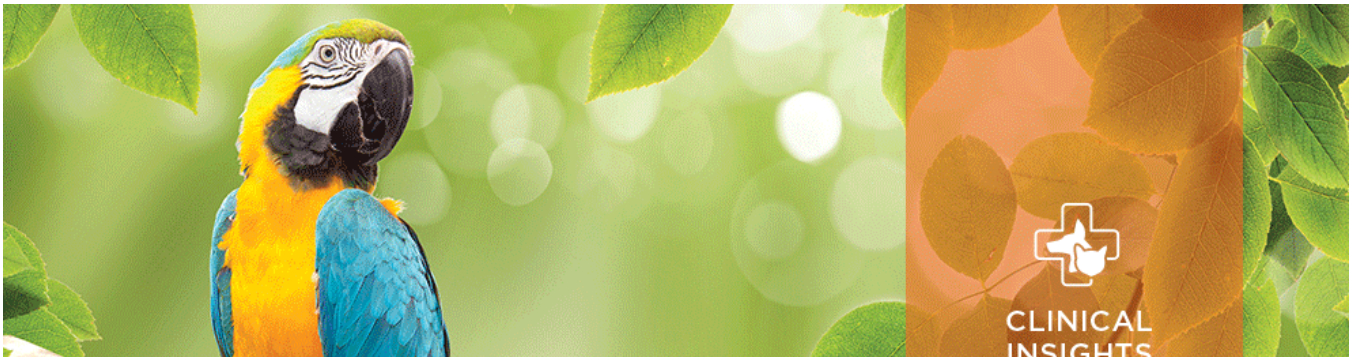
MANAGEMENT STRATEGIES, SMALL ANIMAL/EXOTIC MEDICINE

Avian Aspergillosis: What Every Veterinarian Needs to Know



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BIRD'S EYE VIEW

Certain avian species such as captive psittacines have been reported to be more at risk for *Aspergillus* infection.

WHAT IS IT?

Aspergillosis, a noncontagious, opportunistic fungal infection, is caused by *Aspergillus* species. It is also known as a **mycotic infection**, which may cause a fungal pneumonia. The spores are ubiquitous in the environment, and most birds can be considered exposed; outdoor environments pose a higher risk than does being kept completely indoors.[1] It is a common disease in captive birds, and the most common causative species is *Aspergillus fumigatus*.[2] The clinical disease typically appears as a result of immunosuppression.[1,2]

An acute presentation of aspergillosis can occur from an overwhelming concentration of fungal spores, whereas a chronic case is typically due to immunosuppression. Aspergillosis initially affects the air sacs because of the bird's unique respiratory system.

SIGNALMENT

The fungus is nondiscriminatory—all species and ages and both sexes can be affected. However, certain species have been reported to be more at risk for *Aspergillus* infection.[2] Captive psittacines (such as African grey parrots, amazons, and macaws), birds of prey (merlins, gyrfalcons, red-tailed hawks, golden eagles, rough-legged hawks, goshawks, snowy owls), waterfowl (swans), penguins, pheasants, turkeys, bird of paradise, and mynahs are some species known to have been infected with aspergillosis.[1-4] Risk factors are listed in **BOX 1**. Humid environments propagate excessive fungal growth, and very dry and dusty ones with poor ventilation favor spore formation; both can predispose birds to aspergillosis because of the increased potential for fungal growth. Associated conditions include anorexia, depression, dyspnea, weakness, and nasal granulomas.[1]

BOX 1

Risk Factors for Avian Aspergillosis[1,4,5]

- Stress
- Environmental conditions
- Inappropriate husbandry
- Nutritional deficiencies
- Immunosuppression
- Corticosteroid use
- Long-term antibiotic use
- Wild-caught animal
- Trauma
- Physical exertion (eg, migration)
- Toxicosis
- Genetics (eg, inbreeding)
- Preexisting disease

PRESENTATION

Typically, birds present with vague and nonspecific signs (depression, inappetence, difficulty breathing, reluctance to fly/perch, drooped wings). Initial physical examination findings typically include weight loss, respiratory abnormalities (dyspnea, tachypnea, cyanosis), lethargy, polyuria/polydipsia, vocalizing, open-beak breathing, tail bobbing, and/or enlarged nares.

The patient's respiratory system should be examined. Infection in the lower respiratory tract should be associated with an audible expiration, while inspiratory stridor may be due to an upper respiratory tract or tracheal infection. A sudden change in voice pitch during vocalization is often observed in psittacines with a granuloma in the upper respiratory tract. Some affected birds can have biliverdinuria (green discoloration of the urates).[1,2]

Birds have a unique respiratory system in which air sacs direct airflow in one direction through the lungs. This makes respiration extremely efficient; it is also the reason aspergillosis typically starts in the air sacs before reaching the lungs. Lack of an epiglottis, diaphragm, and surface macrophages, along with limited

pseudostratified ciliated columnar cells, may be predisposing factors in the spread of aspergillosis after initial infection.[4] Hyphae can also penetrate the air sacs and/or invade into blood vessels, consequently leading to a systemic infection through hematogenous spread.[4,5]

Signs of ocular aspergillosis typically include discharge, dull/cloudy cornea, blepharospasm, photophobia, swelling, and/or conjunctival yellow exudate.[4,5]

DIAGNOSIS

Diagnostic testing includes blood work (complete blood count, biochemistry), fungal culture, serology, imaging, endoscopy, and histopathology.[1]

Blood work may reveal moderate to severe leukocytosis with heterophilia (25,000–100,000 cells/mcL) with a reactive left shift.[1,2,4] Repeated blood work can be used to evaluate disease progression and treatment success. Chronic inflammation may reveal nonregenerative anemia.[3,4] Elevated liver values (aspartate aminotransferase and lactate dehydrogenase), elevated creatine kinase, hypoglycemia, hypoalbuminemia, and hyperglobulinemia (beta and gamma) are characteristic. Increased uric acid or electrolyte abnormalities can be seen as well. Protein electrophoresis can be used to obtain an overview of inflammatory changes.[1,2] A decreased albumin:globulin ratio (<0.5) should raise suspicion for aspergillosis.[1]

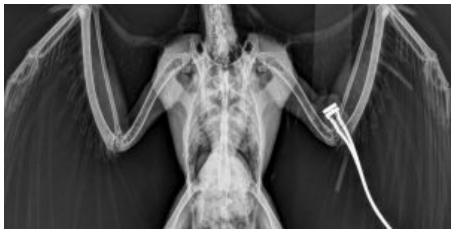

FIGURE 1. Ventrodorsal radiograph of an eclectus diagnosed with aspergillosis. Soft tissue opacities can be appreciated in the cervical region of the coelom.

Cytology and fungal culture can be useful for detecting fungal spores. To reduce sample contamination, an aseptic technique must be used. Cytology may show septate, 5- to 10-mcm-thick hyphae with straight parallel sides, ball-shaped terminal ends, and 45° branching.[2] Culture of samples taken from granulomas or the respiratory tract can help confirm aspergillosis.[1]

Signs of ocular aspergillosis typically include discharge, dull/cloudy cornea, blepharospasm, photophobia, swelling, and/or conjunctival yellow exudate.[2,4]

Serologic assays can be used to monitor treatment response and fungal exposure. An active *Aspergillus* infection can be better diagnosed with paired-titer serology than with a single titer because of the ubiquitous nature of the fungus.[1,2]

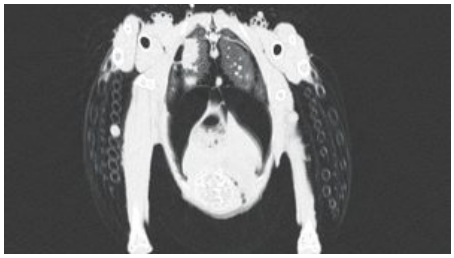

FIGURE 2. CT scan of the eclectus parrot shown in Figure 1 diagnosed with aspergillosis. Note the detailed view of the lesion compared with the radiograph in this image.

Noninvasive imaging—radiography, computed tomography (CT), and magnetic resonance imaging (MRI)—can help determine the location and distribution of potential lesions; however, images from these technologies cannot confirm the disease. Lateral and dorsoventral radiography is helpful for evaluating the lungs and air sacs (lower respiratory tract).[2] A late-stage infection can have radiographic evidence of multiple soft tissue densities (granulomas; **FIGURE 1**). Asymmetry, the thickness of air sac walls, hyperinflammation, consolidation, and soft tissue density in the lungs/air sacs can be observed.[1,2] Radiographic evidence is not ideal for detecting short-term improvement.[3] CT and MRI can be useful for viewing exact lesion locations (**FIGURE 2**); however, such testing is associated with a higher financial burden and often requires anesthesia or heavy sedation.

Endoscopy, while invasive, provides the substantial benefit of enabling acquisition of representative samples (biopsy and/or culture) from lesions (**FIGURE 3**). It also helps visualize granulomas and air sac plaques.[1,2] Granulomas can be localized in the nares, trachea, lungs, and/or air sacs.[1] In addition, endoscopy allows direct treatment of granulomas by endoscopic removal and application of antifungal agents via the treatment channel of the endoscope.[1,2]

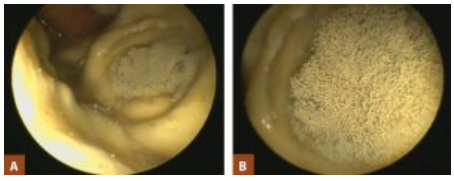

FIGURE 3. (A) Endoscopic photo of an aspergillosis granuloma in a wild red-tailed

hawk. (B) Close-up view of the same granuloma.

On pathology, lesions typically involve the respiratory system; chronic lesions usually involve the entire respiratory system, but acute cases can have lesions in the lungs and air sacs. Birds with aspergillosis typically have white or yellow plaques or nodules/granulomas and a mold-like lesion, or a general cloudiness, in the air sacs.[2,4] Aspergillosis can disseminate into other body systems, but this is rare. Invasive forms have been reported to be localized to the trachea or syrinx (**FIGURE 4**).[2]

Initial supportive treatments typically include stabilization, stress reduction, and collection of adequate samples to confirm the diagnosis.

Histopathology with periodic acid-Schiff or Gridley staining can demonstrate the fungal structure inside granulomas, and immunohistochemistry can help identify specific fungal species. Histopathology can be used to diagnose granulomatous air vasculitis and/or pleuritis, a thickened air sac with inflammatory cells and germinating conidia in macrophages, heterophilic and lymphohistiocytic lung lesions, and/or pneumonia with edema and hemorrhage.[2]

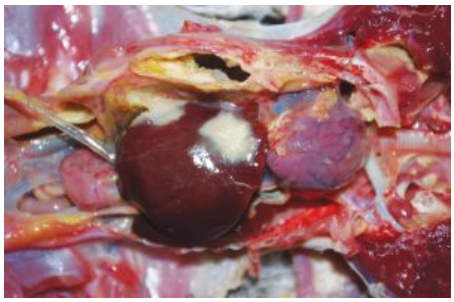

FIGURE 4. Necropsy photo of aspergillosis lesions in the coelomic cavity (liver, air sacs, heart lesions) of the hawk in Figure 3.

Other tests, such as acute-phase proteins, specific antigen detection, serologic assays, and *Aspergillus* toxin identification, are available but require further research of their diagnostic value.[2]

TREATMENT

Initial supportive treatments typically include stabilization, stress reduction, and collection of adequate samples to confirm the diagnosis. Once the patient is stabilized and the diagnosis is confirmed, specific treatment can be administered.

Acute treatment includes fluid therapy with crystalloids (SC, IV, or intraosseous) at 50 to 150 mL/kg q24h (maintenance) and correction of fluid deficiencies. The fluid rate should be 10 to 25 mL/kg over 5 minutes or 100 mL/kg q24h as a constant-rate infusion. Alternatively, the daily requirement can be calculated and one-third of this dose can be given via the SC route q8h. Environmental changes include increasing the humidity (relative humidity, ~40%–50%) and keeping the temperature between 85°F and 90°F. Nutritional support should also be considered depending on the needs of the individual patient.[1]

Antifungal therapy is typically prolonged and can last several months.[1,3] Routes of administration include nebulization, oral, parenteral, and topical. Medications of choice include amphotericin B, itraconazole, fluconazole, clotrimazole, and terbinafine hydrochloride.[1] Ideally, antifungal choice should be based on a sensitivity test. Dr. Mayer uses the Fungal Testing Laboratory at the University of Texas in San Antonio to verify that the fungus is susceptible to the chosen antifungal agent (**strl.uthscsa.edu/fungus**).

Amphotericin B can act as a fungistatic or fungicidal depending on its dosage, and it must be diluted with water before administration.[2,3] It can be systemically toxic because it binds to cholesterol.[3] Because of poor bioavailability, it must be given via the IV route. A variety of dosages can be given (**BOX 2**). Amphotericin B is the drug of choice that can be administered directly into the granuloma during endoscopic evaluation.

BOX 2

Dosages of Antifungal Drugs Commonly Used to Treat Aspergillosis

Amphotericin B

- IV route (typical): 1.5 mg/kg IV q8h for 3 to 5 days combined with itraconazole at 5–10 mg/kg PO q12h for 5 days
- Nebulized: Administer with 1 mg/mL sterile water/saline for 15 min q12h
  Intratracheal: 1 mg/kg q8–12h1

Itraconazole

- Recommended: 5–10 mg/kg PO q12h for 5 days, then q24h until treatment is complete

Fluconazole

- Oral: 5–15 mg/kg PO q12h1

Clotrimazole

- Nebulized: 1% aqueous solution for 30 min q24h for localized aspergillosis
- Topical or administered directly into the tracheal or air sac lesion: 10 mg/kg1,3

Terbinafine hydrochloride

- Oral: 10–15 mg/kg PO q12–24h in conjunction with itraconazole
- Nebulized: 1 mg/mL aqueous solution for 20 min q8h1

Itraconazole can be administered alone (**BOX 2**); however, its effectiveness increases when it is combined with nebulized clotrimazole and/or IV or nebulized amphotericin B.[1] African grey parrots are very sensitive to itraconazole, and toxicosis has occurred at higher doses in this species. In this species, the dose should not exceed 5 mg/kg q24 h.1 Inappetence and depression are the most common adverse effects associated with itraconazole in African grey parrots.[3]

Fluconazole is typically less effective than itraconazole.[1] It is fungistatic and typically used for ocular or central nervous system mycosis.[1,3] It is the only antimycotic that can be administered via the SC route, but its therapeutic effect is limited.[3]

Clotrimazole, a fungicidal and fungistatic, and **terbinafine hydrochloride**, known to penetrate mycotic granulomas, may also be good therapeutic choices (**BOX 2**).

Other medications that can be considered include the following:

- **Ketoconazole**, a fungistatic with known resistance in the population.
- **Enilconazole**, a fungistatic and fungicidal that can be used as a prophylactic or aerosolized treatment at a dose of 2 mg of medication per 1 mL of saline q12h for 30 minutes or an intratracheal dosage diluted and administered at 0.5 mL.
- **Voriconazole**, which has been reported to be more effective than amphotericin B and itraconazole, but is hepatotoxic.[3]
- **F10**, a newer medication available in the United States that can be used at a dilution of 1:250 to 1:50 for nebulization and as a sinus flush.[6,7] F10 contains the active ingredients benzalkonium chloride (0.22 mg/mL) and polyhexanide (0.02 mg/mL), which have not been shown to have adverse reactions at the recommended solution.[7] F10 super concentrate has been useful in treating secondary infection of respiratory aspergillosis.[8]

No current antifungal has been developed for nebulization, but terbinafine, amphotericin B, enilconazole, and clotrimazole have been diluted and used. Systemic side effects are rare. This route of administration is useful because of the minimal stress it causes and its ability to provide both prophylactic and prolonged treatment. Oral administration is common and preferred due to potential organ toxicity associated with IV administration. Absorption, however, varies by species. Topical applications, including natamycin, enilconazole, and clotrimazole, can be formulated as ointments and are used more often for dermal or ocular infections.[3]

Treatment of granulomas typically involves debulking and/or excision through surgery or endoscopy.[1] Surgical removal of granulomas can be an option to improve the treatment response.[3,4]

Vaccination (eg, killed, whole cell) has been attempted through various routes (intramuscular, transcutaneous, subcutaneous), but results were variable and inconclusive.[4,9] No vaccine has yet been developed for

immunization.

Prognosis depends on the severity of each case (based on such factors as chronicity, immune status, and species).[1]

PROGNOSIS

Prognosis depends on the severity of each case (based on such factors as chronicity, immune status, and species).[1] An uncomplicated case typically has a good prognosis. Months-long treatment is not uncommon. If the underlying source is not identified, a bird can be reinfected after successful treatment.

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Julia Dobros • **2 months ago**

Hello, I would appreciate your thoughts on the following situation. A euroasian eagle owl is being treated for

aspergillosis, 70% of her lungs are affected. She is been given antifungals in injections and orally, and her vets are concerned that clearing the lungs in the process of treatment, "coughing things up" while the antifungals work can lead to suffocation. Are there any measures that could help with that? Is it relevant to the humidity and temperature recommendation in your article? I am not a veterinarian, just searching all possible sources in order to help a friend. Thank you.

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