Pulmonary and Systemic Fungal Infections*

Allison J. Stewart, BVSc(hons), MS, DACVIM
Elizabeth G. Welles, DVM, PhD, DACVP
Tricia Salazar, MS, DVM
Auburn University

ABSTRACT: Pulmonary or systemic fungal infections in horses are associated with a high mortality rate. The diagnosis can be difficult; the clinical signs depend on the extent of organ dysfunction. For pulmonary infections, thoracic radiography and collection of fluid samples by tracheal wash or bronchoalveolar lavage are useful. Biopsy samples may be obtained percutaneously or during laparoscopy/thoracoscopy or laparotomy/thoracotomy. Cytologic or histologic examination of lesions may identify characteristic morphologic features of fungal organisms. The etiologic agent can be definitively identified by microbiologic culture, immunohistochemistry, or polymerase chain reaction. Serologic titers can provide a noninvasive presumptive diagnosis for many conditions. Candidemia has been diagnosed by blood and urine cultures. Assessment of immune function is warranted to identify possible immunodeficiencies before long-term treatment. Although mortality rates are high, there have been some recent successful outcomes after treatment with amphotericin B, itraconazole, or fluconazole.

Systemic fungal infections can have an insidious progression, often presenting with nonspecific clinical signs. A thorough clinical evaluation is usually required to confirm the diagnosis. Historically, fungal disease has been associated with a poor prognosis in horses and other species. However, with earlier diagnosis and the increasing availability of affordable antifungals with known pharmacokinetic profiles, guarded prognoses and successful outcomes are likely to be more common in horses with fungal infections.

Fungi
There are more than 70,000 species of fungi, but only 50 species have been identified as causes of disease in people or animals. Fungi are eukaryotic organisms with a definitive cell wall made up of chitins, glucans, and mannans. Within the cell wall, the plasma membrane contains ergosterol—a cell membrane sterol that is frequently targeted by antifungal agents.

Clinical Signs and Gross Lesions
Patients with pulmonary fungal infections that cause pulmonary granulomas, diffuse pneumonia, or pleuropneumonia can present with signs similar to those of bacterial infection. Signs may include coughing, nasal discharge,
tachypnea, respiratory distress, and, if the condition is chronic, weight loss. Fungal pneumonia sometimes affects horses that are immunocompromised or neutropenic or that have enteritis/colitis, bacterial pneumonia, or neoplasia. Systemic infections can have variable clinical signs depending on the location and extent of the infection. Fungal infections can affect multiple organ systems and body cavities. Weight loss, colic, and diarrhea often occur with infection within the abdominal cavity. Immunodeficiency, either congenital or acquired, or glucocorticoid therapy may predispose a horse to fungal infection.

**DIAGNOSTIC DIFFERENTIALS**

Diagnostic differentials for a pulmonary or thoracic mass include bacterial abscess, neoplastic mass, and granulomatous mass. The radiographic appearance of fungal pneumonia can be variable, although a miliary or diffuse alveolar pattern is frequently observed. Differentials include bacterial pneumonia, recurrent airway obstructive disease, silicosis, granulomatous disease complex, and neoplasia.

**DIAGNOSIS**

**Diagnostic Samples**

Masses in the mediastinum or lungs may be observed radiographically. Ultrasonographic imaging may detect pleural or peritoneal fluid that can be aspirated or parenchymal abnormalities, from which biopsy samples can be obtained percutaneously. Fungal pneumonia may be diagnosed from samples obtained from tracheal wash or bronchoalveolar lavage fluid or from a lung biopsy (Figure 1). Lung biopsy is associated with significant risk...
because a pulmonary vessel may accidentally be dissected. The biopsy should be performed with ultrasound guidance and obtained from the periphery of the lung. (Some horses have experienced fatal hemorrhage associated with biopsy of a vessel only 2 cm from the periphery.) The lungs are rich in plasminogen, so bleeding complications may be severe. Spring-loaded biopsy needles are suitable for lung biopsy. Cytologic or biopsy samples from other organs may be obtained during exploratory laparoscopy, thoracoscopy, laparotomy, or thoracotomy.

**Cytology**

Fungal hyphae may be identified in airway, peritoneal, or pleural fluid or in impression smears obtained from biopsy samples of masses. Some fungi can be found in tracheal aspirates from healthy horses (Figure 2). Barn fungi such as *Alternaria* spp are nonpathogenic and rarely incite an inflammatory response in the host. The organisms often have a block-like appearance and may be colored. A normal predominance of macrophages and lymphocytes as well as less than 10% nondegenerate neutrophils would be expected. With fungal pneumonia, the aspirate may contain intracellular fungal hyphae and predominately neutrophils that are often degenerate. If processing of the sample is delayed, extracellular fungi may be phagocytized, which confuses the interpretation. Some fungi have characteristic morphologic features that can lead to an early presumptive identification.

**Histopathology**

Hyphae of certain fungi may be poorly visualized using routine hematoxylin–eosin stain; therefore, special stains (e.g., periodic acid–Schiff, Gridley’s fungus, Grocott–Gomori methenamine–silver nitrate) can be useful in identifying histopathologic specimens. With chronic infection, there is often evidence of extensive fibrosis.

**Microbiologic Culture**

Some fungi that have fastidious growth requirements may be overgrown by contaminant bacteria and may take up to several weeks to grow on culture media. To transport tissue for microbiologic culture, the sample should be placed in a prepared culture media and transported at room temperature. Specific culture media such as Sabouraud’s dextrose agar, inhibitory mold agar, or mycobiotic agar containing cycloheximide and chloramphenicol are useful.
Molecular Techniques

Serologic tests that use immunodiffusion,\(^1\) radioimmunoassays, complement fixation, or ELISAs\(^2\) are available to detect circulating antibodies against several fungal organisms (\textit{Cryptococcus neoformans},\(^3\)\(^–\)\(^5\) \textit{Coccidioides immitis},\(^6\)\(^–\)\(^7\) \textit{Blastomyces dermatitidis},\(^8\) \textit{Aspergillus} spp,\(^9\) \textit{Histoplasma capsulatum}). These tests can also help monitor response to treatment. Titters often decrease with resolution of disease. Immunohistochemistry,\(^10\)\(^–\)\(^13\) fluorescent in situ hybridization,\(^12\) and DNA probes\(^8\) can be used to diagnose fungal organisms in histopathology sections.

IMMUNE-FUNCTION TESTING

Several fungal infections have been associated with host immune suppression caused by severe malnutrition, congenital immunodeficiency, or acquired immunodeficiency.\(^14\)\(^–\)\(^16\) Blood can be tested for immunoglobulin quantification by radial immunodiffusion and lymphocyte subpopulation phenotyping via flow cytometry.\(^16\)\(^,\)^{17}

ANTIFUNGAL THERAPEUTICS

Antifungals used in horses have been reviewed.\(^18\) Amphotericin B is one of the most efficacious antifungals, but its use is limited because of the risk of nephrotoxicity. Benzimidazole derivatives from the azole class that can be administered systemically include ketoconazole, itraconazole, fluconazole, and voriconazole. They destroy fungi by inhibition of ergosterol biosynthesis in the fungal cell membrane (Table 1).
Cryptococcosis

Cryptococcosis is commonly caused by *C. neoformans* (var *neoformans*, var *grubii*, var *gattii*), a ubiquitous, saprophytic, round, basidiomycetous yeast-like fungus (5 to 10 µm) with a large heteropolysaccharide capsule (1 to 30 µm) that does not take up common cytologic stains (Figure 3). The capsule forms a clear halo when stained with India ink. The capsule is immunosuppressive and antiphagocytic. Capsular antigens that are secreted into the host’s body fluids bind opsonizing antibody before it reaches the organism. Equine cryptococcosis is relatively common in Western Australia, and there is an epidemiologic relationship between *C. neoformans* var *gattii* and the Australian river red gum tree (*Eucalyptus camaldulensis*) and between *C. neoformans* var *neoformans* and bird (particularly pigeon) excreta. Cytologic or histopathologic identification is very reliable for diagnosis because of the characteristic morphology. Serologic testing with latex agglutination to identify cryptococcal capsular antigen is useful (92% sensitivity and 98% specificity in small animals), and resolution of lesions is correlated with declining serum titers.

Cryptococcosis in horses is associated primarily with pneumonia, rhinitis, meningitis, and abortion. However, successful medical treatment has rarely been reported. Surgical removal of a localized jejunal lesion was successful in one horse. A pony with multiple pulmonary cryptococcomas, from which *Cryptococcus neoformans* var *gattii* was cultured from transtracheal washings and lung mass aspirate, was treated successfully with daily infusions of amphotericin B for 1 month. One year after ces-

### Table 1. Systemic Antifungals Used to Treat Horses

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>Successfully Treated Conditions in Horses</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amphotericin B</td>
<td>0.3 mg/kg in 1 L 5% dextrose, increasing every 3 days by 0.1 mg/kg until a dose of 0.9 mg/kg IV infusion is given for 30 days^a^</td>
<td>Histoplasmosis^29^ Pulmonary cryptococcosis^1^ Pulmonary aspergillosis^2^</td>
<td>Nephrotoxic: consider diuresis with intravenous fluids. Phlebitis: use a catheter.</td>
</tr>
<tr>
<td>Ketoconazole</td>
<td>30 mg/kg via nasogastric tube q12h mixed with 0.2 normal hydrochloric acid^40^</td>
<td>Scopulariopsis pneumonia^40^</td>
<td>Low oral bioavailability in the nonacidified form. ^39^</td>
</tr>
<tr>
<td>Itraconazole (Sporanox solution)</td>
<td>5 mg/kg PO q24h^27^</td>
<td>Coccioidoides immitis infection^37^</td>
<td>Compounding is not recommended.</td>
</tr>
<tr>
<td>Fluconazole</td>
<td>Loading dose of 14 mg/kg followed by 5 mg/kg q24h^38^</td>
<td><em>C. immitis</em> infection^14^ Candida bacteremia^42^</td>
<td>Minimal activity against filamentous fungi (<em>Aspergillus and Fusarium</em> spp.). Compounded fluconazole formulations are very stable.</td>
</tr>
<tr>
<td>Voriconazole</td>
<td>3 mg/kg PO q12h^21^ 4 mg/kg PO q24h^26^</td>
<td>—</td>
<td>Potent in vitro activity against <em>B. dermatitidis, C. immitis,</em> and <em>H. capsulatum.</em> Good activity against <em>Candida</em> and <em>Aspergillus</em> spp. One of the safest antifungals used in humans.</td>
</tr>
<tr>
<td>Enilconazole</td>
<td>1.2 mg/kg aerosolized q12h in 125 mL of saline (extrapolated dose)^40^</td>
<td>Part of the successful treatment of Scopulariopsis pneumonia^40^</td>
<td>Only available for poultry in the United States.</td>
</tr>
</tbody>
</table>

sation of treatment, clinical signs had resolved and the cryptococcal antigen titer decreased from 4096 to 256.4

**Aspergillosis**

Aspergillosis in horses has been reviewed.20,21 *Aspergillus* spp have broad (2 to 4 µm in diameter), septate hyphae with parallel sides and acute right-angled branching. They have a propensity for vascular invasion. A definitive diagnosis can be made by culture or staining by immunohistochemistry or immunofluorescence (*Fusarium* spp and *Pseudallescheria boydii* look similar on histologic examination).10,13 *Aspergillus* spp are very common in the environment, especially in moldy feed and bedding.2 They are opportunistic pathogens and often cause disease in horses that are immunosuppressed from debilitating conditions (e.g., enterocolitis, septicemia, neoplasia, Cushing’s disease, equine protozoal myeloencephalitis) or major surgery or that have been treated with immunosuppressive drugs10,20–23 (Figure 4).

Infection is by inhalation of an overwhelming number of spores or by translocation of organisms across an inflamed gastrointestinal tract. *Aspergillus* pneumonia is almost uniformly fatal, often with no or mild respiratory signs. The two forms of *Aspergillus* pneumonia probably reflect the two portals of entry, with fungal proliferation and invasion of the small airways occurring secondary to inhalation, and angioinvasive aspergillosis with lesions centered around large blood vessels likely due to hematogenous infection originating from the gastrin-
testinal tract. In two retrospective studies of invasive pulmonary aspergillosis, 41 of 49 cases were associated with enterocolitis.\textsuperscript{21,22}

Pulmonary aspergillosis is characterized grossly by multiple nodules throughout the lungs. On histologic examination, there is often necrosis and purulent inflammation. Necrosis is due to toxin and enzyme production as well as vascular obstruction. Fungal invasion of blood vessels is common and results in vasculitis, thrombosis, infarction, and necrosis. Chronic lesions are granulomatous, with macrophages, neutrophils, and multinucleated giant cells predominating.

Antemortem diagnosis of pulmonary aspergillosis is rare. In a retrospective study of 30 cases of \textit{Aspergillus} pneumonia, only two cases were diagnosed or suspected antemortem.\textsuperscript{21} Transtracheal aspirate or bronchoalveolar lavage may not be helpful because hyphae and spores are often present extracellularly or within macrophages in aspirate and lavage from healthy animals.\textsuperscript{22} False-negative results can also occur. Two days before euthanasia, cytologic examination of a transtracheal wash specimen obtained from the foal in Figure 4 failed to identify \textit{Aspergillus} hyphae. Serologic diagnosis has occasionally been useful\textsuperscript{9} but is often unreliable. Development of a commercial ELISA is promising.\textsuperscript{2,20}

Fifty percent to 90% of humans with invasive aspergillosis die despite treatment. For decades, amphotericin B has been the mainstay of treatment of invasive infection with \textit{Aspergillus} but is associated with nephrotoxicity in about 50% of patients. Nephrotoxicity is reduced using liposomal amphotericin B. Amphotericin B colloidal dispersion is not recommended because of the risk of infusional toxicities.\textsuperscript{24}

Voriconazole, a new azole antifungal, is now considered the drug of choice in treating human aspergillosis, while caspofungin (in the new class echinocandin antifungals) shows promising results in patients with refractory infections.\textsuperscript{24} The pharmacokinetics of voriconazole have recently been determined in horses, with excellent absorption after oral administration and high concentrations achieved in several body fluids.\textsuperscript{25,26} Voriconazole is still prohibitively expensive; therefore, oral itraconazole is currently preferred for treating aspergillosis in horses.\textsuperscript{27}

In humans, the use of itraconazole has shown response rates comparable to those associated with the use of amphotericin B.\textsuperscript{24} There is a limited number of reports of horses surviving pulmonary aspergillosis. One horse with \textit{Aspergillus} pneumonia survived with amphotericin B therapy (the dose and duration were not reported).\textsuperscript{2}

### Blastomycosis

Blastomycosis is caused by inhalation of conidia of the thermally dimorphic saprophytic fungus \textit{B. dermatitidis}. \textit{Blastomyces} yeasts can be identified on cytologic examination, often within multinucleated giant cells. They are spherical and 15 to 17 µm in diameter with basophilic protoplasm and unstained, uniformly shaped refractile walls. Unilateral, broad-based budding is characteristic.

Blastomycosis reportedly caused pulmonary abscessation, pyogranulomatous pneumonia, pleuritis, peritonitis, and abscesses in a 5-year-old horse.\textsuperscript{8} \textit{B. dermatitidis} was positively identified from transtracheal wash fluid by use of a DNA probe, and serology was strongly posi-
granulomas in a horse dying of chronic *Yersinia* colitis and in another horse with intestinal salmonellosis. It has also been associated with abortions and severe granulomatous pneumonia in neonatal foals and a yearling.

Successful treatment with amphotericin B was reported in a filly with pulmonary histoplasmosis diagnosed by cytologic identification of the organism from lung aspirate and a tracheal wash smear. The filly was treated with increasing doses of amphotericin B over a 4-week period. After every treatment, the filly became extremely lethargic for 18 to 24 hours. In the 4th week of therapy, there was transient polyuria and polydipsia; however, there was no azotemia or loss in urine-concentrating ability.

**Coccidioidomycosis**

Coccidioidomycosis is a systemic fungal infection caused by *C. immitis*—a soil saprophyte that grows in areas with sandy, alkaline soils and semiarid conditions. In the environment, *C. immitis* exists as a mycelium with thick-walled, barrel-shaped arthroconidia. Inhalation of airborne arthroconidia can result in infection. Inhaled arthroconidia can enlarge to form nonbudding spherules, which incite an inflammatory reaction in the lungs and lymph nodes. Affected horses can experience weight loss, fever, abdominal pain, and signs of respiratory disease. Localized, recurring nasal granulomas have also been reported. Diffuse infections with granulomas in the lungs, liver, kidneys, or spleen have a grave prognosis.

Przewalski’s horses may be more susceptible. *C. immitis* is difficult to culture, and spherules may not be observed histologically from antemortem lung biopsies. However, serology is very useful to diagnose infection, and decreasing titers are associated with clinical improvement. Serum antibodies are rarely detected in healthy horses. Antifungals that have been used successfully to treat infected dogs include ketoconazole, fluconazole, and itraconazole. A very low dose of unacidified ketoconazole (3 to 6 mg/kg/day PO) did not achieve serum concentrations above the minimal inhibitory concentration and was unsuccessful in treating several cases of coccidioidomycosis in horses. Itraconazole (2.6 mg/kg PO q12h) was effective in treating coccidioidomycotic vertebral osteomyelitis in a foal. Fluconazole administered at the recommended dosage for 5 to 6 months was successful in treating two geldings with pulmonary coccidioidomycosis. Oral therapy with acidified ketoconazole at recommended dosages or with itraconazole could be considered in future cases.

**Scopulariopsis**

In a 2-year-old quarter horse filly, *Scopulariopsis* pneumonia was diagnosed by culture of bronchoalveolar lavage fluid. The filly had extensive granulomatous lesions within the pulmonary parenchyma and pleural effusion visible on thoracic ultrasonography. The infec-

---

**Figure 5.** A photomicrograph of small intestinal submucosa infiltrated by activated macrophages, many of which contain multiple *Histoplasma* yeasts. These yeasts characteristically measure approximately 2 to 4 μm and appear with a basophilic center and clear halo. (Hematoxylin-eosin stain; bar = 30 μm; Courtesy of Arno Wünschmann, University of Minnesota)

**Figure 6.** Disseminated histoplasmosis was diagnosed in an 11-year-old quarter horse stallion that presented with severe weight loss. *Histoplasma* organisms were observed on the peripheral blood smear. Severe respiratory distress developed, and thoracic radiographs showed a coalescing alveolar pattern around the hilar region, with air-filled cavitory lesions in the caudodorsal lung fields. The disease progressed rapidly, and the stallion was euthanized. (Courtesy of Peggy Marsh, Texas A&M University)
tion resolved following multimodal therapy with ketoconazole for 9 days, which was discontinued because of expense and replaced with aerosolization of enilconazole for 23 days.40

**Adiaspiromycosis**
A horse was diagnosed by percutaneous lung biopsy with adiaspiromycosis miliary fungal pneumonia caused by the saprophytic soil mold *Emmonsia crescens*. No treatment was attempted, and the horse was euthanized.41

**Candidiasis**
Systemic candidiasis was diagnosed and successfully treated in four neonatal foals. Each foal had prior sepsis attributable to gram-negative bacteria that had been aggressively treated with numerous antibiotics and parenteral nutrition. *Candida albicans* was cultured from a transtracheal wash from one of the foals. Three of the foals had *Candida* glossitis, and one had panophthalmitis and fungal keratitis. Two of the foals were treated with intravenous amphotericin B for 8 days (total dose: 2.6 mg/kg) and 29 days (total dose: 10.3 mg/kg), respectively. Fluconazole (5.5 mg/kg PO q24 h for 6 weeks and 4 mg/kg PO q24 h for 28 days) was used to treat the other two foals.42 Superficial *Candida* infections of the mucous membranes (thrush)43 can occur in isolation or as part of a systemic infection, and further microbiologic culturing of the blood, tracheal wash fluid, urine, or joint fluid may be indicated to rule out systemic infection.42 *Candida* glossitis can be treated by rinsing the mouth with either potassium permanganate (0.025% q24 h) or nystatin (0.3 g in 10 mL of water q8 h).

Candidemia is the most frequent fungal infection in humans who undergo complex abdominal surgery, receive total parenteral nutrition, are neutropenic with malignancies, have been burned, or receive long-term corticosteroid therapy. *Candida* spp account for 8% to 10% of all blood culture isolates and rank fourth among the most frequently isolated pathogens in blood cultures from humans.24 The mortality rate of patients with candidemia is 40% to 75%.24 More than 60% of isolates are *C. albicans*.24 Fluconazole is generally considered the preferred drug in treating *Candida* infection, although *Candida krusei* is resistant to fluconazole. Itraconazole, amphotericin B, caspofungin, and voriconazole are alternative antifungals recommended in humans.24

**Pneumocystosis**
*Pneumocystis carinii* has been reclassified from a protozoan to a saprophytic fungus based on the DNA sequence of its 16S-like RNA subunit. Some researchers even consider it a plant because it lacks ergosterol, the major fungal sterol.44 *P. carinii* exists in two parasitic forms. The yeast form (trophozoite) is ameboid and 2 to 5 µm in diameter with filopodia that attach to the surface of type I pneumocytes. The sporangia (cystic form) are 4 to 6 µm in diameter and contain eight uninucleate spores (intracystic bodies). The yeast cell stains well with hematoxylin–eosin stain, while sporangia can be identi-
fied with Grocott–Gomori methenamine–silver nitrate and periodic acid–Schiff stains. *P. carinii* cannot be cultured, and diagnosis of *P. carinii* infection is based on the identification of characteristic morphologic features. A fluorescent in situ hybridization method with an oligonucleotide probe that targets the 18S ribosomal RNA has been developed to detect *P. carinii* in histologic sections. Immunohistochemistry can also be used.

*P. carinii* infection causes diffuse interstitial pneumonia, especially in immunocompromised patients such as Arabian foals with severe combined immunodeficiency. It has also been diagnosed in immunocompromised adult horses and in an immunocompetent foal. Three-quarters of humans with AIDS are infected with *P. carinii*, and people undergoing immunosuppressive therapy after organ transplantation are predisposed. *P. carinii* infection is best diagnosed by cytology using specimens obtained from bronchoalveolar lavage rather than tracheal wash. Trimethoprim–sulfamethoxazole (25 to 30 mg/kg PO q12h) is the treatment of choice. Dapsone (3 mg/kg/day PO for 2 months) was used to successfully treat a foal with *P. carinii* infection that developed *Salmonella* enterocolitis after treatment with trimethoprim–sulfamethoxazole.

**Pythiosis**

*Pythium insidiosum* is a fungus-like aquatic organism in the kingdom Stramenopila and phylum Oomycota that affects mammalian species living in tropical and subtropical climates. Pythiosis is generally associated with large, ulcerative, proliferative, pyogranulomatous lesions that affect cutaneous and subcutaneous tissues of the extremities, ventral abdomen, and face. However, infection can disseminate to the intestines, bones, arteries, lungs, liver, and spleen. *P. insidiosum* lesions are characterized by the presence of sparsely septate hyphae within eosinophilic granulomatous lesions. The hyphae resemble those of fungi in the class Zygomycetes (*Conidiobolus* and *Basidiobolus* spp), but *P. insidiosum* does not have ergosterol in its cell membrane and is, therefore, not a true fungus. This explains why most antifungals are generally ineffective at treating pythiosis. There is one report of successful treatment of periorbital pythiosis in a child by using a combination of terbinafine and itraconazole for 1 year, and there are anecdotal reports that this drug combination was successful in treating 20% to 25% of canine pythiosis cases.

In one case of pulmonary pythiosis in a 3-year-old...
mare, a pruritic, proliferative, ulcerated lesion consistent with *Pythium* spp was surgically excised from the metatarsal region 1 year previously. The horse presented again with a 3-month history of bilateral sanguineous nasal discharge and coughing during exercise. A large amount of pleural fluid was observed by radiography, and transtracheal wash cultures were positive for only β-hemolytic *Streptococcus* spp. At necropsy, multiple white to pale yellow masses that measured 1 to 20 cm in diameter were observed throughout the pulmonary parenchyma. Branching hyphae characteristic of *Pythium* spp were cultured from the sequestered tissue.

Three cases of subcutaneous pythiosis that disseminated to internal organs (the lungs, liver, and spleen) were described in Brazilian horses. The subcutaneous lesions had been treated with radical surgery or immunotherapy but had returned or progressed after several months of treatment. All the horses eventually suffered severe weight loss and were euthanized. Granulomatous lesions were found in the lungs and liver at necropsy in all three horses and in the spleen and lymph nodes of one horse that had a primary *Pythium* granuloma of the nasal septum. Lesions observed in the internal organs had the typical infiltration of eosinophils around necrotic masses (kunker).

Although there are no reports of antemortem diagnosis or treatment of pulmonary pythiosis, immunotherapy should be recommended. One study showed a 72% success rate in treating subcutaneous pythiosis with the use of immunotherapy that contained *P. insidiosum* exoantigens and cytoplasm. Immunologic changes observed in cured horses suggest that immunotherapy may induce a change from a helper T cell type 2 to a helper T cell type 1 immune response, which allows the horse’s own immune system to destroy the *Pythium* organisms. The *P. insidiosum* antigens are injected intramuscularly, and a strong (>10 cm) reaction at the injection site is associated with a greater likelihood of successful outcome in treating subcutaneous pythiosis. Disease resolution was also associated with a shorter duration of clinical signs. Unfortunately, pulmonary pythiosis in horses is likely to be diagnosed late in the disease process. Pythiosis immunotherapy has been used to treat systemic pythiosis in humans and was curative in a young boy with arterial pythiosis. The *P. insidiosum* allergenic extract is available from Pan American Veterinary Laboratories. Equine pulmonary pythiosis could be diagnosed using serology (ELISA, immunodiffusion, or Western blot), histopathology using immunohistochemical staining, culture, or polymerase chain reaction of a lung biopsy sample.

**REFERENCES**

11. Perron LePage MF, Gerber V, Suter MM. A case of interstitial pneumonia

---

Pan American Veterinary Laboratories (pythium.pavlab.com; phone 800-856-9655).


---

**ARTICLE #1 CE TEST**

This article qualifies for 2 contact hours of continuing education credit from the Auburn University College of Veterinary Medicine. Subscribers may take individual CE tests or sign up for our annual CE program. Those who wish to apply this credit to fulfill state relicensure requirements should consult their respective state authorities regarding the applicability of this program. CE subscribers can take CE tests online and get real-time scores at CompendiumEquine.com.

### 1. An association (41 of 49 cases) exists between invasive pulmonary Aspergillus infection and:

- a. hepatitis.
- b. laminitis.
- c. nephritis.
- d. pleuritis.
- e. colitis.

### 2. Blastomycosis can be identified cytologically by observing:

- a. spherical, broad-based budding yeasts with basophilic protoplasm and unstained, refractile walls that are often located within multinucleated giant cells.
- b. round yeasts with large capsules that do not take up common stains.
- c. round or crescent-shaped organisms with thin, clear halos and basophilic cytoplasm.
d. all of the above

e. None of the above. 
Blastomyces spp cannot be readily identified via cytology alone. A DNA probe or serology is required for diagnosis.

3. Which of the following is recognized as a cause of funga glossitis?
   a. B. dermatitidis  
   b. H. capsulatum  
   c. Aspergillus spp
   d. C. immitis  
   e. Candida spp

4. Which statement regarding P. carinii is incorrect?
   a. Culture of P. carinii is impossible.
   b. P. carinii infection can be confirmed using in situ hybridization on histopathology sections.
   c. P. carinii was originally classified as a protozoan but is now considered to be a saprophytic fungus.
   d. Interstitial pneumonia caused by P. carinii has never been diagnosed in an immunocompetent horse.
   e. all of the above

5. Przewalski’s horses appear to be more susceptible to infection with
   a. C. immitis  
   b. H. capsulatum  
   c. Conidiobolus coronatus  
   d. C. neoformans  
   e. B. dermatitidis

6. The treatment of choice for P. carinii infection is
   a. amphotericin B.
   b. trimethoprim–sulfamethoxazole.
   c. itraconazole.
   d. fluconazole.
   e. caspofungin.

7. An epidemiologic association between _________ and both the Australian river red gum tree and bird droppings has been described.
   a. C. immitis  
   b. H. capsulatum  
   c. Conidiobolus coronatus  
   d. C. neoformans

8. Nonpathogenic _________ is/are commonly found in tracheal aspirate from healthy horses.
   a. Alternaria spp  
   b. H. capsulatum  
   c. Aspergillus spp
   d. C. immitis  
   e. Candida spp

9. The current drug of choice in treating human aspergillosis is
   a. trimethoprim–sulfamethoxazole.
   b. ketoconazole.
   c. amphotericin B.
   d. voriconazole.
   e. fluconazole.

10. The prognosis for systemic fungal infections in horses is
    a. excellent.
    b. good.
    c. guarded.
    d. fair.
    e. that these conditions are uniformly fatal.