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Clinical Management of Avian Renal Disease

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INTRODUCTION

As in mammals, avian renal disease may be classified as acute or chronic. Acute renal failure results from an abrupt decrease in renal function, often caused by an ischemic or toxic insult.1 Chronic kidney disease is characterized by loss of functional renal tissue owing to a prolonged and usually progressive disease process.2

Causes of kidney disease may be classified as prerenal, renal, postrenal, or of mixed origin. A prerenal origin is characterized by hypoperfusion of the kidney. Conditions that commonly lead to the development of prerenal hyperuricemia include dehydration, hypovolemia, and congestive heart failure. Renal origin of kidney disease refers

KEYWORDS

- Avian • Fluid therapy • Nutrition • Supportive care • Allopurinol • Antifungal drugs • Chelation therapy • Chemotherapy

KEY POINTS

- Fluid therapy is one of the most important treatments in cases of kidney disorders in birds. The choice between oral, subcutaneous, intravenous, and intraosseous routes depends on the patient and its needs.
- Elevated dietary protein alone does not seem to be the underlying etiology of gout in all avian species because diets as high as 70% protein failed to induce gout in adult cockatiels.
- The efficacy of allopurinol remains controversial in avian medicine and its use has not been reported in many avian species.
- Surgical procedures, such as nephrectomy or renal transplantation, are not advisable in birds owing to the anatomic constraints of the avian kidney.
- No effective therapy is recognized in birds with renal neoplasia.

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to an intrarenal process, leading to a dramatic decrease in the glomerular filtration rate. In birds, a decrease in glomerular filtration rate can either be a sign of renal disease or an appropriate physiologic response to water restriction. Causes of renal disease in the avian patient include infectious nephritis, hypovitaminosis A, heavy metal intoxication, and renal neoplasia. Postrenal hyperuricemia occurs when there is a disruption of the integrity of the urinary tract or an obstruction of urine outflow (eg, urolithiasis).

The treatment of avian renal disease relies on supportive care such as fluid therapy and nutritional support. Analgesia and adaptations of the environment are indicated in cases of renal disease associated with painful joints or spinal nerve compression. Other treatments vary with the underlying etiology and may include systemic antibiotics, antifungal therapy, vitamin A supplementation, chelation therapy, and agents to lower uric acid levels such as allopurinol. Potentially nephrotoxic drugs should be used with extreme caution in patients with renal disease. Additionally, drugs that are excreted through the kidney may fail to reach therapeutic plasma levels in polyuric birds or reach toxic levels if drug excretion and elimination are impaired.

GENERAL THERAPY FOR RENAL DISEASE

Fluid Therapy

As in mammals, fluid therapy constitutes one of the most important treatments in cases of kidney disorders in birds. Uric acid is eliminated by active tubular secretion and water is needed to flush the suspension through the renal tubules. Without regular removal by diuresis, urates can accumulate within the kidneys. Fluid type is selected based on results of biochemical analyses, evaluation of blood electrolytes, glucose, and acid–base status. When these values are not known, a balanced isotonic crystalloid solution, such as lactated Ringer’s solution may be used for rehydration and hemodynamic support. Caution is recommended when using colloid fluids in patients with renal disease by extrapolation from mammals.

Route of administration

Depending on the clinical circumstance, fluids can be administered by oral, subcutaneous, intravenous (IV), and/or intraosseous (IO) routes. Fluids are often administered by mouth by gavage with liquid oral nutrition. This route is generally safe and adequate for avian patients that are not in shock or debilitated. In birds with mild dehydration, fluids can also be provided subcutaneously. Subcutaneous fluids can be administered in the inguinal (Fig. 1), interscapular, or axillary regions. Volumes as great as 20 mL/kg may be administered in 1 location. Subcutaneous fluids are easily delivered using a butterfly needle, which allows the animal to move without the needle being pulled out. Practitioners unfamiliar with avian anatomy should beware of the thin skin and the presence of abdominal air sacs close to the inguinal region. Thus, it is key to remain steady during the procedure and to firmly hold the leg in extension to avoid inadvertent coelomic puncture. Fluids given subcutaneously and by mouth are poorly absorbed if hypovolemic shock is present.

The vasculature in birds can be accessed via IV or intraosseous (IO) routes. The choice between these routes depends on patient size, patient temperament, and the volume of fluids needed. IV catheters may be used for initial fluid therapy, but do not have the stability of an IO catheter. Permanent supervision of birds with IV catheters is also required to prevent fatal hemorrhage in case of accidental removal of the catheter. IO catheters can be placed quickly, are stable and reliable, and are relatively easy to maintain, but placement is more painful. Fluids can also be provided
in a larger bolus by the IO route than the IV route. Unlike IV catheter placement, IO catheterization can also be performed even in very small birds.

IV catheters may be placed in ulnar (Fig. 2) and medial metatarsal veins (Fig. 3), or more rarely in the jugular vein. IV catheterization often requires sedation or general anesthesia to avoid stressful physical restraint. Jugular and ulnar catheters must be sutured in place. Medial metatarsal catheters can be secured using tape only. All catheters should then be covered with a nonadhesive bandage. Wing catheters are protected with a figure-of-eight bandage (Fig. 4).

IO catheter sites include the proximal tibiotarsus and the distal ulna (Box 1). Pneumatized bones, such as the humerus and femur, should be avoided. Rarely, in large birds such as pelicans, California condors (Gymnogyps californianus), and turkey vultures (Cathartes aura), the ulna is also pneumatized.

Some birds may benefit from an Elizabethan or cervical restraint collar; however, these devices can be extremely stressful to some birds and may adversely affect
patient condition. The ability to tolerate a collar should be assessed in each patient\(^\text{11}\) (see Box 1).

**Fluid requirements**

Daily maintenance fluid requirements have not been determined in birds; however, the recommendations of different authors range from 50 to 150 mL/kg/d, with the higher
end of the range expected in smaller species.\textsuperscript{14,15} Maintenance plus one-half of the estimated fluid deficit is generally administered over the first 12 to 24 hours, with the remainder of the deficit replaced over the following 48 hours.\textsuperscript{9} Fluids for maintenance and correction of dehydration are given as a constant infusion, using a pediatric Fig. 4. A cockatiel (\textit{Nymphicus hollandicus}) receiving fluid therapy via an IO catheter in the right ulna. The wing has been taped to the body. The patient is weak and thus does not need an Elizabeth collar. (Courtesy of C. Grosset, médecin, CES, IPSAV, DACZM, Saint-Hyacinthe, Canada.)

Box 1

\textbf{IO catheter placement in the bird}

\textit{Placement of an IO catheter in the distal ulna}

- Palpate the styloid process of the distal ulna on the dorsal aspect of the wing.
- Pluck the feathers over the surrounding site and prepare aseptically.
- Ideally use a 20- to 25-gauge short spinal needle.
- Flex the distal wing tip and grasp the ulna between the fingers of one hand. With the other hand, the spinal needle is inserted just ventral to the condyle and directed proximally toward the elbow along the ulnar shaft (Fig. 5A, 5B).
- Apply gentle pressure as the bevel of the needle is rotated, allowing the needle to cut through the cortex of the bone and enter the medullary cavity.
- If the lumen of the needle becomes plugged, the needle may be removed and replaced.
- Check the patency of the catheter with a small amount of heparinized saline. Visualize flow in the ulnar vein as the fluid is injected (Fig. 5C).
- Two orthogonal radiographic views may also be obtained to confirm correct placement.
- Secure the catheter with butterfly taping and by suturing this tape to the skin, if necessary.
- Place a figure-of-eight wing bandage to minimize wing movement.

\textit{Placement of an IO catheter in the proximal tibiotarsus}

- Flex the stifle, and palpate the cnemial crest at the proximal anterior surface of the tibiotarsus, just distal to the knee joint.
- Insert the needle at the cnemial crest at, or to either side of, the insertion of the patellar tendon, to avoid penetration of the stifle joint.
- Secure the catheter in place with tape.

Data from Refs.\textsuperscript{9,10,12}
infusion pump or syringe pump. Fluids should be warmed to body temperature. Depending on the patient’s condition and species, the author will typically give 50 to 100 mL/kg of fluid twice a day subcutaneously, IV, IO, or via a combination of routes.

Outpatient measures to maintain or improve proper hydration
Various tips may be given to clients to promote adequate hydration at home for avian patients with renal disease. Owners may offer fruit juice without added sugar or infant electrolyte replacement solution (Pedialyte, Abbott, Saint-Laurent, Quebec, Canada) full strength or diluted with water. Owners can also increase the proportion of fruits and vegetables in the diet or offer moistened seeds or other foods like warm, unsalted vegetable soup. Caretakers may float seeds in the water bowl to encourage drinking behavior. Regular access to a shower or bath can also promote drinking, acknowledging that individual birds vary greatly in the ways they choose to bathe. Some birds love the feeling of a trickling shower, some enjoy daily misting with a spray bottle, and some like to dunk themselves in a pool of water. If none of these measures prove adequate and the bird is still not drinking in sufficient amounts, the

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**Fig. 5.** Placement of an IO catheter in the ulna of an avian patient (see Box 1). (A) Computed tomography scan of an African gray parrot (Psittacus erithacus). Dorsal view of the right wing. The white arrow indicates the site and axis of insertion of the catheter in the ulna. (B) After aseptic preparation of the site and appropriate analgesic protocol administration, the ulna is grasped between the fingers. Palpate the styloid process of the distal ulna on the dorsal aspect of the wing. The needle is inserted in the distal ulna and directed proximally. (C) Check the patency of the catheter by using a small amount of heparinized saline flush. Visualize the flow in the ulnar vein as the fluid is injected. (Courtesy of [A] S. Larrat, mé’d v ét, MSc, DES, DACZM, Brech, France; and [C] M. Desmarchelier, DVM, MSc, DACVB, DACZM, DECZM, Saint-Hyacinthe, Canada.)
owner can use a plastic eyedropper, syringe, or straw with finger kept over 1 end to slowly offer fluids directly into the beak, followed by positive reinforcement like verbal praise. Reserve this method as a last resort and inform owners of the risk of fluid aspiration.

**Nutritional Supportive Care**

Patients with renal disease should be monitored for weight loss and appropriate nutritional support should be offered as needed.16

**Dietary protein**

Clinical studies in dogs and cats have demonstrated that dietary protein restriction can slow chronic kidney disease progression and improve survival.19 By extrapolation, few commercial diets low in proteins have been formulated for birds with renal insufficiency (eg, Roudybush AK formula; Woodland, CA), although evidence-based data on whether protein restriction is beneficial in birds are lacking. Precise protein content and composition is also not disclosed for this diet.

Renal lesions, such as gout, have been associated with excess dietary protein in birds, but only under specific conditions.16 In 1 study, a 42.28% protein diet fed to 18-day-old broiler chicks for 15 weeks induced multiple renal abnormalities, primarily nephrosis and visceral gout.16 In another study, diets high in urea were linked to outbreaks of nephritis in poultry,16 however, cockatiels (*Nymphicus hollandicus*) fed high dietary protein (up to 70%) for 11 months did not develop renal lesions. The cockatiels were able to upregulate enzymes associated with amino acid catabolism and uric acid synthesis.6 Of note, these cockatiels received a gradually increasing protein concentration in their diet over 3 weeks. Uric acid increased linearly with dietary protein levels, but remained within normal limits in these birds, indicating that hyperuricemia is specific of renal disease or severe dehydration in granivorous avian species. Because the nutritional requirements vary among avian species, it is unknown if these conclusions can be extrapolated to other birds. Unlike carnivorous birds, granivorous species have low requirements for dietary amino acids and seem to be able to conserve amino acids by tight regulation of amino acid catabolism.6 Frugivorous birds have lower rates of nitrogen loss compared with granivorous birds and, thus, even lower dietary protein requirements.20 A safe recommendation is that birds with hyperuricemia should not consume diets with protein levels greater than what is considered normal for the given species.16

**Fatty acid supplementation**

Omega-3 fatty acid supplementation has been shown to decrease the risk of chronic renal disease and delay the progression of disease in dogs and humans.16,20 Cytokines derived from membrane-bound omega-6 fatty acids like arachidonic acid include prostaglandins, thromboxanes, and leukotrienes.19 These cytokines are proinflammatory and vasoactive, which promotes chronic kidney disease progression, owing to renal free radical production and antioxidant depletion.19

In humans, the positive effects of the polyunsaturated fatty acid eicosapentaenoic acid (EPA) are more pronounced than those of α-linolenic acid, another omega-3 fatty acid.21 Concentrated sources of longer chain omega-3 fatty acids (such as EPA and docosahexanoic acid) are limited to fish and other marine products and algal-based sources.21 Flaxseed is also a source of EPA, but is less commonly used in feed manufacturing because of susceptibility to oxidative rancidity.

In avian medicine, only anecdotal information exists regarding the use of omega-3 fatty acids in renal disease.16 Most psittacine diets are highly enriched in omega-6
fatty acids (primarily linoleic acid) and limited in omega-3 fatty acids (Table 1). Of note, diets high in polyunsaturated fatty acids require additional antioxidants to prevent lipid peroxidation during storage.\textsuperscript{14}

Incorporation of omega-3 into cockatiel red blood cells was greater after supplementation with fish oil\textsuperscript{22,23}, however, the palatability of fish oil may be an issue when supplementing psittacine birds at home. Being carnivorous, some birds of prey are more likely to accept fish oil in their diet. In cases of concomitant gout, ensure the patient receives a plant-based source of EPA or docosahexanoic acid rather than a fish oil source, which may have higher purine levels\textsuperscript{17} (see Table 1).

**Management of Hyperuricemia**

Severe dehydration and many forms of renal disease, including obstructed ureters, can result in decreased uric acid elimination thus causing hyperuricemia.\textsuperscript{16} Fluid therapy (combined with medications for hyperuricemia if needed) is generally continued until uric acid decreases to either normal or mildly increased levels (10–20 mg/dL) and the bird demonstrates signs of improvement, such as eating or increased activity.\textsuperscript{16}

The use of medications for hyperuricemia is extrapolated from human medicine, and the safety and efficacy of these treatments are often lacking in birds. These drugs have been poorly studied in psittacine birds and should only be used with close monitoring of uric acid levels.

**Xanthine oxidase inhibitors**

Xanthine oxidase inhibitors, such as allopurinol and febuxostat, decrease uric acid synthesis. The efficacy of allopurinol in avian medicine is controversial; information is available for only a limited number of species. In broilers, uricemia was reduced as well as xanthine oxidase and xanthine dehydrogenase activity in the kidney in birds treated with allopurinol (25 mg/kg by mouth).\textsuperscript{24,25} Allopurinol was unable to completely inhibit xanthine oxidoreductase activity.\textsuperscript{24}

Toxicity has been reported following administration of allopurinol in red-tailed hawks (Buteo jamaicensis). Vomiting developed at 50 mg/kg by mouth every 24 hours and was attributed to the accumulation of oxypurinol, a metabolite that worsens renal gout.\textsuperscript{26} Allopurinol given at 25 mg/kg by mouth every 24 hours to red-tailed hawks was shown to be safe, but had no significant effect on plasma uric acid concentrations. Based on the lack of response at a dose of 25 mg/kg and the toxic effects at

| Food Items                | Omega 3 Concentration (g) Value per 100 g | Omega 3/Ω 6 Ratio Value per 100 g |
|---------------------------|------------------------------------------|----------------------------------|
| Flax seeds                | 22.8                                     | 3.86                             |
| Chia seeds                | 17.6                                     | 3.03                             |
| Walnut                    | 9.1                                      | 0.24                             |
| Soybean oil               | 6.8                                      | 0.13                             |
| Lafeber Senior Bird Nutri-Berries® | 0.48                                     | 0.16                             |
| Edamame (green soybean)   | 0.3                                      | 0.16                             |

Data from United States Department of Agriculture Agricultural Research Service Database (USDA). Available at: https://ndb.nal.usda.gov/ndb/.
50 mg/kg, allopurinol is not recommended in the red-tailed hawk. It is unknown whether this finding should be extrapolated to psittacine birds.

**Uricase**
Uricase oxidizes uric acid to allantoin in humans. Little information is available in veterinary medicine. Poultry on a high-protein diet developed hyperuricemia, which was reversed with uricase injection. In a more recent study, the uricolytic properties of uricase were studied in a granivorous bird (pigeon, *Columba livia domestica*) and a carnivorous avian species (red-tailed hawk). Plasma concentrations of allantoin and uric acid were determined in experimental groups before and after receiving 100, 200, and 600 UI/kg uricase intramuscularly once daily. All regimens caused a significant decrease in plasma uric acid concentrations within 2 days after the first administration, when compared with controls. Plasma allantoin concentrations were also significantly higher when compared with controls, suggesting a similar mechanism of action in these species.

**Xanthine dehydrogenase inhibitor**
The xanthine dehydrogenase inhibitor, colchicine, is used for its antigout activity in humans. Colchicine has also been used to treat amyloidosis and renal fibrosis in small animals. In turkeys diagnosed with articular gout, colchicine administered at 0.18 mg/kg by mouth every 24 hours for 7 days failed to influence uric acid concentrations. No controlled study on colchicine has been published in birds.

**Uricosuric drugs**
Uricosuric drugs, such as probenecid, promote uric acid excretion by the kidneys. Uricosuric drugs are contraindicated when tubular urate crystals are present, which is frequently seen in birds. Probenecid has been shown to inhibit uric acid tubular secretion in chicken proximal tubule epithelium in vitro. It has also been studied in vivo in chicken; depending on the dose given intravenously, the drug increased or decreased uric acid clearance. Probenecid use has been reported anecdotally in psittacine birds and reptiles with gout, but no efficacious dose is currently published.

**Pain Management**
Birds with renal disorders may suffer from pain caused by articular gout or nerve compression secondary to renal masses. Affected birds are likely to spend more time on the cage floor and suffer from impaired locomotion. Husbandry adaptations and pain control are required to improve their quality of life.

**Enclosure modifications**
Water and food dishes can be placed as close to the bird as possible. Containers of different shapes and depths can stimulate consumption. Replace standard perches with perches of a larger diameter and ladders or ramps that allow the bird to use its beak. Once the bird is unable to perch normally, the claws may need to be trimmed and shaped more frequently than in a healthy bird. Patients with gout should not be restricted in their movements, and instead should be housed in as large a cage as possible. The minimum size considered adequate allows the bird enough space to spread its wings without hitting either the sides of the cage or other perches.

**Analgesia**
Pain management is paramount in birds with articular gout or nerve compression by renal masses. Long-term treatment with opioids may be considered. Intra-articular injections of corticosteroids are administered to humans with only 1 joint affected by gout, but this treatment modality has not been investigated in birds.
The effectiveness of intra-articular bupivacaine injections in the suppression of osteoarthritic pain has also been demonstrated in humans. In an avian model of acute gouty arthritis, local anesthesia was effective in suppressing pain-associated behavior. It was concluded that the optimum intra-articular dose of bupivacaine for the treatment of musculoskeletal pain in the domestic fowl was 3 mg bupivacaine in 0.3 mL saline. Physical modalities such as thermotherapy and laser may also be used to diminish pain. Low-level laser therapy (660 nm, 9 J/cm²) has been shown to decrease neuropathic pain.

Alternatively, after discussion with owners of the safety versus quality of life balance, the use of nonsteroidal anti-inflammatory drugs may be considered as a palliative treatment. A study in Hispaniolan Amazon parrots (Amazona ventralis) indicated 1.3 mg/kg by mouth every 12 hours of meloxicam to be a therapeutic dosage for relief of arthritic pain.

Both severe gout and renal tumors carry a poor prognosis; therefore, euthanasia must be considered when analgesia and husbandry modifications fail to ensure an appropriate quality of life for the patient.

Miscellaneous Conditions Associated with Chronic Renal Disease

Hyperphosphatemia is poorly documented in birds in association with renal failure, but it has been reported in some instances. If this condition develops, phosphate binders may be administered at doses extrapolated from small animals.

| Table 2 | Analgesic agents evaluated in Hispaniolan Amazon parrots (Amazona ventralis) by pharmacokinetic studies |
| --- | --- |
| Agent | Dosage | Route | Frequency | Comment |
| Tramadol hydrochloride | 30 mg/kg | PO | q6-12h | – |
| Butorphanol tartrate (long-acting poloxamer 407 gel formulation) | 12.5 mg/kg | SQ | q4-6h | – |
| Gabapentin | 15 mg/kg | PO | q8 h | Neuropathic pain, effects takes days to weeks |

Abbreviations: PO, by mouth; SQ, subcutaneous; q, every.
Although rarely reported with renal disease in birds, gastric ulcers may be treated with omeprazole\textsuperscript{41} (1–10 mg/kg by mouth every 12 hours) and sucralfate (25 mg/kg by mouth every 8 hours) staggered 2 hours apart from other oral treatments.

Chronic anemia owing to decreased erythropoietin secretion is challenging to manage because avian erythropoietin is structurally different from that of mammals.\textsuperscript{42} The effect of epoetin alfa in birds has not been documented but it is likely to cause antibody production.

Colchicine may be administered long term to treat amyloidosis and limit renal fibrosis.\textsuperscript{16} No controlled studies have been published in birds about this drug.

In mammals, peritoneal dialysis or hemodialysis is ideal for cases of renal disease not treatable with other medical options.\textsuperscript{43} The use of dialysis has not been described in birds and coelomic dialysis is not possible in the avian patient owing to the presence of abdominal air sacs. Renal transplantation has also never been described in avian medicine and is unrealistic given the position of the kidneys immediately ventral to the synsacrum, adjacent to air sacs, and in close relation with pelvic nerves.

**SPECIFIC THERAPY FOR RENAL DISEASE**

In avian species, renal diseases are caused by various etiologies, including infectious nephritis (bacterial, viral, parasitic, fungal), renal neoplasms, toxic exposure, and nutritional disorders.\textsuperscript{44} Specific treatment options vary depending on the cause.

**Bacterial Nephritis**

Many bacteria have been reported to cause nephritis in birds, including Enterobacteriaceae, Pasteurella spp., Pseudomonas spp., Streptococcus spp., Staphylococcus spp., Listeria monocytogenes, Erysipelothrix rhusiopathiae, and chlamydial organisms.\textsuperscript{43,45} Mycobacterium spp. have also been rarely reported in the avian kidney.\textsuperscript{43,46,47}

Antibiotics are indicated in suspected or confirmed cases of bacterial nephritis.\textsuperscript{16} Drug choice should ideally be based on a susceptibility panel from blood or histopathologic samples.\textsuperscript{16} Cloacal samples may also be used owing to the possibility of ascending infection but may not be reliable. In cats and dogs, bacterial nephritis is treated for at least 4 to 6 weeks.\textsuperscript{5} This recommendation may be extrapolated to birds in the absence of controlled studies regarding duration of treatment in avian medicine.\textsuperscript{16} Pending culture and sensitivity results, empirical broad-spectrum antibiotics that provide excellent therapeutic levels within renal tissue should be initiated such as β-lactams, trimethoprim-sulfamethoxazole, or fluoroquinolones.\textsuperscript{48,49} Avoid potentially nephrotoxic antibiotics, such as aminoglycosides.\textsuperscript{48,49}

**Viral Nephritis**

Among viral infections, polyomavirus often results in clinically relevant renal disease.\textsuperscript{44} Polymavirus is the most important cause of viral nephritis in the companion psittacine bird.\textsuperscript{43} Many other viruses can cause renal lesions in psittaciformes including, but not limited to, paramyxoviruses,\textsuperscript{43,44} bornavirus,\textsuperscript{50,51} and West Nile virus.\textsuperscript{52} In backyard chickens, infectious bronchitis virus is the most important cause of renal disease.\textsuperscript{43} Treatment of viral nephritis usually relies on nonspecific supportive care.

**Parasitic Nephritis**

Renal coccidiosis is the most common cause of parasitic nephritis. Renal diseases caused by the coccidian Eimeria spp. have been reported in several species, including juvenile waterfowl,\textsuperscript{53} domestic goose (Anser anser domesticus), and less commonly
Although rare, renal cryptosporidiosis has also been reported in birds. Schizonts of *Leukocytozoon* spp., *Plasmodium* spp., and *Haemoproteus* spp. have been identified in avian renal tissue and associated with lymphoplasmacytic inflammation. Renal trematodes and cestodes have also been reported in multiple species of bird housed outdoors, including order Columbiformes, Passeriformes, Anseriformes, Psittaciformes, and Galliformes.

Parasitic diseases associated with the kidneys are typically diagnosed from a fecal parasite examination or renal biopsy. Antiparasitic treatments vary greatly depending on the species and life cycle of the parasite, with ponazuril (20 mg/kg by mouth every 24 hours for 7 days) or toltrazuril (25 mg/kg by mouth once a week) being used for coccidia, and praziquantel (10 mg/kg subcutaneously 2 times 10 days apart) for trematodes and cestodes. Although toltrazuril has been shown to successfully control coccidiosis in broilers with a single 2-day treatment course, its use is not approved in food animal species in many countries. Practitioners should consult local regulations for approved anticoccidial agents. Monensin has been used for the treatment of renal coccidiosis, but is toxic in turkey and guinea fowl. Reports on resistance of *Eimeria* isolates to anticoccidial drugs are increasing, and rotation of anticoccidial drugs is recommended to minimize the risk of resistance. Natural products, such as cider vinegar, are also emerging as alternative strategies to control avian coccidiosis.

**Fungal Nephritis**

**Aspergillosis**

Although predominantly a disease of the respiratory tract, systemic aspergillosis can occur. Renal aspergillosis has been reported in several avian species, including chickens and a black palm cockatoo (*Probosciger aterrimus*). Fungal culture from a biopsy is recommended because treatment options can vary depending on the fungal organism involved. Most systemic fungal infections require long-term therapy over a period of months. Initial IV administration of antifungal drugs followed by oral therapy is recommended.

Amphotericin B is a polyene macrolide that acts by binding to ergosterol, the principal sterol in the fungal cell membrane. Amphotericin B has a broad antifungal spectrum, including *Aspergillus* spp. and *Cryptococcus* spp., although resistance has been reported. IV administration quickly establishes fungicidal concentrations, making amphotericin B a frequent choice for initial therapy. The use of amphotericin B has been associated with nephrotoxicity in mammals; however no evidence of nephrotoxicity has been documented in birds. This difference may be associated with the shorter elimination half-life in birds compared with mammals after IV administration of amphotericin B.

In combination with early, systemic antifungal therapy, topical amphotericin B can be administered through a polypropylene tube during endoscopic or surgical procedures. Topical therapy is recommended when renal lesions can be easily debrided to maximize drug concentrations in tissues; however, in many patients granulomas cannot be reached endoscopically.

Itraconazole, fluconazole, and voriconazole are the most studied azoles in birds. The relative toxicity of an azole depends on the affinity to fungal cytochrome P450 enzyme, compared with its affinity to the avian cytochrome P450. The most common adverse effects associated with azole administration in birds are anorexia, vomiting, and alterations in liver function. Regular bile acid monitoring is recommended during treatment for early detection of hepatic adverse effects. Itraconazole is a first-generation triazole antifungal agent, commonly used in birds for treatment of...
aspergillosis. Voriconazole is a third-generation triazole antifungal agent. Voriconazole is increasingly used to treat invasive aspergillosis in birds, given the broad antifungal spectrum, which includes molds (fungicidal) and yeasts (fungistatic), and its rapid bioavailability. Acquired resistance of Aspergillus fumigatus strains to both itraconazole and voriconazole has been reported. Fluconazole is a watersoluble fungistatic agent that is rapidly absorbed with high bioavailability after oral administration. A blue-fronted Amazon parrot with Aspergillus keratomycosis was successfully treated with oral and topical fluconazole.

Terbinafine is an allylamine, fungicidal agent with activity against several fungal species, including Aspergillus spp. and Cryptococcus spp. Of note, the dose should be decreased in cases of impaired renal function. Studies have documented dose- and species-dependent variability, suggesting that different dosage regimens of antifungals may be required for different species of birds (Table 3). Caution should be applied when extrapolating a dose to a different avian species.

Cryptococcosis
Systemic cryptococcosis may also affect companion psittacine birds. Partial response to treatment with fluconazole (15 mg/kg by mouth every 12 hours) and terbinafine (15–20 mg/kg by mouth every 12 hours) was described in an African gray parrot (Psittacus erithacus) with renal cryptococcosis.

Microsporidiosis
Renal microsporidiosis has been reported in lovebirds (Agapornis spp.), particularly in individuals positive for psittacine beak and feather disease, as well as budgerigar parakeets (Melopsittacus undulatus), eclectus (Eclectus roratus), red-bellied parrots (Poicephalus rufiventris), and other avian species. Treatment of renal microsporidiosis has not been reported in birds, but an umbrella cockatoo (Cacatua alba) with keratoconjunctivitis associated with microsporidia was successfully treated with albendazole (25 mg/kg by mouth every 24 hours) for 90 days. Clinicians should keep in mind potential toxicities associated with benzimidazoles in many birds.

Treatment of Intoxications Affecting Renal Function

Heavy metal intoxication
Lead and zinc toxicosis can cause renal nephrosis and acute tubular necrosis, respectively. Treatment of heavy metal toxicosis must begin with removal of metal from the gastrointestinal tract to halt further absorption. General supportive care is also important. Diets higher in calcium decreased morbidity and mortality in experimentally lead-poisoned ducks. Antioxidative therapies, such as supplemental vitamin C, may also be instituted, because lead induces free radicals.

Various chelation agents have been used in avian species. Careful monitoring of renal parameters is important for the duration of chelation therapy. Elevated uric acid levels can be observed with heavy metal poisoning and improvement of hyperuricemia with therapy has been reported.

Calcium disodium salt of EDTA (CaEDTA) is the main chelator for lead and zinc poisoning in avian species. CaEDTA must be administered parenterally because absorption from the gastrointestinal tract is poor. In a study conducted with children, nephrotoxicity and inducement of acute renal failure were reported as an adverse effect of CaEDTA. Although nephrotoxicity has not been reported in birds treated with CaEDTA, even at 40 mg/kg every 12 hours intramuscularly for 21 days, fluid therapy is still recommended to minimize the risk of renal adverse effects.
| Antifungal Agent | Active Against | Pharmacokinetic Studies | Recommended Doses | Adverse Effects | Comments |
|------------------|----------------|--------------------------|-------------------|----------------|----------|
| **Amphotericin B** |               |                          |                   |                |          |
| C                | A             | Domestic turkey,         | 1-1,5 mg/kg IV q8–12 h | Renal toxicity considered lower than in mammals because elimination phase faster in birds |          |
|                  | Cr            | broad-winged hawk, red-tailed hawk, great-horned owl |                   |                |          |
| **Itraconazole** |               |                          |                   |                |          |
| C                | A             | Humboldt penguin        | 8.5 mg/kg PO q12 h | Anorexia, vomiting, and alterations in liver function are most common. | Itraconazole is better absorbed in an acidic gastric pH; thus, antacid medications should not be administered concomitantly. |
|                | ST            | Blue-fronted Amazon parrot | 20 mg/kg PO q24 h |                      |          |
|                  |               | Racing pigeons          | 5 mg/kg PO q24 h |                      |          |
|                  |               | Red-tailed hawk         | 6–26 mg/kg PO q12 h |                      |          |
|                  |               | African gray parrot     | 10 mg/kg PO q24 h |                      |          |
|                  |               |                          | If itraconazole is used owing to monetary constraints, doses of 2.5 mg/kg PO q12–24 h have been used safely with frequent monitoring of plasma bile acid levels |                      |          |
|                  |               |                          | Voriconazole is usually preferred over itraconazole owing to toxicity reports in African gray parrots |                      |          |
| Voriconazole | ST (yeasts) | Red-tailed hawk\(^{87,88}\) | 10–12.5 mg/kg q8–12h | Anorexia, vomiting, and alterations in liver function are most common.\(^{71,72}\) | Voriconazole induces its own metabolism via cytochrome P450 and doses should be increased over time.\(^{95}\) | Owing to toxicity reports in African gray parrots, voriconazole is usually preferred over itraconazole in this species. |
| --- | --- | --- | --- | --- | --- | --- |
| | | Timneh African gray parrot\(^{89}\) | 12–18 mg/kg PO q12 h | | | |
| | | Hispaniolan Amazon parrot\(^{90}\) | 18 mg/kg PO q8 h | | | |
| | | Mallard duck\(^{91}\) | 20 mg/kg PO q8–12h | Poor bioavailability in chickens\(^{92}\) | | |
| | | Chicken\(^{92}\) | | | | |
| | | African penguins\(^{93}\) | | | | |
| | | Falcon\(^{94}\) | | | | |

| Fluconazole | ST | Cockatiel | 5 mg/kg PO q24 h or 10 mg/kg PO q48 h or 100 mg/L in the drinking water | Fluconazole has the safest therapeutic index of the azoles. | Described doses resulted in plasma levels that exceeded human MIC for most strains of *Candida albicans* generally less effective against aspergillosis than itraconazole.\(^{69}\) |

| Terbinafine | C | A\(^{75}\) | Hispaniolan Amazon parrot\(^{79}\) | 60 mg/kg q24 h | Regurgitation in red-tailed hawk\(^{80}\) | Often combined with azoles\(^{71}\) |
| --- | --- | --- | --- | --- | --- | --- |
| | | Cr\(^{78}\) | Red-tailed hawk\(^{80}\) | 22 mg/kg q24 h | | Dose should be decreased in cases on impaired renal function\(^{57}\) |
| | | | African penguin\(^{81}\) | 15 mg/kg q24 h | | |

*Abbreviations:* A, *Aspergillus* spp; C, Fungicidal ST; Cr, *Cryptococcus* spp; Fungistatic MIC, minimum inhibitory concentration; PO, by mouth; q, every.

*Data from Refs.*\(^{57,69,71,72,75,78-95}\)
Succimer (meso 2,3-dimercaptosuccinic acid or DMA) is an oral chelator, derived from British Anti-Lewisite capable of chelating lead from soft tissues, but not from bone. \(^\text{107}\) Succimer is less efficient in cases of zinc intoxication. \(^\text{101}\) Succimer has a narrow margin of safety, so accurate dosing is important. Doses as low as 15 mg/kg have been reported to be effective. \(^\text{101}\) In an experimental trial with induced lead intoxication in cockatiels, a dose of 40 mg/kg by mouth every 12 hours was found to be safe, whereas a dose of 80 mg/kg by mouth every 12 hours was associated with a high mortality rate. \(^\text{106}\)

**Treatment of intoxication by drugs or plants**

Potentially nephrotoxic drugs include aminoglycosides, \(^\text{48,49}\) fenbendazole, \(^\text{108}\) and nonsteroidal anti-inflammatory drugs, such as diclofenac \(^\text{109}\) and flunixin meglumine. \(^\text{110}\) Ingestion of rhubarb leaves and other oxalic-acid rich plants can also cause kidney failure. \(^\text{102}\)

Treatment options for intoxications include crop lavage \(^\text{111}\) or endoscopic removal of plant material when birds are presented within 1 to 6 hours of ingestion, depending on the avian species. \(^\text{112–115}\) Fluid therapy and supportive care are also indicated. Some authors recommend the use of activated charcoal (1 g/kg or 1–3 mg/g body weight) as an adsorbent. \(^\text{102}\) This treatment is not recommended for acids or corrosive alkaloid agents because it will be useless and may complicate retrieval from the crop. For more information regarding treatment of avian intoxications, the reader should refer to the excellent review by Lightfoot and Yeager. \(^\text{116}\)

**Treatment of Nutritional Diseases Affecting Renal Function**

**Hypovitaminosis A**

Vitamin A deficiency is commonly reported in companion parrots fed seed-based diets. \(^\text{20}\) Hypovitaminosis A can lead to squamous metaplasia of renal epithelium, ureteral mucosa, and collecting ducts leading to obstruction of the ureters and secondary hydronephrosis, hyperuricemia, and oliguric or anuric renal failure. \(^\text{44}\) Vitamin A may be supplemented at 2000 to 5000 IU/kg intramuscularly, then repeated every 1 to 3 weeks depending on patient condition and response. Of note, fat-soluble vitamin A is considered safer than water-soluble vitamin A. \(^\text{117}\) Vitamin A supplements are also available in powder form. Beta-carotenes and other provitamin A carotenoids can serve as a safer alternative to potentially toxic vitamin A in psittacine birds. \(^\text{20}\) Seeds and nuts are generally low in carotenoids, whereas some orange-colored fruits and vegetables, such as carrots, melon, and butternut squash, can provide large quantities thereof. \(^\text{14}\) A study in cockatiels demonstrated that vitamin A deficiency can be prevented with 4000 IU vitamin A/kg diet or 2.4 mg β-carotene/kg diet. \(^\text{118}\) Levels of less than 10,000 IU vitamin A/kg do not significantly influence plasma levels in cockatiels. \(^\text{116}\) Some avian species, such as recessive white canaries (Serinus canaria), are unable to convert β-carotene to vitamin A and require 3 times as much vitamin A as colored canaries. \(^\text{119}\)

**Hypervitaminosis D**

Excess vitamin D\(_3\) promotes metastatic mineralization of viscera, including the kidneys. Vitamin D\(_3\) is considered toxic at 4 to 10 times the recommended dose. Any bird species can potentially be susceptible to hypervitaminosis D \(^\text{16}\); however the dietary requirements for vitamin D vary among avian species, with optimum levels at 200 IU/kg in poultry, 900 IU/kg in turkey, and 1200 IU/kg in Japanese quail. \(^\text{14}\) In cases of hypervitaminosis D associated with hypercalcemia, fluid therapy and treatments stimulating calciuresis, such as bisphosphonates and corticosteroids, are recommended in dogs and cats. \(^\text{120,121}\) Unfortunately, the use of corticosteroids is controversial in
birds owing to the risk of associated immunosuppression and safe doses of bisphosphonate have not been described in birds. Because metastatic calcifications are irreversible, prognosis is guarded.

**Iron overload**

Iron storage disease results from the accumulation of iron in various tissues, including the kidneys. High dietary iron has been implicated in the development of iron storage disease in susceptible species, such as hornbills, toucans, lories, and lorikeets, as well as mynahs and other Sturnidæ. It is generally recommended that the iron content of commercial diets be maintained at less than 100 mg/kg. Iron-sensitive species require even lower amounts of iron, ranging from 19 to 25 mg/kg. The high vitamin C content of many fruits also enhances dietary iron uptake. Frugivorous species should be offered fruits low in vitamin C to minimize uptake of iron from commercial diets. Another common strategy is to soak commercial pellets in black tea (first discard the water after initial infusion to avoid caffeine administration, then add water again to the cup and let the pellets soak) to increase the amount of tannins in the food and thereby decrease iron absorption. Soaking should be done every other month to avoid causing other mineral deficiencies.

In case of renal hemochromatosis, treatments described in birds include therapeutic venipunctures to decrease hematocrit, oral deferiprone, or intramuscular deferoxamine injections (Table 4).

**Treatments for Obstruction of Outflow**

The underlying cause for urate concretions, such as a cloacolith or ureterolith, is rarely known. In rare instances, changes to digestive microbial flora may affect the cloacal environment and contribute to the formation of cloacoliths. A cloacolith composed of 100% uric acid was reported in a blue-fronted Amazon parrot fed a mixture of table food, seeds, and pellets. Cloacoliths can obstruct the ureteral opening and cause postrenal hyperuricemia. Cloacoliths can usually be disintegrated and removed with forceps via the cloaca with or without endoscopic assistance.

Ureteroliths have also been described in a double yellow-crowned Amazon parrot (Amazona ochrocephala), a chestnut-bellied seed finch (Oryzoborus angolensis), and in poultry. Imbalances in dietary calcium and phosphorus content and coronavirus infection are reported causes of urolithiasis in poultry. Treatment of ureteroliths requires a surgical approach; lithotripsy may be an alternative treatment option.

**Treatment of Renal Neoplasia**

Kidney neoplasms have been reported in several avian species; however, budgerigar parakeets are overrepresented and renal neoplasms account for 17% to 20% of all neoplasms described in this species. Renal carcinoma is the most common renal neoplasm reported. Other renal neoplasms reported include renal adenoma, nephroblastoma, cystadenoma, and lymphoma.

Nephrectomy is the treatment of choice for unilateral renal tumors in dogs. In birds, unless the renal neoplasm is contained and pedunculated, surgical removal is virtually impossible because of the kidney’s dorsal location, its intricate relationship with adjacent vessels and nerves, the limited access to the renal arteries, and the short distance between the renal artery and the aorta, which make ligation or hemostasis difficult if not impossible. Regional invasion by renal neoplasms into the synsacrum bone and sacral nerve plexus is also reported, precluding surgical excision.
| Therapeutic agent | Species | Doses | Action | Adverse effects | Comments |
|-------------------|---------|-------|--------|----------------|----------|
| Deferiprone       | Chickens and pigeons | 50 mg/kg PO q12 h | Significantly reduced iron concentration in liver and feces | Weight gain, decreased serum zinc levels, 30% mortality in chickens | Good gastrointestinal absorption at this dose |
|                   |         | 70 mg/kg PO q24 h | Significantly reduced iron concentration in liver and feces | Weight gain, decreased serum zinc levels, 30% mortality in chickens |          |
|                   | Hornbills (n = 3) | 75 mg/kg PO q24 h for 90 d | Significantly decreased hepatic iron concentration | | |
| Deferoxamine      | Chestnut-fronted macaw (Ara severa) (n = 1) | 50 mg/kg IM q12 h for 14 d | Reduced hepatic iron concentration | | Associated with a low-iron diet |

Abbreviation: PO, by mouth; q24 h, every 24 hours.
Data from Refs. 125-127
No effective therapy for the management of renal tumors is recognized in birds. Palliative treatment is often selected, including the use of analgesics (see Pain management) and corticosteroids. Corticosteroids may predispose birds to opportunistic infections and should be used with caution. Prophylactic antibiotic and antifungal therapy are recommended whenever immunosuppressive drugs are used in avian species.

In mammals, chemotherapy has not been shown to be effective against renal tumors other than lymphosarcoma. Chemotherapy has not been thoroughly evaluated for avian renal tumors. Carboplatin was used to treat renal adenocarcinoma in a budgerigar, resulting in a short-lived clinical improvement but the mass continued to grow. In this case, carboplatin was used at 5 mg/kg IV every 4 weeks without side effects. A few cases of lymphocytic leukemia affecting the kidneys and treated with chemotherapy have been described in psittacine birds.

Radiation therapy for renal tumors has been rarely performed owing to questionable tolerance of adjacent tissues. In the case of a black swan (*Cygnus atratus*) presented with chronic T-cell lymphocytic leukemia affecting the kidneys, whole body radiation therapy with 2 Gy was performed over 31 days, in addition to chemotherapy with chlorambucil, followed by lomustine, l-asparaginase, and prednisone. The swan survived more than 1 year after treatment initiation and was euthanized owing to hyperviscosity syndrome associated with the leukemia. The white blood cell count decreased after radiation therapy and no adverse effects to radiation were detected clinically or at necropsy in this swan. The dose received was much lower than tolerable radiation doses evaluated in ring-necked parakeets (*Psittacula krameri*). Further studies are needed on the use of radiation therapy in birds for radiosensitive neoplasms.

**SUMMARY**

The clinical management of bird with renal disease may prove challenging. Treatment choice is highly impacted by the cause and chronicity of the disease. The specific physiology of avian kidneys, and the large variety of species encountered in clinic implies that only a small part of the knowledge about mammalian therapeutics can be extrapolated to birds. More studies on renal disease treatments and their specific applications are warranted.

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