural pouch infections.

Treatment of fungal infection is invariably difficult. Treatment with antifungal agents including amphotericin B, konazoles

and iodides form the basis of management. In some cases such as nasal fungal infection surgical debridement can be helpful in reducing the bulk of the damaged and removing the greater part of the fungal infection. However, the surgical option is not likely to be effective on its own in most cases and in any case it is often impossible for anatomical reasons to remove the total affected region.

There are some aspects of the treatment of guttural pouch mycosis that are particularly interesting. Several research clinicians have suggested that ligation/occlusion of the carotid (or maxillary artery where this is the affected locus) results in a dramatic "die-back" of the fungal growth. This implies that there is some local requirement for arterial contact. However, it is hard to understand why this should also result in control of fungal plaques over the other areas of the guttural pouch. The main problem with topical treatment of fungal infections of the pouch are that the lesions are usually (if not invariably) situated on the roof of the pouch and irrigation with antifungal solutions is largely a waste of effort. Dry powder of nystatin or enilconazole can be insufflated into the pouch very easily. This can be done in the standing horse without any need for concurrent endoscopy. It is important however to remember that the lesions may be in a severe danger of disruption and extreme fatal bleeding. Therefore surgical occlusion of the relevant vessels should always be performed prior to instigating topical insufflation therapy.

Pulmonary aspergillosis is probably best regarded as untreatable in the horse although in theory at least Amphotericin B may be effective. The residual pathology however, and the poor therapeutic efficacy of the drug coupled with its extreme cost make this an unrealistic option in most cases. The prognosis in any case is poor at best.

Probably the most practical therapy is daily oral administration (in feed) of potassium iodide (usually a dose of 10 - 15 g per day for a 450 kg horse and 5 - 10 g/day for a pony). The treatment is usually continued for 30 - 60 day, stopping only when signs of iodism are seen (these include lacrimation, a silt productive cough and a dry scurfy coat with some hair loss). It is very important to remember that this medication is contraindicated in pregnant mares and in very young foals. Intravenous doses of sodium iodide can be used but are logistically more difficult and have no obvious clinical advantage.

The konazoles have a poor reputation in the treatment of fungal pneumonia but can be tried. Treatment with Amphotericin B is difficult. A dose of 0.3 mg/kg is administered intravenously on day 1 and on each subsequent day the dose is increased by 0.1 mg/kg. Every fourth day no treatment is given and the treatment is continued for at least 21 - 35 days [5]. The drug is very nephrotoxic and so renal function must be monitored and the drug withdrawn if renal dysfunction is detected.

Prevention has to be the best approach because of the extreme difficulty of treatment and because the disease has a very poor prognosis. Avoidance of any contact with fungal spores is unrealistic but horses with upper airway Aspergillosis and those with immunocompromising disease should be managed with the direct intention of preventing pulmonary contamination with large numbers of spores. Horses that are being medicated with steroids are at considerable risk and where this is combined with antibiotics the risk is correspondingly higher. Good quality forage (free of fungal/mouldy growths) fed off the floor, and good air hygiene programmes are the basic requirements of prevention.

## References

1. Peardson EG, Watrous BJ, Schmitz JA, et al. Cryptococcal pneumonia in a horse. *J Am Vet Med Assoc* 1990; 196:106-107.
2. Blue J, Perdrizet J, Brown E. Pulmonary aspergillosis in a horse with myelomonocytic leukemia. *J Am Vet Med Assoc* 1987;190:1562-1564.
3. Beech J, Sweeney CR. Infections caused by bacteria, mycoplasmas, parasites, and fungi. In: Beech J, ed. *Equine Respiratory Disorders*. Philadelphia: Lea & Febiger, USA, 1991; 181-207.
4. Sweeney CR. Fungal diseases of the lower airway. In: Robinson NE, ed. *Current Therapy in Equine Medicine*. 4th ed. Philadelphia: WB Saunders Co, 1997; 439-440.
5. Ruoff WW. Fungal pneumonia in horses. In: *Proceedings of the American Association of Equine Practitioners*, 1964; 423.

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