CHAPTER

16

Evaluating and Treating the Kidneys

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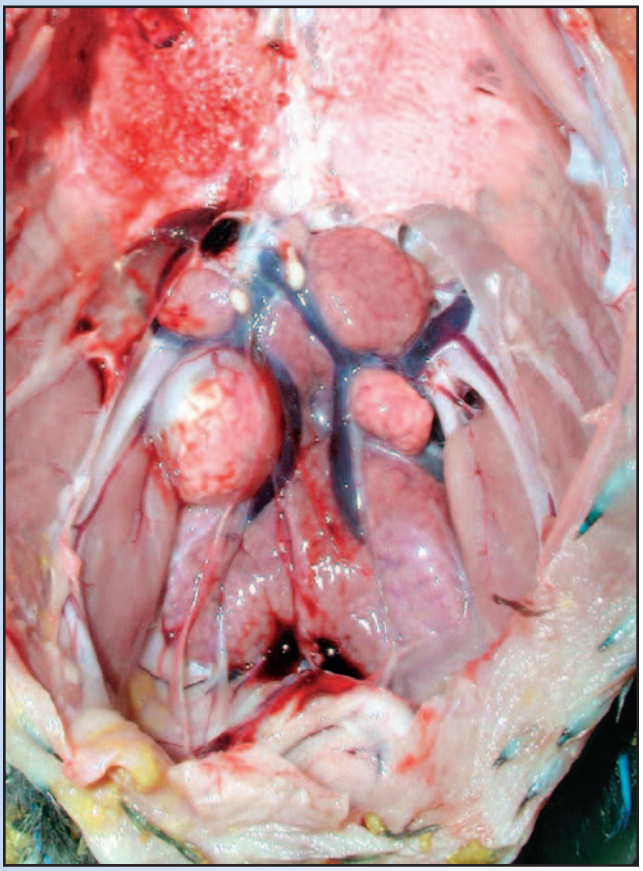

Renal diseases and their various classifications are well documented in the avian literature. The precise pathogenesis of avian renal disease, however, is not nearly as well described as it is in mammals. Renal disease has been shown to be fairly common in avian species. In studied poultry, as much as 29.6% of all disease conditions had abnormal pathology associated with or attributable to renal disorders.[20,214,251] Amyloidosis, urate nephrosis and gout were the most common diseases associated with mortality in a 4-year retrospective study conducted at a waterfowl park in Ontario, Canada.[210] Thirty-seven percent of all avian cases presenting with renal tissue for histopathological examination, included over a 15-month period at the Schubot Exotic Bird Health Center, had one or more histologically identified kidney lesions.[187] Nine of 75 pheasants (*Phasianus colchicus*) died with nephritis, one or both ureters impacted, and visceral gout in another comprehensive study on avian mortality.[186] These case reports and retrospective studies support the conclusion that renal diseases are relatively common and are clinically significant in multiple avian species.

When compared to mammalian counterparts, the avian urogenital system has many structural and functional differences, which have been described previously.[77,90,118,181,187,227] Differences including gross anatomy, renal portal blood flow and protein waste elimination should be considered when reviewing this chapter, as findings obtained from mammalian studies may not necessarily be applicable to birds. By better understanding the pathophysiology of renal disease, practitioners will be able to better diagnose, clinically evaluate and treat kidney disorders in birds.

Part one of this two-part chapter will combine mammalian and avian literature to help describe the pathogenesis and progression of renal disease. Various forms of specific kidney disorders that have been reported in birds are described. Discussions of treatments will be deferred to the second half of this chapter.

Part two will focus on methods of diagnosis and management of specific avian renal diseases. Many of the diagnostics and treatments discussed are rationalized and based on avian renal anatomy, physiology and an understanding of the pathophysiology behind kidney disease, all of which are covered in the first half of the chapter.

PART 1: Pathophysiology, Pathogenesis and Classification of Avian Renal Disease

ANATOMY

Kidneys

The avian renal system is quite unique among vertebrate kidneys. In-depth discussions of gross and microscopic avian kidney anatomy have been covered elsewhere as referenced, but pertinent features will be discussed here.[27,38,39,90,113,141] In general, avian kidneys comprise 1 to 2.6% of body weight compared to an average of 0.5% of body weight in mammals.[77] Kidney mass also is relatively larger in those birds with active salt glands.[77,110] At least in Pekin ducks (*Anas platyrhynchos*), females have more and larger nephrons and bigger kidneys relative to body mass.[15] Finally, the left kidney in laying hens tends to be heavier and have a higher rate of renal portal blood flow than the right.[248]

Birds have paired kidneys located within a cavity formed by the ventral surface of the synsacrum. The kidneys extend from the caudal edge of the lungs to the caudal synsacrum.[36] An abdominal air sac diverticulum extends between the synsacrum and kidney. Normal bird kidneys are surrounded by air.[36] In most birds, the kidney is composed of three divisions: cranial, middle and caudal. Figs 16.1a,b demonstrate basic gross renal anatomy. The middle and caudal renal divisions of most passerines are fused, while the caudal renal divisions are connected across the midline in herons, puffins and penguins.[36] Additional variations in gross renal anatomy can be found in other avian species.

Within each division are numerous renal lobules, each containing a cortex and a cone-shaped medulla (medullary cone). Avian medullary cones have no inner and outer regions as described in most mammalian kidneys.[40]

One of the most unique features of avian kidneys is the presence of two types of nephrons, with and without a loop of Henle.[38] The loop of Henle allows for urine concentration and is the primary reason that birds and mammals are the only classes of vertebrates that can consistently produce hyperosmotic urine.[38,39] In birds, only about 10 to 30% of the nephrons are of the mammalian type.[40,77,141,248] Most avian nephrons are loopless ("reptilian" type) and stay within the cortex.[141] The looped nephrons ("mammalian" type) extend from the cortex into the discrete medullary areas known as medullary cones. Since birds have primarily "reptilian" type nephrons, which produce isoosmotic urine, urine concentration is limited.

Neurovascular System (Including the Renal Portal System)

The vascular system surrounding avian kidneys is quite complex and is one of the main reasons that renal surgery is difficult in birds. Another unique feature of avian kidneys is the presence of an arterial and venous, or dual, afferent blood supply.[141] (See Figs 16.1a-e for anatomy of the gross renal neurovascular system). The arterial afferent blood supply to the kidneys is as follows. The cranial renal division is supplied by the cranial renal arteries, which branch off the aorta. The glomeruli and postglomerular tubular network of the middle and caudal renal divisions are supplied by the middle and caudal renal arteries, which branch off the ischiadic or external iliac arteries.[77,141]

The renal portal system forms the second afferent blood supply, which is venous, to the kidneys.[141] The external iliac, ischiadic and caudal mesenteric veins supply blood to the renal portal system.[248] A ring is formed on the ventral side of the kidneys by the cranial and caudal portal veins, which branch off the external iliac and common iliac veins.[141]

The renal portal system works by either directing blood to or shunting it past the kidneys as directed by the renal portal valve. For example, venous blood from the limbs is shunted straight to the caudal vena cava when the renal portal valve, within the common iliac vein, is open.[141] The opposite is true when the renal portal valve is closed, as venous flow from the legs is directed to the afferent venous system of the kidneys.[129] This, of course, means that blood may pass through the kidneys prior to any other organ. Additional shunting either to the caudal mesenteric vein (caudally) or internal vertebral sinus

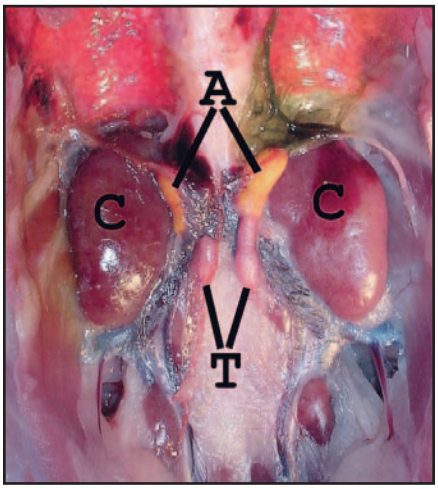

Fig 16.1a | Gross renal anatomy of a normal immature male red-tailed hawk (*Buteo jamaicensis*) that died from head trauma. Note the testes (T), adrenal glands (A) and cranial renal divisions (C). This hawk has a moderate amount of fat covering the middle and caudal renal divisions.

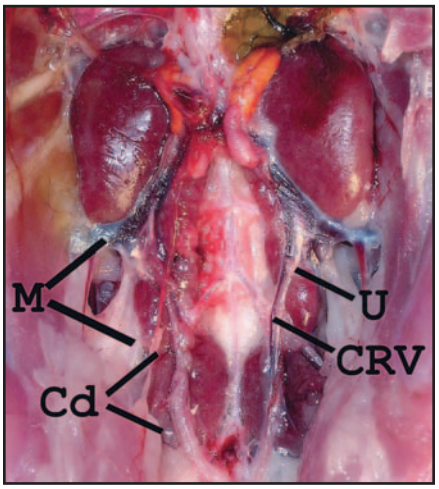

Fig 16.1b | The excess ventral perirenal fat has been removed. The middle (M) and caudal (Cd) renal divisions are now visible. The immature ductus deferens runs alongside the ureter (U) and caudal renal vein (CRV), but is not distinguishable in this young bird.

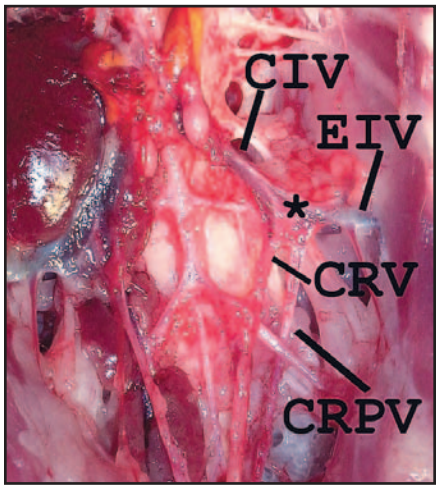

Fig 16.1c | The left kidney, ductus deferens and ureter have been removed, leaving the large vascular structures intact. The external iliac (EIV), caudal renal portal (CRPV), caudal renal (CRV) and common iliac (CIV) veins and the approximate location of the renal portal valve (*) are identified.

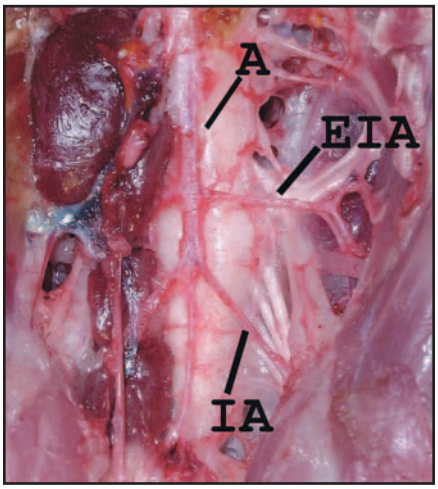

Fig 16.1d | The venous system has been removed to demonstrate the aorta (A), external iliac (EIA) and ischiadic (ischiatic) (IA) arteries.

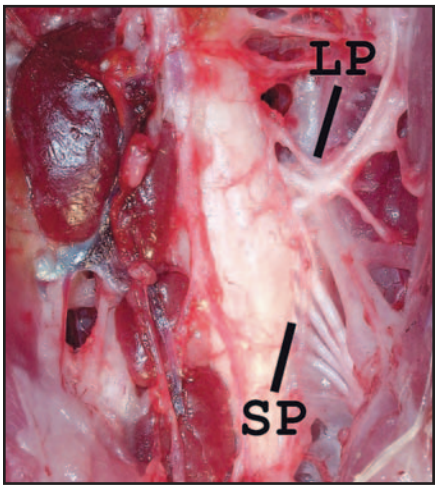

Fig 16.1e | The left renal, vascular, reproductive and endocrine systems have been removed, revealing the overlying renal fossa of the synsacrum and lumbar (LP) and sacral plexi (SP).

(cranially), again bypassing the kidneys, also may occur once blood has entered the renal portal ring.

By route of the afferent caudal and cranial renal portal vein branches, blood is delivered to the peritubular capillary network.[141] While virtually all renal arterioles terminate in the glomerular capillary beds, renal portal blood flow does not.[248] This system allows only arterial blood into the glomeruli and both postglomerular arterial and renal portal vein venous blood to the renal tubules. Blood is ultimately drained out of the kidneys via the centrolobular to the cranial and caudal to the renal and finally common iliac veins just proximal to the renal portal valve.[141]

This unique system accounts for some clinical concerns.[141] First is the fact that blood can be directed from the lower limbs straight into the renal parenchyma. This may increase the effect of nephrotoxic drugs and/or enhance elimination by taking the compound directly to the kidneys. Some drugs eliminated by tubular secretion and given into the leg may enter the renal portal system and be eliminated without ever entering systemic circulation.[223] As a general rule, parenteral drugs probably should be given in the cranial half of the body. Because some of the venous afferent blood comes from the caudal mesenteric vein (*v. coccygeomesentericae*), which drains the lower intestines, alimentary tract disease may ascend into and have an effect upon the kidneys. As

addressed under Part 1: General Mechanisms and Consequences of Renal Injury, Gastrointestinal Complications, the effect of lower intestinal disease upon the kidneys should be considered and treatment such as antibiotics for colitis instituted.

Hemodynamics

Studied birds have an impressive ability to maintain renal blood flow, even with severe hemodynamic alterations. Chickens seem to be able to "autoregulate" (keep constant) glomerular filtration rate when the arterial blood pressure range is within 60 to 110 mmHg.[73] Arterial pressures below this "autoregulatory" range result in decreased glomerular filtration rate until urine flow ceases at pressures below 50 mmHg.[73] Also of interest is that renal perfusion does not decrease in chickens (*Gallus domesticus*) until nearly 50% of the blood volume has been removed.[23] Despite severe hemorrhage, birds are able to maintain their blood pressure, suggesting other compensatory mechanisms such as extravascular fluid mobilization are utilized to ensure normal renal blood flow.[23]

Local Renal Neurologic System

The lumbar and sacral nerve plexi are closely associated with the kidneys. The lumbosacral plexus is formed by the ventral rami of about eight spinal nerves.[180] From these rami, the first three form the lumbar plexus, which produces the femoral and obturator nerves. In turn, these nerves provide innervation to the stifle extensors and leg adductors.[180] The lumbar nerve plexus forms dorsal to the cranial renal division and exits the pelvis cranial to the hip joint.[59]

The sacral plexus is formed by the caudal five to six spinal nerve ventral rami.[180] These nerves go on to supply innervation to the lower leg and some of the proximal leg muscles. The sacral plexus runs through the middle renal division parenchyma and exits the pelvis via the ischiadic foramen.[59,180]

Pressure on the nerve plexi can result in non-weight-bearing lameness.[180] This is the reason why some birds with renal diseases, especially those that cause renomegaly such as cancer, result in one-leg lameness in clinically affected birds. Other causes of one-leg lameness in birds include egg-laying disorders, bumblefoot, testicular cancer and trauma, and should be considered before making a diagnosis of renal disease.

Salt Glands

Salt glands are present in almost all birds, but have important functional significance in waterfowl, marine birds, and some raptors and desert avian species.[15,34,200,213] Birds have limited ability to produce hypertonic urine. As a compensatory mechanism, the extrarenal salt glands allow birds to adapt to brackish and saline environments and maintain normal electrolyte balance. There is likely an intimate association between renal function and extrarenal NaCl excretion.[110]

In chickens, the gland appears vestigial, but its anatomical features have been studied. The (supraorbital) salt gland is approximately 2 cm long and 2.5 mm in diameter. The caudal portion is located above the orbit, adjacent to the frontal bone, while the rostral extent is in the lateral wall of the nasal cavity, next to the dorsal and medial turbinates.[200] The salt gland's draining duct crosses under the nasal cavity and opens from the nasal septum, adjacent to the rostral part of the ventral turbinate, into the nasal cavity.[200] Fluid is then removed by shaking movements of the head or by passively dripping from the tip of the beak.[213] Similar features also have been noted in the turkey nasal salt gland.[200]

The salt glands function by providing an extrarenal pathway for the excretion of sodium chloride when the bird must consume salt quantities greater than its relative ability of renal clearance.[34,110] In some birds, the secreted sodium chloride can reach 10 times plasma concentrations.[213] The salt glands may remove more than 20% of the sodium chloride delivered by blood and have been considered one of the most efficient ion-transporting organs in the animal kingdom.[213] One reference notes that active salt glands can remove 60 to 88% of sodium and chloride eliminated by the bird's body.[77] Salt encrustation may be noted around the nares of dehydrated, heat-stressed birds and represents a gross manifestation of the gland's function.[141]

The gland size depends on the bird's salt consumption, and a hyperplastic response is considered normal in some species.[213] By adding high levels of sodium to the drinking water, salt gland hyperplasia can be induced in aquatic birds, but not in chickens.[200] In general, birds exposed to little salt have small salt glands. Once a bird is exposed to high salt loads, there is a rapid and profound hyperplasia and hypertrophy response that results in a greatly enhanced salt-secretory capacity within 1 to 7 days.[213]

Diseases of the salt glands are rarely described. This may imply that salt glands either are infrequently evaluated or are truly uncommonly affected by disease conditions. One study found that domestic ducks induced with plumbism had high concentrations of lead in the salt glands.[34] The authors hypothesized that in ducks, salt glands are involved in the elimination of lead. Also, lead toxicity results in obvious renal impairment and possibly damages the salt glands, making it difficult for wild waterfowl to adapt to different saline environments.[34] High cadmium intake significantly increased salt gland

mass in Pekin ducks (*Anas platyrhynchos*) and, combined with the toxic renal effects, was believed to adversely affect osmoregulation.[15] Salt gland enlargement from hyperplasia and inflammation are noted incidentally in range-reared tom turkeys.[200] Reported clinical signs are mild and consist of localized or unilateral swelling above the eye.[200]

PHYSIOLOGY

Roles of the Avian Kidney

Undoubtedly, the kidneys play numerous vital roles in birds. One primary role of the kidney is elimination of metabolic wastes. The kidneys also aid the liver in detoxification.[248] Because the kidneys are responsible for eliminating numerous metabolites, tissue concentrations of antibiotics (apramycin and ciprofloxacin) and toxins (lead and cadmium) are often highest in renal tissue.[3,7,10,178] As a result, various compounds are best identified and quantified in the kidney tissue.

Renal regulation of water via electrolyte (Na^+, K^+, Cl^-) balance is essential to maintaining intra- and extracellular fluid volumes and osmolalities.[248] By regulating fluid volume, the kidneys also regulate blood pressure. Arginine vasotocin is likely the primary mediator in response to dehydration, but norepinephrine, aldosterone, rennin, angiotensin II and prolactin also may each have an effect on avian kidneys and osmoregulation.[27,88,89,96,131,204,205]

The avian kidney has other endocrine functions and it is likely that future studies will elucidate more roles of this complex organ. One function of the kidney is the production of the active form of vitamin D (1,25- $[OH]_2D_3$) via the renal enzyme ($25[OH]D_3$)-1-hydroxylase.[66,244] Parathyroid hormone also has been shown to have a profound effect on renal excretion patterns of calcium and phosphate in birds.[61,70] As a result, the kidney is partly responsible for mineral metabolism.[248] The avian kidney also is the target organ for numerous growth factors, the functions of which are not yet known.[57] In addition to production in the liver, chick kidneys secrete apolipoproteins and are believed to contribute to the plasma lipoprotein pool.[232] This may be a functional response to the lipids coming from the terminal ileum, via the renal portal system, that contributes to production of lipoproteins.[232]

Fluid Regulation

Fluid regulation in birds is complex, as is true in many other animals. Birds have the ability to absorb and secrete various electrolytes and nutrients, which have some effect on fluid regulation. These osmoregulatory mechanisms are covered in depth in other references.[38,39,90,223,248] As mentioned previously, birds have the ability to produce concentrated urine, but because avian nephrons are primarily loopless, urine concentration within the kidney is limited. In birds, the process for concentrating urine is believed to be similar to that in mammals, but in avian species, sodium chloride acts as the major solute, not urea or potassium. The end effect is that sodium chloride does not have as much osmotic force as does urea, further limiting the concentration of avian urine.[223] Although birds inhabiting arid environments generally produce more concentrated urine than those from the tropics, many exceptions exist.[38,39] This leads to other water conservation methods that are variable between species.

In response to dehydration in birds, glomerular filtration and urine flow rate are consistently decreased while solute concentration increases. In studied birds, arginine vasotocin is the natural avian antidiuretic hormone and is believed to be the primary mediator in response to dehydration.[88,89,204] Increased plasma osmolarity is likely the major stimulus for release of arginine vasotocin.[131] Arginine vasotocin acts by controlling tubular water permeability, and thus the concentrating capacity of the avian kidney.[33]

As a component of water and possibly protein conservation, birds have the ability to absorb significant amounts of excreted (renal) water in the colon and ceca.[28] This system also allows some birds to regulate electrolyte loss through the urine.[248] The ureters empty into the urodeum where reverse peristaltic waves of the cloaca cause a reflux of urine into the cloaca and ceca, which are sites of water reabsorption.[28,220,236]

The amount of water reabsorbed is highly variable among different avian species. Rock ptarmigan (*Lagopus mutus*) ceca play a minimal role in digestion, but account for 98% of water absorbed in the hindgut.[252] In domestic turkeys (*Meleagris gallopavo*), 20 to 40% of the urine is refluxed into the ceca, from which 80% of all fluids that enter are absorbed. It has been shown that 77% of the water, 72% of sodium and 82% of potassium from ureteral urine in Gambel's quail (*Callipepla gambelii*) is subsequently reabsorbed in the ceca, lower intestine, cloaca and rectum.[28,252] In domestic fowl, it has been estimated that 13 to 28 ml/kg body weight per day of fluid is absorbed in the cloaca.[248]

Cecectomized birds often have changes in fluid regulation. Cecectomized Gambel's quail and great horned owls (*Bubo virginianus*) temporarily drank more water than controls. Water intake gradually returned to preoperative levels, suggesting a compensatory response either in the intestines or kidneys.[252] Cecectomized great horned owls and chickens also have shown a transient increase in water excretion (in the droppings).[220,252]

While the lower intestines appear to play a significant role in water and possibly electrolyte reabsorption, the ceca apparently do not have an obligatory role in osmoregulation in some species.[252] Additionally, many birds have no functional or anatomic ceca.

No studies were found that demonstrate the effect of lower intestinal disease on osmoregulation. Regardless, diseases such as typhlitis and colitis may adversely affect water and electrolyte balance beyond simple intestinal fluid loss, and should be a consideration when treating affected birds. Aside from nephrotoxic drugs such as aminoglycosides, no studies were found that show a clear correlation between antibiotic use for treatment of colitis/typhlitis and altered osmoregulation.

Uricotelism

Uricotelism is simply the excretion of uric acid as the end product of nitrogen metabolism. Birds lack carbamyl phosphate synthetase, an enzyme needed to synthesize urea from amino acid nitrogen.[99] While birds produce very little urea, the avian urea cycle is important, but is primarily related to renal detoxification processes and not nitrogenous waste excretion.[248] In birds, xanthine dehydrogenase is the terminal enzyme of purine metabolism and ultimately produces uric acid as the end product of nitrogen metabolism.[106,132] This is an adaptation that allows birds to minimize urinary water loss. Because uric acid is osmotically inactive, little water is required to excrete this nitrogenous waste.[248] The true advantage of water conservation in adult birds is debatable, though. The real advantage of uricotelism may simply be the storage of nitrogenous waste in eggs where a water-soluble product such as urea may prove toxic to the developing embryo.[248]

GENERAL MECHANISMS AND CONSEQUENCES OF RENAL INJURY

Initiation of Renal Disease

Proposed mechanisms of the process of initiation of renal injury and perpetuation of disease are complex, but have been described in mammals. These "mammalian" mechanisms may or may not apply directly to birds, but help form the basis on which some treatments are considered (see Part 2: Treatment, Nutritional Supplementation and Non-steroidal Anti-inflammatories). For this reason, some of the inflammatory cascade that occurs with renal disease is described.

The products resulting from the arachidonic acid cascade have effects throughout the body. For the purposes of this discussion, the cyclo-oxygenase pathway of the arachidonic acid cascade will be briefly covered.

In studied species, the renal medulla and papilla are a rich source of the group of enzymes collectively called prostaglandin synthetases.[62] The action of the prostaglandin synthetase cyclo-oxygenase upon arachidonic acid results in the formation of numerous prostaglandins (PE_2, PGF_{2a} and PGD_2) and thromboxanes (thromboxane A_2 [TXA] and thromboxane B_2), all of which have varying actions on cells. In response to renal ischemia and vasoconstriction, prostaglandin and thromboxane production is altered (primarily increased). These "alterations" subsequently result in varying effects on the body and kidney including changes in renal vascular resistance, blood flow, recruitment of inflammatory cells and other physiologic effects. Non-steroidal anti-inflammatories act to inhibit prostaglandin synthetase and represent another method by which to "alter" these arachidonic acid by-products and their subsequent actions.[62]

Specifically, TXA production, secondary to toxic or ischemic injury, is considered the main cause of renal vasoconstriction associated with acute renal failure and is believed to play a pathogenic role in many forms of kidney disease.[92,93,95] Thromboxane A_2, again an eicosanoid derived from the action of cyclooxygenase on arachidonic acid, is produced by many mammalian cells including glomerular epithelial and mesangial cells, renal medulla tubular cells and especially platelets.[91-95]

In mammals, TXA causes mesangial cell contraction and is a potent vasoconstrictor. Both of these actions can result in decreased glomerular filtration rate (GFR).[31,91,94,95] Renal vasoconstriction decreases GFR and delivery of oxygen and nutrients to tubular cells, resulting in renal damage.[95] Thromboxane A_2 also promotes platelet aggregation and may be partially responsible for hemostatic abnormalities noted with renal disease.[91,190] As histologic progression of renal disease continues when TXA is inhibited, it is possible that TXA only helps initiate kidney pathology.[93]

The above-described outcomes of increased TXA production serve only to show some of the possible negative effects of one by-product created as a result of renal injury. Management of these negative effects may be needed, especially when a clearly identified cause such as bacteria in the kidney parenchyma is not found. This then brings up the reasoning behind using products such as omega-3 fatty acids and low-dose NSAIDs (non-steroidal anti-inflammatory drugs) when managing some forms of renal disease.

Brief Review of Selected Potential Consequences of Renal Disease

Kidneys are dynamic organs and are directly or indirectly associated with multiple body systems. As a result,

renal disorders can lead to or be caused from multiple other disease processes. Some processes, such as hypertension, hypercoagulability and the nephrotic syndrome, are well described in mammalian renal disease, but are never or rarely discussed in the avian literature.

Hemostatic Abnormalities

Abnormalities of hemostasis are noted with some forms of renal disease and may lead to additional kidney or systemic disease. Platelet aggregation and activation occur secondary to complement activated antigen-antibody interactions and renal endothelial damage.[23,86,91,94] Activated platelets may then release vasoactive and inflammatory products (including TXA), growth stimulation factors and facilitate the coagulation cascade.[91,94] These reactions can result in glomerular damage via glomerular basement membrane thickening and, potentially, hyalinization and sclerosis.[94]

Fibrinous renal vessel thrombi have been noted in red-faced lovebirds (*Agapornis pullarius*) with membranous glomerulopathy and in chickens with *Erysipelothrix rhusiopathiae* sepsis. However, thrombus formation has been suggested to be rare in birds compared with mammals.[86,212] Using multiple staining methods, it could not be confirmed that fibrin-like thrombi noted histologically in various psittacine birds with polyomavirus-associated glomerulopathy were truly composed of fibrin.[189]

Gastrointestinal Complications

Gastrointestinal ulcerations are reported in some animals with uremia and advanced renal disease, but are rarely mentioned concurrently in clinical reports of birds with kidney disorders.[26] In chickens, gizzard erosions have been associated with naturally occurring urolithiasis.[148] Due to the overall lack of reports in the reviewed literature, it is unlikely that birds with renal disease develop gastrointestinal ulcers.

Intestinal inflammation may lead to renal disease. In humans, inflammatory bowel disease (IBD) can be related to renal disorders.[183] In humans, those with IBD have a 10 to 100 times greater risk of developing nephrolithiasis compared with other hospitalized patients.[183] Human IBD patients also may have an increased risk of glomerulonephritis and tubulointerstitial nephritis.[183] The avian coccygeomesenteric vein drains the mesentery of the hindgut into the hepatic portal and/or the renal portal vein.[226] Colitis may serve as a source of infectious agents, toxins and inflammatory products to the avian kidney if blood flow draining the colon is diverted into the renal vasculature. As a result, antibiotic therapy should be considered in all cases of colitis, especially when renal disease is suspected or confirmed.

Abnormal Lipid Metabolism

Aberrant lipid metabolism as evidenced by increased serum total cholesterol, low-density lipoproteins and triglycerides has been noted in humans, cats and dogs with renal disease.[31,179] In rats, lipid accumulation is known to stimulate glomerular mesangial cell and excess matrix production known as glomerulosclerosis.[31] Hyperlipidemia has been associated with glomerulosclerosis and/or loss of renal function in rats, guinea pigs, rabbits and dogs.[190] Glomerulosclerosis is histologically similar to atherosclerosis and may share a common pathogenesis.[190] Although scarcely noted in the avian literature, abnormal lipid intake, production and/or metabolism may be associated with renal disease in birds, as described below.

High-cholesterol diets actually may induce renal disease in birds. Pigeons supplemented with dietary cholesterol (0.2%, 0.4% and 0.5% of the diet) had a high incidence of end-stage renal disease, atherosclerosis and increased mortality rate compared with controls.[121] Although specific data was not presented, pigeon mortality was influenced largely by the degree and duration of hypercholesterolemia.[121] The implication herein is that diets high in cholesterol may lead to renal disease, at least in pigeons.

Gout

Renal disease may lead to numerous other conditions including gout, which can further damage the kidneys or additional body systems.[214] Gout reportedly may be caused by reduced excretion of urates or by increased dietary protein (although this has been disputed as discussed under Part 2: Treatment, Dietary Modification).[236] Dehydration and many forms of renal disease including obstructed ureters and general kidney damage can result in decreased uric acid elimination. As blood levels of uric acid rise and exceed the solubility of sodium urate in plasma (hyperuricemia), monosodium urate crystal precipitation is initiated.[236] It has been concluded that gout may not prove to be a nutritional disease in birds except under unusual circumstances such as deficiency of vitamin A.[207]

Visceral gout results secondarily from elevated plasma uric acid levels and its resultant deposition on visceral organs[9] **(Fig 16.2)**. During visceral gout, urate depositions are commonly found on the pericardium, liver and spleen.[134] Additionally, uric acid deposits are noted histologically within the lamina propria of the proventriculus, ventriculus and sometimes intestine and within the kidney, but can be found on or in any tissue. Visceral gout may appear as a white coating when on the capsular surface of affected tissue. Visceral gout has been associated with multiple forms of renal pathology.[9,214] Experimentally, visceral gout has been induced in chickens fed excessive

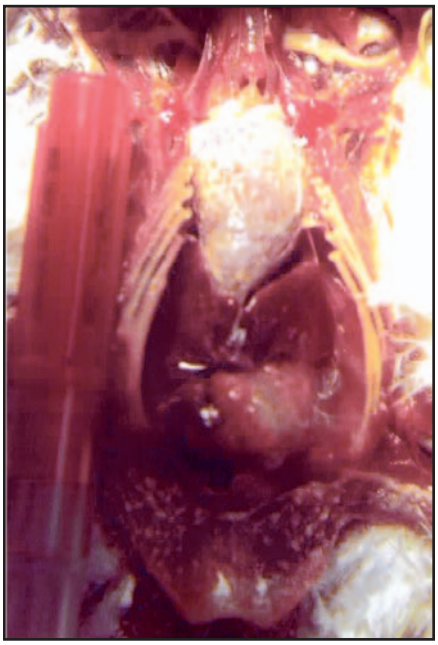

Fig 16.2 | An adult cockatiel (*Nymphicus hollandicus*) with visceral gout. Note the whitish deposits encasing the heart. The bird died with renal failure due to chronic renal fibrosis and interstitial nephritis.

Fig 16.3 | An adult budgerigar (*Melopsittacus undulatus*) with articular gout secondary to renal carcinoma. The postmortem picture shows subcutaneous "gouty" deposits over the dorsal tarsometatarsus and ventral phalanges. The skin has been teased open with a needle.

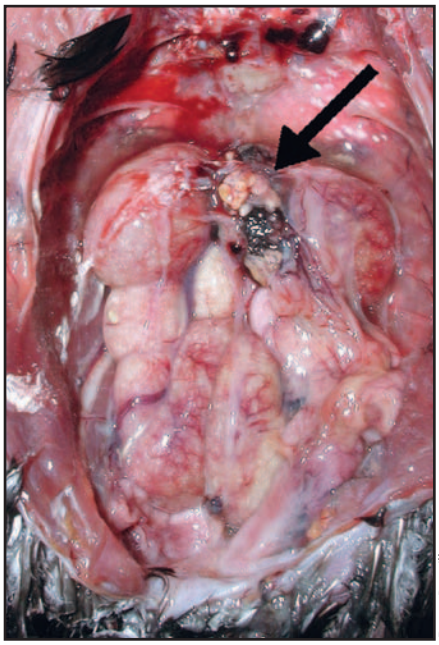

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Fig 16.4 | An adult female black lory (*Chalcopsitta atra*) with severe renomegaly and visceral and articular gout. This female recently laid two eggs, but the ovary (arrow) was quiescent at the time of death. Histologically, renal tubular necrosis with urate stasis and multiple acute "gout tophi" were noted. The etiology was not defined.

dietary calcium and a diet deficient in vitamin A, administered various nephrotoxic agents, and following ureteral ligation and urolithiasis.[9,214]

Articular gout results from the accumulation of urates in the synovial capsules and tendon sheaths of the joints[9] (Fig 16.3). Diffuse urate deposits on visceral surfaces do not occur in articular gout.[214] However, visceral and articular gout can be present in the same bird (Fig 16.4). Gross lesions typically consist of soft swellings on the feet at the metatarsophalangeal and interphalangeal joints.[214] These swellings appear to be painful, as noted in clinical cases. Spontaneous articular gout in birds without underlying renal pathology is relatively uncommon and appears to have a hereditary basis, at least in chickens.[214]

Continuing Damage

Once renal damage occurs, persistent and progressive kidney damage is likely to occur, even if the initial insult is treated and "cured."[114] In humans, 50 to 60% of children with pyelonephritis develop irreversible lesions of the renal parenchyma.[13] Although no refereed literature describes the post-treatment progression of renal lesions in living avian patients, the author reported repeated kidney biopsies in numerous birds in an effort to help evaluate their clinical progression.[64] Repeat biopsies have shown that in birds with histologic confirmation of various kidney diseases, some mild renal lesions persist, even if the patient is clinically normal or improved.[64] When repeating kidney biopsies, the author has noticed no increase in scarring (gross or histologic lesions) or other abnormalities at the prior surgery sites, suggesting some treated birds have good regenerative and/or healing properties. Although these repeat biopsies are encouraging, the long-term health of these patients' kidneys is still unknown.

GENERAL RENAL DISEASE CATEGORIES

Nephritis

Nephritis is simply inflammation of the kidney and may involve the interstitium, tubules and/or the glomerulus (although "glomerulonephritis" is typically reserved for glomerular lesions). While "pyelonephritis" has been described in birds, this term is technically incorrect, as avian species lack a renal pelvis.[116,214] Nephritis is a nonspecific description, but some histological patterns and (especially) identification of infectious organisms help define the etiology.

Glomerulopathies

In the literature reviewed for this chapter, glomerular disease has been loosely termed "glomerulonephritis," but unless inflammation is specifically present, the term "glomerulopathy" would be more appropriate. Glomeru-

lonephritis describes inflammation of the glomerulus, usually considered mediated by the deposition of immune complexes or antiglomerular basement membrane antibodies.[22,94,239] A more accurate description of glomerular lesions, based on light and electron microscopy and immunohistochemistry, helps define the actual type of glomerulopathy present.

Glomerular disease is the most important cause of end-stage renal disease in humans worldwide and of chronic renal insufficiency/failure in dogs.[109,237,239] Proteinuria is the hallmark sign of glomerulonephritis in mammals prior to the onset of clinical renal insufficiency.[94] However, chicken leukocytes lack proteolytic enzymes that would potentially damage the glomerular basement membrane (and allow protein leakage) and birds may, in fact, not develop pathologic proteinuria with glomerulopathies.[22] In one study, no pathologic proteinuria was found in chickens with experimental autoimmune glomerulonephritis.[21] As noted below, glomerulopathies are well documented in avian species, but numerous differences exist when comparing this disease in birds and mammals.

The cause of glomerulopathies is generally assumed to be immune-mediated, but the inciting etiology is often unknown. Membranous nephropathy, the most common cause of nephrotic syndrome in humans, is usually idiopathic and specific etiologies are identified in only 20% of cases.[196] With few exceptions, the causes of glomerulopathies in birds are poorly studied. Polyomavirus infection is associated with membranous glomerulopathy in psittacines.[86,189] Glomerular pathology has been noted in chickens with various septic conditions and naturally occurring multicentric histiocytosis.[102,219] Glomerulopathies also can be induced experimentally in chickens by intravenous fungal injections, *Plasmodium gallinaceum* infections and by feeding aflatoxin.[158,214] Grossly normal 6- to 7-week-old broiler chickens at slaughter have been diagnosed with proliferative glomerulonephritis of unknown etiology.[193] Proliferative glomerulopathy can be induced in pigeons fed diets high in cholesterol.[121] It has been suggested that because of the extensive (dual) renal blood supply, severe chronic glomerulonephritis may persist without any clinical manifestation in birds.[214] It has been further suggested that avian glomerulonephritis may be present in far more birds than it is currently diagnosed.[214]

Although humorally mediated immunity is frequently discussed as the etiology of glomerulopathies, research has strongly suggested that cell-mediated immunity plays an important role in producing glomerular disease in chickens and other animals.[22,109,237] Under experimental conditions, cyclophosphamide bursectomized (humorally deficient) chickens develop glomerulonephritis. Although gross histologic lesions are similar, bursectomized chickens develop no IgG glomerular basement membrane deposits compared to controls when glomerulonephritis is induced in both groups.[22] These and other findings support the conclusion that cell-mediated immunity or some other non-humoral immune response is responsible for inducing glomerulonephritis in chickens.[22,237] Interestingly, in the above described study, even birds with massive mesangial enlargement maintained normal glomerular filtration.[22] Due to the small centrally oriented avian glomerular mesangium, the capillary loops were only slightly displaced to the periphery without compromising function.[22] Given our current knowledge regarding the differences between avian and mammalian species, renal biopsy is the best way to definitively diagnose glomerular (and other) kidney diseases in birds (see Part 2: Diagnostic Tests, Biopsy).

Infectious Diseases

Bacterial

Certain patterns may be expected with bacterial nephritis. Chickens experimentally infected with *E. coli* (*E. coli* $0_1K_{67}[B_{12}]$), *Staphylococcus aureus* and *Actinomyces pyogenes* developed a fairly consistent pattern and progression of renal disease.[219]

Birds inoculated subcutaneously developed more severe renal lesions and these lesions were noted earlier than those exposed to bacteria per os. Additionally, lesions were more severe in birds infected with *E. coli* and *S. aureus* compared to the slight reaction induced from *A. pyogenes*. Gross renal changes included congestion, enlargement and hemorrhagic foci. Although specific timelines were not given in regard to lesion development, bird kidneys were histologically examined at 4, 7, 10, 14 and 21 days postinoculation. The early-stage lesions consisted of acute interstitial nephritis (mainly lymphocytes, plasma cells and macrophages), prominent congestion and hemorrhage. The lesions progressed to nephrotoxic nephritis and included tubular epithelial cell degeneration and necrosis with the formation of hyaline casts and eosinophilic material. Later histology showed decreased congestion, persistence of mononuclear cells, introduction of connective tissue running around hyperplastic tubules and glomerular lesions.[219]

Certain renal histologic characteristics, with or without organisms present, may suggest an ascending or hematogenous bacterial infection in the avian kidney. The typical lesions suggestive of bacterial nephritis include tubular dilatation and impaction with inflammatory cells.[214] As nephritis becomes chronic, tubular necrosis, cyst formation, distortion and interstitial fibrosis with mononuclear cell infiltration become evident.[214]

Using sterile collection and culture methods, bacterial nephritis is definitively diagnosed by recovering bacterial organisms from affected kidneys. Light microscopic identification of bacteria within renal tissue may be difficult, as has been noted in dogs and swine with renal disease.[26,54] In a *Coturnix* quail processing plant outbreak, *Erysipelothrix rhusiopathiae* was cultured from multiple organs.[169] While the kidneys were swollen and congested, no organisms were specifically noted histologically, which emphasizes the importance of tissue culture.[169] Specifically, *Escherichia coli* has been identified in chickens as a cause of bacterial nephritis (pyelonephritis).[116] As a component of systemic paratyphus, *Salmonella typhimurium* var. *Copenhagen* was identified in kidney tissue and most frequently caused interstitial nephritis in a study of 78 experimentally infected pigeons.[87] The same organism also was recovered from kidney tissue, as a component of systemic salmonellosis, in pigeons from a large production colony.[121] As is likely true of most viral and fungal renal diseases, bacterial nephritis is often a component of systemic infection and multiple organs may be involved.[187] In summary, any septicemia can potentially result in kidney infection and inflammation (Fig 16.5).

Viral

Viruses perhaps have the most varied effect on avian kidneys. Numerous viruses may infect and affect avian kidneys (Table 16.1). Histologic patterns are highly variable, as some viruses, such as pheasant coronavirus-associated nephritis, directly affect the kidneys while others, like psittacine herpesvirus and polyomavirus, damage renal tissue as part of a more systemic process.[126,186,202]

Other viruses may cause minimal to no renal disease, but can be identified in the avian kidney because of viremia and/or viral replication and transmission through the urinary tract. For example, the reovirus that causes viral arthritis of chickens infects the kidneys within a few days of inoculation, but causes minimal, if any, renal lesions.[174] Some viral infections such as the West Nile virus are best identified in the kidney, and provide an additional reason to save extra renal tissue (frozen and/or formalinized) for later testing[124] (Fig 16.6).

Parasitic

Renal Coccidia

Primary and secondary renal parasites have been noted throughout the avian literature and some contribute to significant morbidity and mortality[18,19,43,69,76,82,83,133,160,175,177,194,217,218,236,253] (Table 16.2). Renal coccidiosis, found predominately in some waterfowl and marine species, is the most frequently reported avian renal parasite in those

Table 16.1 | Viruses Known to Infect or Affect Avian Kidneys

Virus	Common Name	Renal Lesions	Reference(s)
Adenovirus	New gosling virus enteritis virus	Renal hemorrhage	44
	Hydropericardium syndrome in broiler chickens	Renal hemorrhage, tubular nephrosis	2
Astrovirus	Duck astrovirus (aka duck hepatitis II)	Swollen congested kidneys	202
Coronavirus	Infectious bronchitis virus	Interstitial nephritis, urolithiasis, visceral gout and renomegaly	202, 231, 243
Enterovirus	Avian nephritis virus	Renal disease of young chickens and turkeys	202
Herpesvirus	Marek's disease	Renal lymphoma, renal masses	202
	Psittacine herpesvirus	Renomegaly	202
	Pigeon herpesvirus-1	Renal necrosis	202
Orthovirus	Influenza A of ratites	Renomegaly and green urate-filled ureters	202
Paramyxovirus	Pigeon paramyxovirus-1	Renomegaly, lymphoplasmacytic nephritis	202
Polyomavirus	Hemorrhagic nephritis enteritis of geese	Nephritis	101
	Avian polyomavirus	Basophilic and amphophilic mesangial cell intranuclear inclusion bodies, minimal lesions	126
	Psittacine polyomavirus	Membranous glomerulopathy	202
	Passeriforme polyomavirus	Renomegaly and perirenal hemorrhage	202
Reovirus	Viral arthritis or tenosynovitis of chickens	None to minimal inflammation	174
Retrovirus	Avian Leukosis/lymphoid leukosis	Cancer-nephroblastomas, renal lymphoma/adenoma/carcinoma, leukemia	202
	Reticuloendotheliosis virus	Renal tumors	202
Togavirus	West Nile virus	Neptritis (Fig 16.6)	124
	Avian viral serositis (EEE)	Pale kidneys	202
	Chukar alphavirus (EEE and WEE)	Urate-distended kidneys	202
	Turkey alphavirus (EEE)	Renal necrosis	202
	Guinea fowl alphavirus (EEE)	Renomegaly	202
	Crane alphavirus (EEE)	Necrotic nephritis and visceral gout	202
	Emu WEE	Renomegaly, necrotic nephritis	202

This table should serve only as an example of the large variety of viruses known to be associated with the avian kidney.
EEE = eastern equine encephalitis WEE = western equine encephalitis

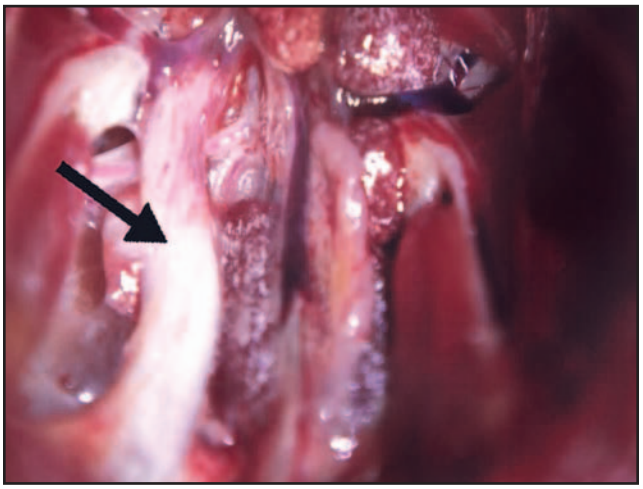

Fig 16.5 | A cloacal carcinoma, right ureteral obstruction (arrow) and *Streptococcus* sp. nephritis in an adult female *Amazona* sp. parrot. The *Streptococcus* sp. isolated from the kidney and heart blood was resistant to enrofloxacin, with which this bird was being treated chronically for cloacal straining.

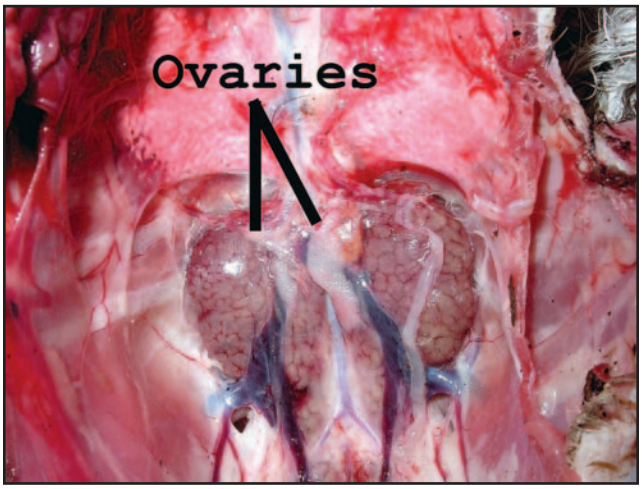

Fig 16.6 | West Nile virus-associated nephritis in an immature female Swainson's hawk (*Buteo swainsoni*). Note the moderate deposition of fat indicating the bird was in good overall body condition prior to acute death. The kidneys are pale. Two ovaries also are present as indicated by the lines.

Table 16.2 | Reported Incidence of Renal Coccidia in Various Avian Species

Affected Avian Species	*Eimeria* Species	Associated with Morbidity/Mortality	Reference(s)
Bufflehead (*Bucephala albeola*)	Unidentified	N/A	84
Canvasback (*Aythya valisineria*)	Unidentified	N/A	84
Duck, long-tailed (*Clangula hymenalis*)	*E. somateriae*	N/A	253
Duck, mallard (*Anas platyrhynchos*)	*E. boschadis*	N/A	253
Eider, common (*Somateria mollissima*)	*E. truncata*, *E. somateriae*	Mortality in ducklings (*E. somateriae*)	217, 253
Gadwall (*Anas strepera*)	Unidentified	N/A	84
Goldeneye, common (*Bucephala clangula*)	Unidentified	N/A	84
Goose, bar-headed (*Anser indicus*)	*E. truncata*	N/A	253
Goose, Canada (*Branta canadensis*)	*E. truncata*	N/A	253
Goose, domestic (*Anser domestica*)	*E. truncata*	Mortality in goslings	83, 84, 177
Goose, greater snow (*Chen caerulescens*)	*E. truncata*	N/A	253
Goose, graylag (*Anser anser anser*)	*E. truncata*	Mortality in goslings	177, 253
Goose, lesser snow (*Chen caerulescens caerulescens*)	Unidentified	Mild morbidity	83
Goose, Ross's (*Chen rossii*)	*E. truncata*	N/A	253
Gull, black-headed (*Larus ridibundus*)	*E. renicola*	N/A	82
Gull, herring (*Larus argentatus*)	*E. wobeseri, E. goelandi*	Incidental finding, nestlings	82
Loon, common (*Gavia immer*)	*E. gaviae*	Inconclusive	82, 160
Oldsquaw (*Clangula hyemalis*)	*E. somateriae*	Unlikely	76
Owl, great-horned (*Bubo virginianus*)	Unidentified	N/A	253
Penguin, little (*Eudyptula minor*)	Unidentified	Mortality	176
Pintail, northern (*Anas acuta*)	Unidentified	N/A	84
Puffin, Atlantic (*Fratercula arctica*)	*E. fraterculae*	Incidental findings, nestlings	133
Redhead (*Aythya americana*)	Unidentified	N/A	84
Scaup, lesser (*Aythya affinis*)	Unidentified	N/A	84
Shearwater, Cory's (*Calonectris diomedea*)	Unidentified	N/A	253
Shearwater, short-tailed (*Puffinus tenuirostris*)	Unidentified	N/A	253
Shoveler, northern (*Anas clypeata*)	Unidentified	N/A	84
Swan, mute (*Cygnus olor*)	*E. christianseni*	N/A	253
Swan, whistling (*Cygnus columbianus*)	Unidentified	N/A	84
Teal, blue-winged (*Anas discors*)	Unidentified	N/A	84
Teal, green-winged (*Anas crecca*)	Unidentified	N/A	84
Widgeon, American (*Anas americana*)	Unidentified	N/A	84
Woodcock (*Scolopax minor*)	Unidentified	N/A	253

N/A = not available

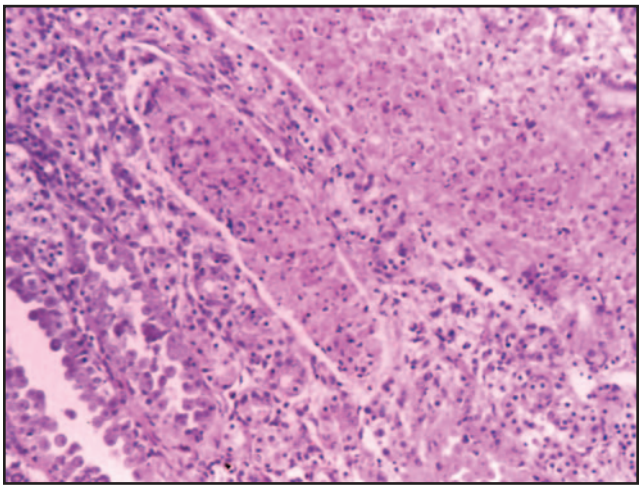
Robert E. Schmidt

Fig 16.7a | Renal coccidiosis in a screamer (*Chauna* sp.). Note the numerous oocysts and various developing stages of the parasite throughout the renal tubules.

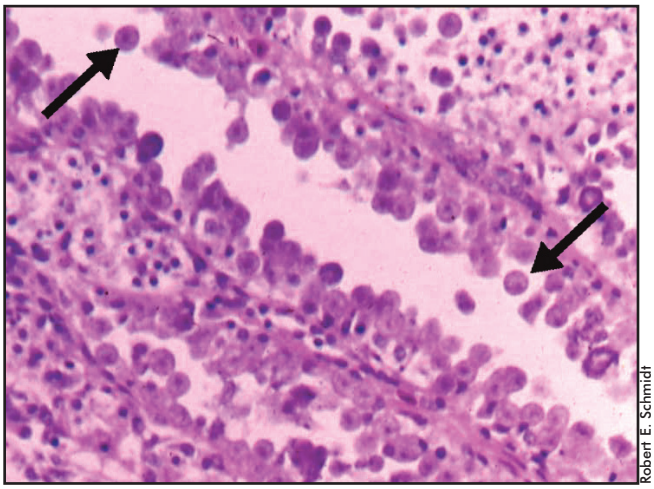
Robert E. Schmidt

Fig 16.7b | Close up of a renal tubule with numerous oocysts being released into the lumen (arrows).

species and has been clearly associated with disease in some cases.[76,82-84,133,160,176,177,217,253] Reports of various other parasitic diseases affecting the kidneys are noted, but their significance is not well established.

Several renal coccidia species have been identified and primarily include *Eimeria truncata*, *E. somateriae*, *E. christianseni*, *E. boschadis*, *E. gaviae*, *E. fraterculae*, *E. goelandi* and *E. wobeseri*.[82,83,133,160] Disease has ranged from mild histologic changes found incidentally (most species) to acute renal failure and death, such as in juvenile eiders (*Somateria mollissima*) and domestic geese (*Anser domestica*).[76,83,217] Flock mortality in domestic geese due to *E. truncata* has been reported to be as high as 87%.[76]

Renal *Eimeria* spp. oocysts are passed in feces via the ureter and sporulate rapidly in the environment.[217] Affected birds typically breed in large colonies or are otherwise under crowded conditions, which likely favors transmission of this parasite.[177,217] The prepatent period appears to range between species and has included 5 to 21 days.[83] Although transmission between different avian species is not clear, one study suggested that renal coccidia of geese do not infect ducks.[83]

The clinical gross and histologic abnormalities noted with renal coccidiosis seem to be fairly consistent across affected species. Most clinically affected species are young birds.[177,217] Clinically affected birds are typically emaciated and may have diarrhea with or without blood.[83,160,177,217] It should be kept in mind that many reported birds are wild and also have had intestinal parasites that may contribute to the described clinical signs. Grossly, the kidneys are often enlarged with white to yellowish nodules containing urates and/or oocysts.[76,83,160,217]

Cytologic smears of renal tissue and ureters often contain different endogenous stages of coccidian oocysts.[160,177,217] The renal tubules are parasitized and histologic lesions vary from mild dilatation to severe tubular destruction with associated degrees of inflammatory cell infiltrate (unusually mononuclear).[76,83,160,177,217] The tubules are often distended with endogenous developmental stages (micro- and macrogamonts, macrogametes) and maturing *Eimeria* spp. oocysts[217] (Figs 16.7a,b). In severe cases tubular nephrosis, necrosis and interstitial nephritis, potentially causing significant renal dysfunction, may be noted.[217]

Sarcocystis

Numerous other parasites have been noted in the kidneys of birds, but oftentimes association with disease is not clear. Canaries (*Serinus canaria*) experimentally infected with *Sarcocystis falcatula* developed mild multifocal interstitial renal infiltrates and glomerular hypertrophy with mesangial hyperplasia that modestly progressed with duration of infection.[218] While precystic merogony was primarily noted in the pulmonary tissue, infected canaries had low levels of merogony in the kidney and other tissues. Similarly infected pigeons developed no renal lesions.[218] Sarcocystis organisms also have been noted histologically in the renal parenchyma of cockatiels, but again the significance is unclear (T. Lightfoot, personal communication, 2003).

Microsporidia

Microsporidia (*Encephalitozoon* spp.) have been reported in numerous avian species with variable effects on the kidney. A psittacine beak and feather virus-positive eclectus parrot (*Eclectus roratus*) had heavily parasitized (*Encephalitozoon hellem*) kidney cells with associated renal tubular distension. As has been noted in other reported cases, renal cellular reaction was minimal

in the eclectus. Similar histological lesions and parasite morphology and locations (liver, kidney, intestines) also have been reported in three species of lovebirds, budgerigars (*Melopsittacus undulatus*) and a double-yellow headed Amazon parrot (*Amazona ochrocephala*).[175,192,194] The author also has seen renal microsporidiosis in a canary (*Serinus canaria*) that presented for acute illness and died shortly thereafter. Histology confirmed that numerous microsporidial organisms (not further defined) were present in the renal tubules and were associated with tubular necrosis. Other histologic lesions were minimal to mild, placing renal failure as the likely cause of death. Although it is not clear what role the kidney plays in disease, some believe that *E. bellem* is an avian and human pathogen, and may be primarily found in immunocompromised individuals.[194]

Cryptosporidia

Urinary tract cryptosporidiosis also has been noted in multiple bird species with varying associated disease. Although renal cryptosporidiosis is infrequently reported, it has been directly associated with kidney lesions in a 4-month-old black-throated finch (*Poephila cincta*), an 8-week-old Sonnerat's junglefowl (*Gallus sonneratii*), 4-month-old pullets and adult laying hens.[19,85,170,199,236] Four-day-old chickens co-infected with Marek's disease virus also have been studied.[1] Clinical signs ranged from acute death (finch and junglefowl) to thinning, depression, leg weakness and respiratory distress (4-month-old pullets and 4-day-old chicks) to slightly increased morbidity and mortality (adult chickens).[1,19,85,170,199,236] Pulmonary cryptosporidiosis also was a common feature of the pullets.[170]

Similarities were noted among gross and microscopic findings. The affected black-throated finch and Sonnerat's junglefowl had pale and swollen kidneys, and all birds had some degree of tubular epithelial tissue change with organism colonization.[1,19,85,170,199,236] The finch, adult layers, pullets and chicks also had interstitial nephritis, while the junglefowl had no inflammatory response.[1,19,85,170,199,236] Although no organisms were specifically found in the kidneys, a diamond firetail finch (*Stagnopleura bella*) with proventricular cryptosporidiosis also had similar tubular lesions in addition to multifocal amyloidosis (kidney included), severe chronic urate nephrosis, and protein and cellular tubular casts.[19]

Increased incidence of visceral gout, 1 to 2% higher than expected mortality, and numerous stages of *Cryptosporidium* sp. organisms within the epithelial cells lining the renal collecting tubules and ureters (of histologically evaluated kidneys) were found in egg-laying chickens from a production facility. Visceral gout was likely caused by the partial ureteral obstruction resulting from heavy diffuse lymphoplasmacytic infiltration in the wall of the ureter and (parasitized) epithelial wall hyperplasia.[236] Regarding the experimentally infected chicks, the authors concluded that *Cryptosporidium baileyi* can be highly pathogenic, and induce mortality and urinary tract infections in chickens infected with Marek's disease virus (an immunosuppressive effect).[1] Several authors have hypothesized that urinary tract *Cryptosporidium* infection originates in the cloaca and retrogrades into the kidneys via the ureters.[170,236] Although relatively uncommon, urinary tract cryptosporidiosis and associated disease seem to be primarily a concern in chickens, especially those with concurrent immunosuppressive illness.

Flukes

Scattered reports of renal flukes are noted in the literature. Spindle-shaped eggs, belonging to the blood fluke *Dendritobilharzia anatinarum*, were identified in kidney tissue pressed between glass slides in mallards (*Anas platyrhynchos*). The birds died from severe enteritis associated with blood fluke eggs, but no renal histology was described.[43] Eggs of other schistosomes may occasionally cause granulomatous ureteritis in waterfowl.[188] Parasites of the genus *Renicola* also may parasitize the renal tubules of several waterfowl species.[188,225] The renicolid flukes appear to have an indirect life cycle, and likely first infect mollusks and then mature in the renal tubules of susceptible species.[225] Eucotylid renal flukes may reside in the dilated ducts of the renal medulla of pigeon and passerine kidneys. They seldom cause problems and their eggs may be found in the feces and confused with other fluke eggs.[98] Clinical descriptions of affected animals are poorly described.

Miscellaneous Parasites

Other parasitic diseases also may be found incidentally in the kidneys of birds. Visceral larval migrans lesions consisting of a granulomatous reaction surrounding intact or degenerate *Baylisascaris procyonis* larvae in the renal (and other tissue) parenchyma of the house sparrow (*Passer domesticus*) were noted in one study. As most of the mixed species of birds had neural larval migrans only, the renal lesions seemed comparatively uncommon.[69] Chickens and pigeons have been experimentally infected with *Toxoplasma gondii* oocysts and evaluated for disease. While infected chickens developed no clinical signs and minimal evidence of infectivity, pigeons showed rapidly progressive disease (diarrhea, trembling, incoordination, death) and toxoplasma organisms in the kidney and other tissues. The authors stressed the importance of the pigeon crop in shedding the organisms with no emphasis on the kidneys.[18] It is probable that other parasites can affect the avian kidney and should be kept as an unlikely or rare differential diagnosis for renal disease.

Fungal

Fungal nephritis is uncommonly reported in birds. One chicken with renal and pulmonary cryptosporidiosis had *Aspergillus* sp. lesions in the lungs, air sacs, thoracic walls and kidneys.[170] In a separate study of 4-day-old chicks co-infected with *Cryptosporidium baileyi* and Marek's disease virus, one bird had necrotic renal aspergillosis.[1] Fungal nephritis, caused by *Aspergillus flavus-oryzae* group, was the only lesion seen in a moribund grey-headed albatross.[235] While focal coagulative necrosis, fibrous tissue and pronounced cellular reaction consisting of macrophages and multinucleated giant cells surrounding occasional fungal hyphae were noted, the lesions spared most of the renal tissue and did not account for the bird's poor condition.[235] Given the close association between the air sacs and kidneys, direct extension from the respiratory system (rather than primary renal invasion) is the likely cause of the necrotic fungal lesions in the kidneys.

Nephrosis

Nephrosis is a non-specific histopathologic change characterized as any degenerative, non-inflammatory lesion of the kidney, from cloudy swelling to necrosis, whatever the cause.[214] **(Figs 16.8, 16.9)** This is a microscopic diagnosis that cannot be made with gross observation. Due to its role in elimination, the avian kidney is vulnerable to the effects of many chemical toxins.[214] Inflammatory changes may develop, especially if the condition persists, and may confuse the diagnosis.[214] It was noted that tubular lesions may be reversible if the noxious substance is removed, provided the pathologic changes are not too advanced.[214] Causes of avian nephrosis have included avian malaria and hemoglobinuria, adenovirus infections, *Clostridium welchii* enterotoxemia, and lead, zinc, cadmium, calcium, aminoglycosides, phenoxyacid, sodium, ochratoxin A, ethylene glycol, 2,4-D, cadmium and 3-chloro-p-toluidine (avicide) toxicities.[2,14,15,16,30,55,72,125,154,161,178,214,224,242] This list is incomplete and serves only to emphasize the diversity of potential avian nephrosis-inducing agents. Although many toxins have been shown to induce nephrosis and other kidney diseases, renal lesions caused by specific toxicities are difficult to prove outside of a controlled study.

Hypertonic solutions also may cause a specific osmotic nephrosis in birds.[214] Hypertonic sucrose solutions (concentration not recorded) given intravenously have caused extensive vacuolation of the proximal convoluted tubules in birds.[214] Similar renal findings have been noted in other animals and man when injected with hypertonic sugar solutions and dextran intravenously.[214]

Selected Toxic and Nutritional Diseases

Also see Chapter 4, Nutritional Considerations: Sections I and II.

Vitamin D Intoxication

Vitamin D intoxication has been discussed in birds.[181,187] Vitamin D is converted in the liver to 25-hydroxycholecalciferol and then further hydroxylated to 1,25-dihydroxycholecalciferol in the kidney. Avian macrophages have the capacity to convert vitamin D to its active form 1,25-dihydroxycholecalciferol.[119] It is 1,25-dihydroxycholecalciferol that enhances the intestinal absorption of calcium and phosphate.[208,211]

As a result of excessive calcium uptake, visceral calcinosis, nephrocalcinosis, visceral gout and urate nephrosis are considered frequent complications of vitamin D intoxication in birds.[187] Symptoms of hypervitaminosis D include hypercalcemia, anorexia, nausea, polyuria, polydipsia, demineralization of bones, disorientation, painful joints and muscle weakness.[211] In normal animals experimentally subjected to hypervitaminosis D, 25-hydroxycholecalciferol, and not 1,25-dihydroxycholcalciferol, increase in the serum.[208] Chicks fed *Cestrum diurnum* leaves, which contain an analog of 1,25-dihydroxycholecalciferol, develop nephrocalcinosis and hypercalcemia, but the ultrastructural lesions are different than is noted with vitamin D toxicity.[208]

Hypervitaminosis D & A may occur when feeding developing birds vitamin D containing supplements **(Fig 16.10)**. A 3.5-month-old blue and gold macaw (*Ara ararauna*) and 5.5-month-old salmon-crested cockatoo (*Cacatua moluccensis*) from the same household developed polyuria, polydipsia and anorexia after being fed a diet (including supplements) with excessive vitamins A and D_3 and of calcium.[211] The cockatoo was hypercalcemic and had radiographic evidence of renomegaly. Hypercalcemia, hyperphosphatemia, hyperuricemia and elevated plasma creatine kinase were noted in the macaw. The calculated levels of vitamins A (119,000 IU/kg feed) and D_3 (26,790 IU/kg feed) were over 20 times the recommended levels (5000 IU/kg feed and 1000 IU/kg feed, respectively). Vitamin D_3 is considered toxic at 4 to 10 times the recommended amount. The cockatoo died 6 days after presentation and had chronic interstitial nephritis and calcifications in the kidney, proventriculus and lung. The macaw improved gradually and became disease free after discontinuing the supplemental vitamins and minerals. Hypercalcemia was attributed to oversupplementation with calcium and the vitamin mixture.

It has been suggested that African grey parrots (*Psittacus erithacus*) may be susceptible to hypervitaminosis D,[211] although no reviewed papers support this statement. Any bird species can potentially be susceptible to hypervitaminosis D.

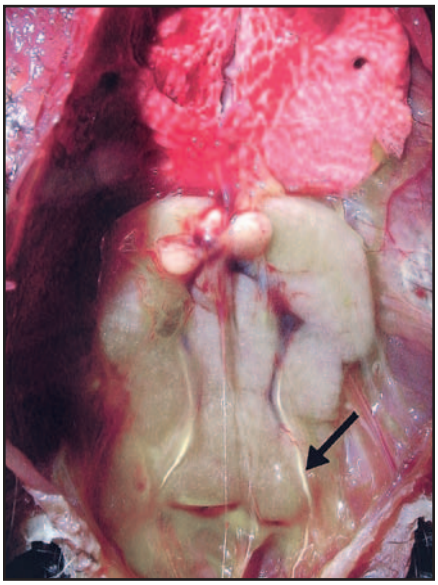

Fig 16.8 | A young adult male canary (*Serinus canaria*) with tubulonecrosis, mineralization and urate stasis of unknown etiology. Note the pale swollen kidneys with almost indistinct renal divisions. Urates are seen in both ureters (arrow points to left ureter).

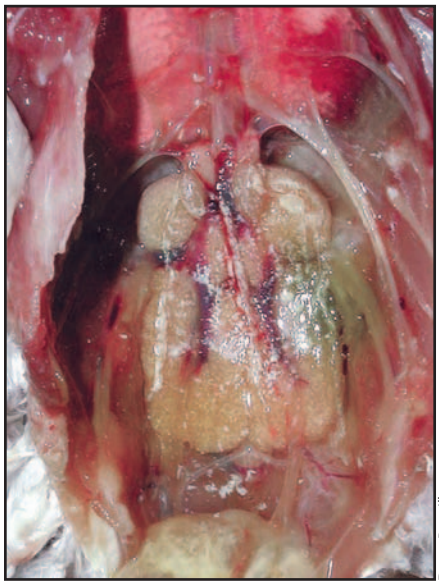

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Fig 16.9 | An adult male cockatiel (*Nymphicus hollandicus*) with severe renal tubular mineralization and necrosis. All renal divisions are pale. The etiology is undefined.

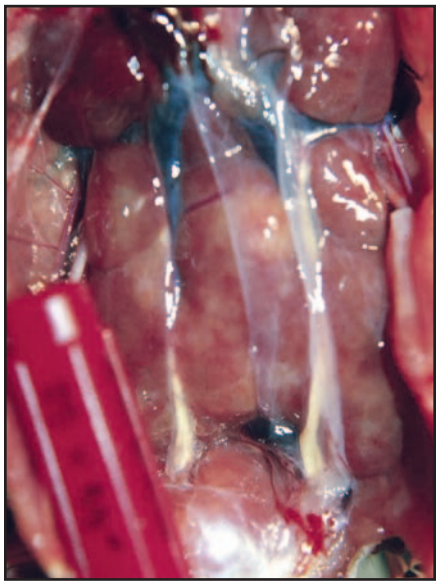

Fig 16.10 | A young blue and gold macaw (*Ara ararauna*) with suspected vitamin D_3 toxicity from excess supplementation in the diet. All renal divisions are severely swollen and indistinguishable from each other. The primary histologic lesion was nephrosis.

Hypercalcinosis

High calcium intake also has been directly correlated with renal disease in birds. Broiler chicks fed 3.27% calcium in the diet for 15 weeks, starting at 18 days old, developed numerous renal lesions throughout the study.[41] Nephrosis was noted by 7 weeks and progressed to nephritis (10 weeks), visceral gout (11 weeks) and replacement of the kidney parenchyma with urate granulomas (12 weeks).[41] In two separate studies, some growing chickens fed 3% calcium and 0.38% and 0.4% phosphorous, respectively, developed renal lesions such as nephritis, and ureteral and collecting duct occlusion due to probable calcium urate salts.[162] Limestone sand substrate (13.48% calcium and 0.02% phosphorous) was associated with rickets and nephrocalcinosis in young ostriches. Clinically affected birds returned to normal and no new cases developed once the substrate was changed to acid-washed sand (0.03% calcium and 0.02% phosphorous).[162]

In a study involving young and adult budgerigars (*Melopsittacus undulatus*), increasing dietary calcium levels were shown to be more renal toxic than was excess vitamin D_3 (D. Phalen, personal communication, 2003). Parent birds were fed diets containing 0.3%, 0.7% and 1.5% dietary calcium with a range of 500, 1000, 1500 and 3000 IU of vitamin D_3 per kg/feed. The adults subsequently fed the young the same diet. When fed a diet containing 3000 IU of vitamin D_3 per kg/feed, there was a questionably increased mortality rate only in the birds receiving 1.5% dietary calcium. However, there was a clear correlation with mild and severe metastatic (renal) mineralization in birds fed 0.7% and 1.5% calcium, respectively. The young birds fed 0.7% and 1.5% calcium died by 24 to 32 days old and never fledged (32 to 35 days). Growth rate and hatchability were poor only in the groups fed 1.5% calcium. While only a few adults died by 5 months on diets containing 1.5% calcium, most had metastatic renal mineralization when fed 0.7% calcium. Birds fed 0.3% calcium had no evidence of metastatic mineralization, and had good hatchability and growth rates (D. Phalen, personal communication, 2003). This study suggests that some species, such as budgerigars, may be very sensitive to dietary calcium levels and that supplementation should be used cautiously.

Hypovitaminosis A

Hypovitaminosis A also may lead to renal disease in avian patients. In birds with hypovitaminosis A, the ureters and renal collecting ducts may undergo metaplasia, changing the normal double-layered epithelium to keratinized stratified squamous tissue.[214] These epithelial changes can result in decreased mucin production and excessive keratin leading to plug formation and ureteral obstruction.[214] The consequential (secondary) lesions include renal tubular dilatation and necrosis, tophus formation and interstitial fibrosis.[214] Nephrosis, nephritis, visceral gout and severe replacement of the kidney parenchyma by urate granulomas were noted in broiler chicks fed vitamin A-deficient diets for 15 weeks starting at 18 days old.[41] See Chapter 4, Nutritional

Considerations: Section II, Nutritional Disorders, for Hypervitaminosis A.

High-Cholesterol Diets

Cholesterol supplemented in the feed can induce significant renal disease in pigeons.[121] Crystalline cholesterol and 10% lard were added to the diets of these pigeons under experimental conditions. The kidneys of some affected birds are firm, diffusely off-white, have an irregular capsular surface and may be enlarged up to 3 times their normal size. All renal components are susceptible and lesions may include tubular degeneration and dilatation, glomerular hypercellularity and hypertrophy (proliferative glomerulopathy), periglomerular fibrosis, lipid-laden cells within the glomeruli and multifocal, acute intersitial nephritis.[121] Since only mortality and necropsy results were reported, clinical information such as diagnosis and management/treatment were not provided. However, this does bring up the potential complication of feeding some birds high-cholesterol foods.

High-Protein Diets

High-protein diets have been associated with renal disease in birds, but only under specific conditions. Compared to a low-protein diet group, pigeons fed a high-protein diet had an observed increase in drinking rates and urine production.[153] Unfortunately, too little information was present to draw any conclusions relating dietary protein to renal disease. It has been shown that feeding 18-day-old broiler chicks a 42.28% protein diet for 15 weeks did induce multiple renal abnormalities (primarily nephrosis and visceral gout).[41] Extraordinarily high protein levels in the diet of genetically predisposed chickens have been shown to cause gout, but a direct relationship with renal disease has not been established. A more detailed discussion of the effects of dietary protein and hyperuricemia are discussed under Part 2: Serum or Plasma-based Biochemistries, Uric Acid, and Part 2: Dietary Modification, Protein.

Diets high in urea also have been linked to nephritis outbreaks in poultry.[42] Fish meal adulterated with urea was linked to high (6-8%) mortality in two separate farms. Clinically affected birds had gross lesions that ranged from pale nephromegaly and hepatosplenomegaly to urolithiasis and visceral gout. Histologic lesions ranged from interstitial, perivascular and pericapsular nephritis to proliferative glomerulopathy, and severe tubular and glomerular atrophy and fibrosis in severe cases. The disease was termed "nephritis-nephrosis syndrome in poultry" and was eliminated when the urea-adulterated feed was replaced with a different balanced diet.[42] See Chapter 4, Nutritional Considerations for more on protein levels in birds.

"Diet-Induced Renal Disease of Color Variety Psittacine Birds"

Although not formally entered into the veterinary literature, there appears to be a form of renal disease induced by feeding predominately pelletized diets to various color variety psittacine birds (M.S. Echols, unpublished data). All affected birds observed by the author have been color variety cockatiels (*Nymphicus hollandicus*), lovebirds (*Agapornis* spp.), budgerigars and parrotlets (*Forpus* spp.) and have eaten a predominately commercial pelletized diet. As most of the major brands of commercial pelletized diets have been involved, there appears to be no predilection toward any one manufacturer's product. With the exception of a history of predominately commercial pelletized diet, affected birds do not display any characteristics pathognomonic for "diet-induced renal disease." Of the birds with suspected "diet-induced renal disease," in which the kidneys have been histopathologically examined (pre- and postmortem), lesions have been limited to non-specific tubular nephrosis and were reversible after feeding a non-pelletized diet for 1 to 3 months. The diet should be converted to one appropriate for the species being treated.

Mycotoxic Nephropathy

Mycotoxic nephropathy, due primarily to ochratoxin A, has been reported in chickens and ducks.[63,149,224] Ochratoxin A is produced by several species of *Aspergillus* and *Penicillium*.[149] Ochratoxicosis occurs primarily because of ochratoxin A buildup in chick feed stored under conditions of excessive moisture, and has been identified from moldy feed, rice, groundnuts and foods prepared from these materials.[149,157,224] Ochratoxicosis causes liver and kidney damage, and specifically induces degeneration and vacuolation of hepatic cells and distension, enlargement and hypertrophy of renal proximal convoluted tubules, respectively.[63] Because of the multiple potential sources of the toxin, it is reasonable to assume that multiple avian species, other than chickens and ducks, can be exposed to and damaged from ochratoxin.

Other mycotoxins also have been closely correlated with renal disease in birds. Oosporein, a toxic pigment produced by *Chaetomium trilaterale*, *C. aureum* and several other species of filamentous fungi, is considered to be primarily a renal toxin.[184,185] The importance of oosporein is that the toxic isolates have been found in various agricultural commodities such as animal feeds, cereal grains and food products. Moldy corn in particular, growing *C. trilaterale*, may yield high concentrations of oosporein toxin. In studied young broiler chickens and turkey poults, oosporein toxicosis is dose-dependent and can cause dehydration, stunted growth, pale nephromegaly and death, and appears to severely affect uric acid secretion leading to hyperuricemia and visceral

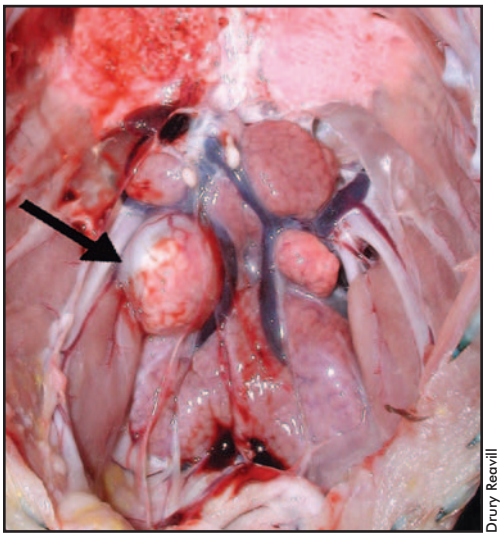
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Fig 16.11a | A young male hyacinth macaw (*Anodorhynchus hyacinthinus*) has a large renal cyst (arrow) deforming the right middle renal division.

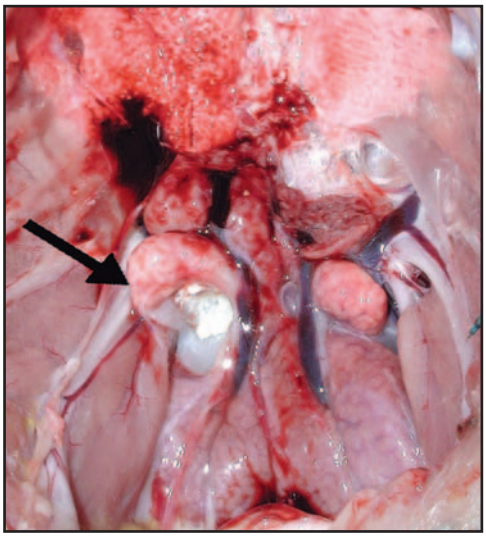
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Fig 16.11b | The cyst (arrow) is opened, revealing a white, pasty interior.

and articular gout.[184] Although still severely affected, turkey poults seemed to tolerate higher doses of oosporein before toxicosis was apparent than did broilers, bringing up the issue of physiological differences between these two species.[185] Sterigmatocystin (STG) is produced by multiple fungal species and has caused acute liver and renal disease and death in 10- to 12-day-old leghorn chicks.[222] Chicks given intraperitoneal STG developed tubular nephrosis and hepatic necrosis and died within 21 hours of injection.[222]

Lead Nephropathy

Lead toxicity is the most common cause of metal poisoning in waterfowl and affects a wide variety of other bird species.[151] Although neurological and gastrointestinal clinical signs are usually seen, lead can have severe effects on avian kidneys. Renal lesions may include proximal tubular necrosis and degeneration (nephrosis), visceral gout and, in some birds, acid-fast intranuclear inclusion bodies.[55] Kidney, liver and brain tissue concentrations of 3 to 6 ppm wet weight are suggestive and greater than 6 ppm is diagnostic for lead poisoning.[125] Also see Chapter 31, Implications of Toxic Substances in Clinical Disorders and Chapter 17, Evaluating and Treating the Nervous System.

Congenital and Hereditary Defects

Multiple congenital renal defects are reported in birds.[214,238] Heritable renal diseases such as X-linked hereditary nephritis in Samoyed dogs and Alport's syndrome in humans are discussed in many mammals, but are poorly described in the current avian literature.[100] In some large poultry flocks, up to 20% of the necropsied birds have had evidence of "faulty kidneys" considered to be congenital in nature.[238] Reported renal abnormalities include complete or partial kidney agenesis, ureteral dilatation, structural glomerular changes and predilection toward hyperuricemia (due to presumed proximal tubule defects).[9,214,238] Renal cysts are occasionally seen and may be congenital or acquired[188] (Figs 16.11a,b). Polycystic renal disease has been noted in chickens, pigeons and a bald eagle (*Haliaeetus leucocephalus*).[228] Renal agenesis is the most frequently described inherited defect and has been attributed to a simple recessive gene with variable penetrance in brown leghorn chickens.[214] With partial renal agenesis, the cranial renal division is most likely affected.[214] Although birds usually die with neurological signs or massive interrenal hemorrhage, emus (*Dromiceius novaebollandiae*) with inherited neuronal storage disease (gangliosidosis) develop unusual large vacuoles in the renal tubular epithelial cells of the proximal convoluted tubules.[17] Congenital renal diseases have been reported in chickens, pigeons, quail, a canary and a mandarin duck but likely exist in numerous other species.[187,214,238]

Fatty Associated Diseases

Lipids are not histologically evident in normal avian renal tissue, but may be noted under certain pathologic circumstances.[214] Fasting (water and food) may result in reversible lipid deposition within the renal tubular epithelium.[214] Defects in lipid metabolism or storage also may account for renal tubule cell lipidosis.[187]

The now rare fatty liver and kidney syndrome of broiler flocks and turkeys (due to biotin deficiency) can cause heavy lipid accumulation within the proximal convoluted tubules.[214,247] At necropsy, the liver, kidneys and

sometimes other organs are often pale and swollen with deposition of sudanophilic lipid droplets.[247]

A fatty liver-kidney syndrome also has been reported in merlins (*Falco columbarius*).[48,72] Only captive birds have been affected.[48] Most affected merlins have been approximately 5% above normal body weight and fed a diet predominately of day-old chicks for several months prior to death. Most affected merlins died suddenly either while eating or with the keeper. A few became lethargic a few hours before death.[48] As is seen in broiler chicks, merlins with fatty liver-kidney syndrome develop excess fat in the liver, kidneys and spleen. One-day-old (feeder) chicks contain appreciable avidin, which may bind dietary biotin, in turn leading to (a theoretical) biotin deficiency. Biotin and other deficiencies, high-fat diet, hepatic anoxia and various toxic agents, have been proposed as causes of fatty liver-kidney syndrome of merlins, but a definitive etiology has not been confirmed.[72]

Neoplasia

The avian kidney, just as with other animal tissue, is susceptible to neoplastic conditions. Nephroblastomas are the most commonly reported avian renal tumor.[214] Nephroblastomas and renal adenocarcinomas comprise the majority of kidney tumors in budgerigars (*Melopsittacus undulatus*).[173,187] Renal carcinomas are the most frequently reported tumor of the urinary system in non-domestic free-ranging and captive birds.[130] Malignant renal tumors are more commonly seen in males than females and are more commonly observed in psittacine than passerine species.[79] In one study of 74 budgerigars suspected of having coelomic tumors, one-legged lameness and abdominal enlargement were the primary clinical signs. In the same study, 47 birds (63.5%) had renal tumors and were diagnosed most commonly within 5 years of age.[173]

Lymphoid, myeloid and erythroleukemias, lymphoma, ovarian, liver and oviductal adenocarcinomas, hemangioma, lipoma, histiocytic cell sarcoma, neurofibroma, granulosa cell tumor, cystadenoma with bone, squamous cell carcinoma, unclassified carcinoma and osteogenic sarcoma have all been reported either as primary or secondary renal neoplasms in birds.[121,193,214,241]

Like other cancers, there are likely many causes of renal tumors in birds, but there is little information regarding definitive etiologies. Avian leukosis virus (ALV) can induce renal tumors in chickens. While ALV has been found in budgerigars with renal tumors, a definitive association has not been made.[173]

A common presentation with renal cancer is unilateral to bilateral leg weakness or paralysis and slight ataxia.[241] Other clinical signs may vary, but often include diarrhea, dyspnea, abdominal distension and weight loss.[130,241]

The lumbar plexus lies dorsal to the cranial renal division, while the sacral plexus runs through the middle division parenchyma.[180] Because of this close association, any parenchymal inflammation or pressure on or from within the kidney can potentially result in nerve dysfunction and resultant lameness. Additional neoplastic extension to the overlying spinal column also may result in nerve dysfunction. Peripheral neural compression should result in peripheral neuropathy with eventual loss of the withdrawal reflex, not seen with most spinal cord lesions.[79] In addition to lameness and muscle atrophy, ipsilateral osteopenia was noted in a cockatiel (*Nymphicus hollandicus*) with a renal adenocarcinoma.[79]

Unfortunately, avian renal tumors carry a poor prognosis. In reported cases of renal cancer, most birds lived less than 3 months following diagnosis.[79] It has been stated in reference to budgerigar renal tumors that the course of the disease may take weeks to several months.[241]

Urolithiasis and Ureteral Obstructive Disease

In birds, urolithiasis refers to the formation of large urate "stones" in the ureters, is primarily seen in pullets and caged laying hens, and can result in increased mortality and decreased egg production.[50] Urolithiasis has been reported primarily in the poultry literature on numerous occasions, but is rarely described in other avian species.[20,42,214,251]

Common findings include atrophic ipsilateral renal tissue, a normal to hypertrophic (compensatory) contralateral kidney and a dilated ureter obstructed with one or more urate stones.[20,214,251] Histologic lesions noted with urolithiasis have included glomerular nephritis, tubular nephrosis, ureteritis and pyelonephritis with interstitial mononuclear infiltrates.[50] One study noted that virtually every cull hen or out-of-production hen examined at affected layer complexes (sites with high incidences of urolithiasis) had gross kidney lesions and kidney stones.[50] In birds, ureteral obstruction (as may occur with ureteroliths, cloacal masses, urodeal fold thickening, etc) may cause a postobstructive form of renal disease. Simple ligation of a bird's ureter results in ipsilateral renal atrophy and this result is similarly expected with urolithiasis.[214] Naturally occurring ureteroliths in chickens are known to contain uric acid, urates, calcium and ammonia.[148] These statements suggest that the kidney should be closely evaluated (eg, via biopsy) when urolithiasis is present.

The cause of urolithiasis in poultry flocks has not been definitely identified.[214] However, it is known that coronavirus-associated nephritis in pheasants can induce inter-

stitial nephritis, tubular dilatation, ureteral impaction and subsequent visceral gout.[186] In addition to infectious bronchitis virus infection (IBV — a coronavirus), other proposed causes of urolithiasis in poultry include water deprivation, excess dietary calcium and nutritional electrolyte imbalances.[50] One group reported that by changing the form of calcium from small particle size to flakes, adding additional phosphorous and by modifying the IBV vaccination protocol, the investigators were able to significantly reduce the incidence of urolithiasis in a previously affected layer flock. However, they could not determine which management change resulted in the beneficial effect.[50]

Urolithiasis in psittacine species is rare, but has been reported. A 21-year-old male double-yellow headed Amazon parrot (*Amazona ochrocephala*) with a lifelong history of straining to void and chronic intermittent vomiting for a "few years" was diagnosed with septic ureteral fluid and ureterolithiasis.[56] Dorsocaudal coelomic radiodense opacities were noted on screening radiographs, but the diagnosis was ultimately made via exploratory celiotomy. Multiple surgeries were required to remove the stones. A kidney biopsy was not collected and a relationship to renal disease could not be made. The ureteroliths were composed of monosodium uric acid crystals and proteinaceous material mixed randomly or forming irregular laminae. Although the bird had dry, flaky skin, a urate-pasted vent, dull feathers and heterophilic (28,840 cells/μl) leukocytosis (32,000 cells/μl), the authors concluded that the clinical signs associated with ureterolithiasis in this bird were non-specific and may result in delayed diagnosis.[56] The cause was not determined.

Amyloidosis

Amyloidosis is occasionally noted in association with avian renal disease. Amyloid deposits are often related to chronic inflammatory disease and usually found systemically, but can affect specific tissues.[29] Typically, amyloid presents histologically as amorphous, eosinophilic, homogenous material that stains red-orange with Congo red and bright green when examined under polarized light. Amyloidosis is most frequently noted in captive Anseriformes (geese, ducks, swans), Gruiformes (cranes) and Phoenicopteridae (flamingos), but also has been reported in numerous other species.[127,201] See Chapter 15, Evaluating and Treating the Liver for a discussion of amyloidosis.

There are a few reports of amyloidosis involving the kidneys of birds. Multifocal amyloidosis was noted in a diamond firetail finch (*Stagnopleura bella*) with proventricular cryptosporidiosis, and was found specifically in the glomeruli and interstitial tissue around the tubules.[19] Numerous laying Japanese quail with systemic amyloidosis had amyloid deposits in the renal tubules and no to minimal deposition in the glomeruli.[171] While some of the birds had concurrent inflammatory diseases such as egg yolk peritonitis, the etiology of the amyloidosis was not determined.[171] Four days after acute onset illness, a roseate flamingo (*Phoenicopterus ruber*) died with necrogranulomatous and septic air sacculitis, perihepatic serositis and hepatic capsulitis, hemosiderosis, atherosclerosis and systemic amyloidosis.[29] The renal amyloid involvement was severe, resulting in a marked glomerulopathy and was likely the cause of death.[29] Amyloid was found within the connective tissue of mycobacterial tubercles found on the kidney surface of a hooded merganser (*Lophodytes cucullatus*). No details were given regarding the premortem disposition of the bird.[209] The author has noted renal amyloidosis in pet geese. These birds presented in end-stage renal failure and necropsy showed severe renal amyloidosis. The underlying cause was never elucidated.

Renal Hemorrhage

Renal hemorrhage is sporadically reported in the literature and may exist predominantly as a secondary finding. Sudden death syndrome (SDS), also known as "perirenal hemorrhage syndrome," is the main cause of death in heavy turkey flocks from 8 to 14 weeks of age.[24] Primarily male turkeys in good body condition die acutely with SDS and typically have characteristic postmortem lesions including perirenal hemorrhage and organ congestion including the lungs, spleen and liver.[24,75,129] One group noted that most affected birds had hypertrophic cardiomyopathy and proposed that acute congestive heart failure was the cause of death and severe passive congestion accounted for the perirenal hemorrhage.[129] The cause is still unknown, but other theories include severe lactic acidosis and limited cardiac capacity, noted in predisposed turkeys, as contributing factors.[24]

An adenovirus, new gosling viral enteritis virus (NGVEV), has been shown to cause renal hemorrhage and hyperemia 4 days postinfection in newly hatched goslings.[44] Renal tubular and ureteral epithelial cell degeneration and intestinal glandular epithelial cell necrosis and sloughing also were consistently seen in the goslings infected with the rapidly progressive NGVEV.[44]

Hydropericardium syndrome of broiler chickens is a contagious disease caused by an adenovirus and can result in grossly swollen kidneys with extensive renal hemorrhage and hydropericardium.[2] Three- to six-week-old broilers are typically affected and mortality ranges from 10 to 60%. Renal tubular nephrosis and necrosis within the liver, spleen and bursa of Fabricius may be seen microscopically.[2]

Other causes of renal hemorrhage also may be seen. Simple trauma, such as from an animal bite or endoscopic biopsy, may result in renal hemorrhage. If the renal capsule is left intact, a subcapsular hematoma may form, increasing the renal size and possibly placing pressure on the neighboring nerve plexi.[134] Renal petechial hemorrhage resulting from *Clostridium perfringens* toxemia was reported in a rock partridge (*Alectoris graeca*).[134]

Metabolic Renal Disease

Metabolic renal disease includes dehydration, diabetes mellitus, amyloidosis, gout and lipidosis, the latter three of which have already been discussed. Diabetes mellitus has been noted in a variety of birds and is seen with polyuric, polydipsic glucosuria and hyperglycemia.[228] Descriptions of the gross and microscopic effects of diabetes mellitus on avian kidney tissue were not found.

One of the more common metabolic derangements associated with renal disease is dehydration. In chickens, dehydration has been associated with nephrosis characterized by tubular dilatation, with or without proteinaceous casts, epithelial necrosis and rare urate granulomas or casts.[198] Food restriction during dehydration may lessen the nephrosis lesions.[198]

Gross Renal Changes

Gross renal changes including masses, discolorations, and size and shape alteration are non-specific and should be cautiously interpreted.

Differential diagnoses for renomegaly include neoplasia, inflammation (including infectious and non-infectious diseases), cystic formation, ureteral obstruction, toxic changes, metabolic disorders (including dehydration, gout, lipidosis) and congenital abnormalities.[79] Also, non-pathological increase in kidney size has been noted in chickens fed certain dietary precursors such as inosine that increase plasma uric acid levels.[215] In these chickens, the renal enlargement was likely due to the increase in processing of uric acid in the kidney.[215] Renal and ureteral calculi also may be noted.

Postmortem Renal Change

Renal postmortem changes are noted in chickens as soon as 22 minutes following death at 37° C (98.6° F).[163] Early renal postmortem changes occur in the proximal tubular epithelium, followed by collecting tubule epithelium and glomerular nuclei.[163] Even with cooling to 4° C (39.2° F), proximal tubular changes can be observed within 45 minutes of death. The early postmortem proximal tubular changes can be confused with antemortem proximal tubular degeneration and should be interpreted with caution.[163] In effort to decrease postmortem changes, perform a necropsy and fix tissues as soon after death as possible.

PART 2: A Review of Diagnosis and Management

HISTORY AND PHYSICAL EXAMINATION

A historical review of a bird's environment, diet, source, exposure to infectious agents and toxins, genetics and behavior becomes important for both diagnosis and management of avian renal disease. Environmental factors can include exposure to known aerosolized, ingested or topical toxins. Adverse conditions that might lead to dehydration or other stresses also may be identified. The diet should reflect what is appropriate for that species, and the history should include any additional dietary supplementation or changes. Understanding the bird's origin, whether from a specific aviary, store, quarantine station, the wild, etc, may suggest the possibility of problems seen in other avian species from the same source. Known exposure to infectious agents (and again, toxins) is especially important, as definitive diagnosis of bacterial, viral, parasitic, fungal and toxic agents is not always possible without cultures, special stains, electron microscopy, in situ DNA hybridization, PCR probes or other diagnostics. Genetic problems are poorly described in birds, but with intense inbreeding, development of mutations or conservation breeding efforts from an extremely limited gene pool, it is reasonable to assume that hereditary defects will become more common. Behavioral changes including depression, anorexia, anuria, oliguria, polyuria, polydipsia, feather picking over the synsacrum, self-mutilation, seizures and others may be associated with renal disease and should be noted in the history.[181]

Most physical examination abnormalities associated with avian renal disease are non-specific, but there are some key findings that tend to warrant further investigation. It is highly likely that a bird with articular gout has had or currently has some form of renal disease. For this reason, consider renal biopsy in some birds with articular gout to help rule out or specifically identify kidney disease. Not all birds afflicted with articular gout, however, have renal disease. Unilateral leg lameness or paresis may accompany renal disease. This is particularly true if kidney disease causes inflammation or compression on the lumbar and/or sacral nerve plexus that is so intimately associated with the dorsal renal parenchyma. Birds with renal disease also may exhibit dehydration,

generalized weakness, regurgitation and decreased muscle mass with or without historical anorexia, all of which are non-specific signs.[166]

DIAGNOSTIC TESTS

Multiple diagnostic tests are available to help clinicians identify and define multiple disease processes in birds. As diagnostic technology improves, so will our ability to accurately diagnose diseases in birds. The tests listed below are ones that are most frequently discussed or used in diagnosing renal disease in birds. See **Table 16.3** for reported selected plasma-based diagnostics sometimes used in diagnosing renal disease in birds. Many diagnostics such as fecal floatation, which help diagnose renal coccidiosis, are not discussed, but should be included in a minimum database when evaluating sick birds. Some new or unfamiliar diagnostics also are introduced.

Considering all the diagnostic tests available, the author has noticed a pattern of laboratory abnormalities that is often strongly correlated with many forms of renal disease in birds. This includes persistently elevated uric acid (at least two consecutive tests on a well-hydrated and fasted bird), elevated creatinine phosphokinase (CPK), mild anemia and a relative heterophilia with or without a total heterophilia. Elevated CPK is a very non-specific indicator of multiple types of tissue damage and is not mentioned further. Using the currently available diagnostics, the actual type and degree of renal disease can be confirmed only with a kidney biopsy.

Complete Blood Count (CBC)

Some non-specific CBC changes may be associated with avian renal disease. A marked (relative) heterophilia was noted in two chickens with urolithiasis, but no total white blood cell count was given.[20] Heterophilia, monocytosis, lymphopenia and normocytic-normochromic anemia were noted in broiler chicks with various forms of histologically confirmed renal disease, but specific details were not given.[41] In a different study in chickens, clinically affected birds with histologically identified nephritis had significant heterophilic leukocytosis when compared to "normal" birds.[42] The author has reported that many pet birds (geese, doves, various psittacine birds) with different forms of renal disease have demonstrated a mild to marked relative heterophilia with a normal total white blood count.[47,64,65] These changes are non-specific, however, and can be seen in healthy birds under stress alone.[221]

Serum or Plasma-based Biochemistries

Selected plasma biochemistries may provide several useful clues toward renal disease in avian patients. Although many serum and plasma-based tests may be "abnormal" in birds with renal disease, only specific diagnostics are covered.

Table 16.3 | Selected Plasma-based Diagnostics in Birds

Diagnostic Test	Species	Normal Range	Reference(s)
Uric Acid	Pigeon	94-518 µmol/L, 225-574 µmol/L	87, 138, 141
	Peregrine falcon	253-996 µmol/L, 4.3-16.7 mg/dl	
Urea	Pigeon	0.36-0.64 mmol/L, 0.27-0.94 mmol/L	87, 138, 141
	Peregrine falcon	0.8-2.9 mmol/L, 2.2-7.0 mg/dl	
Creatinine	Pigeon	23.7-32.3 µmol/L, 20-56 µmol/L	87, 141
	Peregrine falcon	24-64 µmol/L, 0.27-0.72 mg/dl	
Urea/Uric Acid	Pigeons	1-3	138, 141
	Peregrine falcon	1.7-6.4	
Osmolality (mOsm/kg H_2O)	Pigeon	299.4-312.6	138, 141
	Peregrine Falcon	322-356	

Reference values for the pigeon (*Columba livia domestica*) and peregrine falcon (*Falco peregrinus*) are included. These reported values are highlighted because of their potential use in identifying renal disease and dehydration.

Uric Acid

Plasma uric acid can be useful as a screening tool for advanced renal disease. With the exception of gastrointestinal uricolysis, uric acid and its salts (urate) are the end product of nitrogen metabolism in birds.[9,60,132,214,246] Elevated uric acid has been correlated with histologically confirmed severe renal disease in chickens (tubular nephrosis and interstitial nephritis).[224] In a separate study involving dehydrated chickens, increased serum uric acid was associated with histologic renal lesions.[198] Broilers given oosporein (renal toxin), developed visceral and/or articular gout, swollen, pale kidneys and had a 48% increase of uric acid over control birds.[184] In a similar study with oosporein in turkey poults, intoxicated birds had dose-dependent increases in uric acid (over controls) ranging from 76 to 140%.[185] It was noted that fasting hyperuricemia (>16.7 mg/dl [>1000 µmol/L]) in peregrine falcons (*Falco peregrinus*) indicates renal failure.[141]

Uric acid is produced and secreted in the avian liver, kidney and pancreas.[46,106] Although produced predominately in the liver, at least 17% of the uric acid found in chicken urine may be synthesized in the kidney.[46] Specifically, nephrogenic uric acid synthesis may increase when plasma purine precursors are elevated.[46] These findings suggest the avian kidney has an important role in the synthesis, in addition to elimination, of uric acid, especially when increased precursors are available.[46] Precursors, including body proteins degraded because of poor nutritional status, have been suggested as a cause of elevated uric acid and should be considered in birds with hyperuricemia.[155]

An interesting secondary role of uric acid in birds is its antioxidant capability. In chickens, it has been clearly shown that plasma uric acid concentrations are inversely correlated with oxidative activity.[215] It has been stated that uric acid constitutes one of the most important antioxidants in birds and is directly linked to their longevity.[215]

Uric acid is cleared mainly via tubular secretion and is largely independent of glomerular filtration, water resorption and urine flow rate.[9,140,141,187,195] Blood uric acid levels are mildly affected by a bird's hydration status, but rather reflect the functional capacity of the renal proximal tubules.[187] However, in a study with dehydrated chickens, uric acid levels increased after 24 to 48 hours of water restriction, but only in those birds allowed free access to food.[198] Serum uric acid levels actually dropped within 24 hours in birds denied food and water.[198] It has been estimated that renal function must be below 30% of its original capacity before hyperuricemia develops.[166] Suggested normal avian uric acid levels range from less than 1 to 10 mg/dl (59.48-594.8 μmol/L).[214]

Hyperuricemia is defined as "any plasma uric acid concentration higher than the calculated limit of solubility of sodium urate in plasma." In bird plasma, this theoretical limit of solubility of sodium urate is estimated to be 600 μmol/L (10.8 mg/dl).[143]

In chickens, the uric acid renal tubule transport system does not appear to become saturated until plasma uric acid levels exceed 60 mg/dl (3569 μmol/L)[9] which demonstrates the lack of clarity in the literature and experimental dosages.[9] Chickens genetically predisposed to hyperuricemia and fed high-protein (60%) diets develop an elevated steady state of plasma uric acid (10-60 mg/dl {59.48-3569 μmol/L}) in order to excrete their daily loads of this by-product.[9] The increased basal plasma uric acid made the affected chickens susceptible to articular gout formation.[9] One group suggested that these chickens genetically predisposed to gout had a defective uric acid transport mechanism at the peritubular membrane.[184]

Uric acid represents 80% or more of the nitrogen excreted by birds.[9,214] Therefore, a significant increase in the proportion of nitrogen excreted as uric acid is not likely, even with increased dietary protein consumption. At least in chickens, hyperuricemia is likely due to reduced renal tubular secretion of uric acid and not excessive production as can occur in humans.[9,214] These findings imply that renal tubular diseases are likely responsible for hyperuricemia, and uric acid abnormalities may not be evident until very high-protein diets are fed. Specifically in chickens, dysfunctional proximal convoluted tubules result in reduced urate secretion and can lead to hyperuricemia if severe.[214]

In birds of prey, uric acid production is directly related to the amount of protein consumed and transient rises are noted following high-protein meals.[140,143] Peregrine falcons (*Falco peregrinus*) and red-tailed hawks (*Buteo jamaicensis*) are reported to have a "significant" postprandial increase in plasma uric acid concentration (hyperuricemia) for up to 12 hours after ingesting a natural meal.[140,143] The significant postprandial uric acid increase noted in peregrine falcons was up to 32 mg/dl (reported as 1881 μmol/L) between 3 and 8 hours after being fed.[143] It has been stated that significant postprandial increases in both urea and uric acid persist for up to 15 hours in peregrine falcons.[143] It was not clear why these birds of prey did not develop gout lesions, but the authors recommended a 24-hour fast prior to evaluating serum uric acid in peregrine falcons.[143] The authors further recommend that a 24-hour fast should be considered for all carnivorous avian species prior to blood uric acid testing. Almost identical findings of postprandial hyperuricemia were noted in blackfooted penguins (*Spheniscus demersus*) and represent another species that should be fasted before measuring uric acid levels.[122]

Uric acid production following a high-protein meal has been studied in various psittacine birds. In one study with African grey parrots (*Psittacus erithacus* sp.), plasma uric acid concentrations showed a positive correlation with dietary protein consumption.[105] However, even though the fed protein level was as high as 30%, plasma uric acid levels remained within normal ranges.[105] In cockatiels fed 11, 20, 35 and 70% protein for 11 months, serum uric acid increased linearly with dietary protein levels.[123] However, the serum uric acid level was significantly greater only in birds fed 70% protein diets. Because no histologic or gross renal lesions were found at necropsy, the authors concluded that the rise of uric acid was related to dietary protein concentration and not kidney damage.[123] It was found that feeding diets containing 13.5, 18.2 and 24.6% protein for up to 24 weeks had no effect on serum uric acid levels in parakeets.[8]

In consideration of the above-described causes of elevations in uric acid, this single biochemistry value can help identify significant renal disease. The author prefers to repeat (fasting) uric acid levels on well-hydrated birds before a suggestion of renal disease is made. In birds with suspect renal disease that have a single laboratory value of hyperuricemia, the author will often give a total of 100 ml/kg SQ, SID to BID of isotonic fluids for 2 days and then recheck the uric acid level. In the author's experience, birds with persistent hyperuricemia after fluid therapy and/or fasting have some form of renal disease.

Urea

Unlike mammals, urea in birds is produced only in small

amounts (by renal mitochondrial breakdown of arginine) and does not serve as the end product of protein metabolism.[187] Plasma urea in birds is excreted by glomerular filtration and, unlike uric acid, blood urea concentrations are more significantly affected by the bird's hydration status.[138,140,187] During normal hydration, filtered urea is 100% excreted but is 99% reabsorbed in the tubules during dehydration.[138,141] Plasma urea also has been shown to significantly increase in peregrine falcons for up to 15 hours postmeal.[143] In studied cockatiels, serum urea levels increased linearly with dietary protein levels (11, 20, 35 and 70%).[123] Separate studies involving the domestic fowl and pigeons demonstrated decreased urea elimination and/or increased blood urea levels (6.5- to 15.3-fold increase in pigeons) in dehydrated birds.[138,187] It has been shown that plasma urea nitrogen increased in a dose-dependent fashion (in turkeys) at every level of dietary oosporein (nephrotoxin).[185] These intoxicated turkey poults also were showing signs of dehydration.[185] It has been proposed that plasma urea is the single most useful indicator of prerenal (dehydration) causes of kidney failure in birds.[140]

The urea:creatinine and urea:uric acid ratios can be used to better define pre- and postrenal azotemia. Because reabsorption of urea is disproportionally higher than both creatinine and uric acid, these ratios should be high during dehydration and ureteral obstruction.[138] The formulas for these ratios are listed below:

$$\text{Urea:creatinine} = \frac{\text{urea (mmol/L)} \times 1000}{\text{creatinine } (\mu\text{mol/L})}$$

$$\text{Urea:uric acid} = \frac{\text{urea (mmol/L)} \times 1000}{\text{uric acid } (\mu\text{mol/L})}$$

Creatinine

Birds produce little creatinine from its precursor, creatine.[166] Creatinine is eliminated by tubular secretion but clearance is variable.[81] Clinically, creatinine may be elevated in pet birds by feeding high-protein diets.[81] It was shown that plasma creatinine also will increase significantly in dehydrated pigeons.[138] The relationship between creatine and creatinine in birds with renal disease is poorly understood, and differentiation does not appear to be useful clinically.[81,166,181]

Proteins

Although hypoproteinemia has been noted as being associated with renal failure, few studies have evaluated serum protein levels in birds with renal disease.[141] Biochemically determined low serum protein has been noted in chickens with advanced tubular nephrosis and interstitial nephritis.[224] In two chicken flocks with spontaneously occurring urolithiasis, plasma protein level changes (method of determination not disclosed) were not significantly associated with renal disease.[20,251] While affected birds developed articular and/or visceral gout, gross renal changes and death, broilers intoxicated with oosporein (fungal nephrotoxin) had, with the exception of one group, no significant changes in plasma protein (biuret method) over the normal (control) birds.[184] A single group of broilers receiving a midrange amount of oosporein had a statistically significant rise in plasma protein over controls. The cause for this single discrepancy was not determined.[184] In a similar study using oosporein-intoxicated turkey poults, statistically significant decreased albumin:total protein was noted at all levels of intoxication over controls, but total protein remained unchanged and albumin was not significantly decreased until the highest levels of the toxin were given.[185] These few studies show a couple of important facts: there is limited information properly associating plasma proteins with renal disease, and differing species may have dissimilar plasma protein levels under similar disease conditions. As discussed under Part 2: Electrophoresis, Plasma Protein Electrophoresis, protein levels should be evaluated electrophoretically (in addition to the more common biochemical methods).

PLASMA ELECTROLYTES

The effect of renal disease on plasma electrolytes is poorly studied in birds. Hyperkalemia and hyperphosphatemia have been loosely associated with renal failure, but studies are limited in birds.[141] No significant associations between renal disease and plasma sodium, potassium, calcium, magnesium, chloride and phosphate levels were noted in birds from two chicken flocks with spontaneously occurring urolithiasis.[20,251] Specific sample collection/storage was not discussed and the authors conceded that their handling of the samples might have affected the results.[20,251] Dehydrated chickens allowed free access to food developed significantly elevated serum sodium and phosphorous by 24 hours and after 24 hours, respectively, but maintained normal potassium levels.[198] Histologically, these chickens had mild renal tubular dilatation.[198] Turkey poults intoxicated with oosporein (nephrotoxin) developed significantly decreased plasma potassium and phosphorous, and had no changes in sodium compared to controls.[185] As the avian kidney is responsible for electrolyte regulation, it is reasonable to assume that electrolyte disorders can be present in birds with renal disease.

MICROBIOLOGIC ANALYSIS

Microbiologic assays may be useful in identifying infectious causes of avian renal disease. Bacteria may enter the renal system either hematogenously, ascending from the ureters and cloaca, or as an extension of surrounding organ infection.[187] The avian coccygeomesenteric vein drains the mesentery of the hindgut into the

hepatic portal and/or the renal portal vein.[226] It is conceivable that colitis may serve as a hematogenous source of infectious agents, toxins and inflammatory products to the kidney if blood flow draining the colon is diverted into the renal vasculature. For this reason, collection of a cloacal or fecal microbial culture is a rational portion of the supportive laboratory database in birds with suspected renal disease. Severe ulcerative colitis caused by *Salmonella* infection resulted in ascending bacterial nephritis in four African grey parrots.[187]

Bacterial nephritis in birds is often a component of systemic infection and multiple organs may be involved.[187] In one study, 50% of birds with systemic bacterial infections had kidney involvement, suggesting that any bacterial septicemia can potentially result in nephritis.[187] Identification of bacteria within renal tissue may be difficult, as has been noted in dogs and swine with renal disease putatively associated with a bacterial etiology.[26] Blood cultures are an appropriate consideration if septicemia is suspected. Prior to blood collection, the skin over the venipuncture site is aseptically prepared by thorough cleaning with alcohol and organic iodine (as with surgical preparation).[58,107] The jugular and basilic veins are described as appropriate blood collection sites in septicemic birds.[25,58] Using aseptic techniques, renal biopsy specimens also can be sampled for microbial cultures. The cause of infectious nephritis in birds is not limited to bacteria, and various culture methods and other diagnostic procedures also may be useful for identifying fungal, viral and parasitic organisms.

URINALYSIS

Biochemical and cytological sediment analysis of avian urine has been advocated as potentially useful in diagnosing avian renal disease.[128,166,181,188,228] In birds, hematuria may be noted with renal disease, but should be carefully differentiated from bleeding originating from the gastrointestinal and reproductive tracts.[181] Hemoglobinuria, as noted in *Amazona* spp. parrots with lead intoxication and in other species with differing disorders, may or may not be related to renal disease. Toxic, neoplastic, bacterial and viral nephropathies may be more frequently seen associated with hematuria in birds.[181] White blood cells were seen in 45% of urine sediment from pigeons with paratyphus, many of which had intersitial nephritis.[87] Sediment analysis should be a part of an avian urinalysis and specific cellular urinary components have been discussed.[128,188,228]

Several significant factors complicate interpreting avian urinalysis. First, urine is mixed with feces in the cloaca. The one possible exception is the ostrich, which appears to eliminate urinary waste separate from the feces.[168] Second, in many species ureteral urine is refluxed orad into the lower intestines to the ceca, where water and sometimes electrolyte reabsorption takes place.[252] Additionally, diseases of the lower intestine may alter urine production and composition. Gastrointestinal bleeding, inflammation, normal and abnormal organisms, etc, may end up in a "urinalysis" harvested from a dropping, giving the false impression that red and white blood cells and/or infectious agents, respectively, came from the urinary tract. In short, the "urine" present in a dropping is not the same urine produced from the kidneys. Urinalysis results should be carefully interpreted.

Collection

True urine can be collected in birds only with some difficulty. Once emptied of feces, specially designed cannulas can be inserted into the cloaca for collection of ureteral urine. One group used a Foley catheter to occlude the rectum but not the ureters and successfully collected ureteral urine in chickens.[21] Small closed-end cannulas constructed from micropipette tips were used to collect ureteral urine from house (*Passer domesticus*) and song sparrows (*Melospiza melodia*).[38] The opening of the closed-end cannula was placed over the ureteral orifices.[38] A similar design was used in house sparrows to make cloacal cannulas from PE-240 tubing with a hole cut near the sealed end.[89] The sealed end prevented intestinal fluids from contaminating the urine once the cannula was in place.[89] Under local anesthesia, 1.5-ml microcentrifuge tubes were sutured into the cloacas of chickens to allow collection of ureteral urine.[205] Cyanoacrylate was used to glue cannulas over the ureteral orifices of chickens.[73] Several obvious drawbacks include restraint or sedation of the patient while urine is slowly produced, and the cannulation itself may induce diuresis.[249,252] Clearly, there are numerous methods, with varying degrees of difficulty, used to collect ureteral urine.

Casts

Urinary casts represent cellular and/or acellular material sloughed from the inner lining of various renal tubules. This material is generally in the shape (or a "cast") of the tubule from which it originated. Casts are sometimes noted on histologic sections. Protein and cellular casts were histologically noted in an Australian diamond firetail finch (*Stagnopleura bella*) with *Cryptosporidium* sp. and multifocal amyloidosis.[19] Albuminous casts in renal tubules of pigeons infected with virulent *Trichomonas gallinae* were noted.[172] Hyaline casts were identified in kidney sections of birds experimentally infected with infectious bursal disease (Gumboro disease).[214] Eosinophilic granular casts have been found within the renal tubules of turkeys afflicted with salt toxicosis.[242] Eosinophilic tubular casts, possibly containing myoglobin, in an ostrich with acute muscle necrosis and anuric renal fail-

ure have been reported.[187] A rhea with hemoglobinuric nephrosis developed eosinophilic casts in the renal collecting tubules.[16] Both hyaline and granular tubular casts were present in racing pigeons infected with avian paramyxovirus type 1.[11] Granular, hyaline and albuminous casts were seen in the renal tubules of chickens experimentally infected with several pathogenic bacteria.[219]

Identifying casts in urine is reported as highly significant, a sign of renal disease and/or can be a non-specific indicator of tubular renal disease in birds.[128,134] With that stated, the papers cited above describe histological sections with no discussion of casts in the urine. The author disagrees that urinary casts are highly significant or a definite sign of renal disease, as there is little information correlating casts found in a urinalysis with any type of renal disease in birds. However, casts should be noted and may have correlation with some forms of avian renal disease. Epithelial casts were found in 2 out of 35 ostrich urine samples, but no correlation was made with any renal parameters.[168] Epithelial casts were noted in 20% of urine samples from *Salmonella typhimurium*-infected pigeons.[87] Although many birds did have histologically confirmed renal disease, no correlation was made between those pigeons with kidney lesions and those with urinary casts. The large variety of "types" of casts reported also suggests that an inconsistent naming system exists within the current literature.

Urine Chemistries and Electrolytes

Standard mammalian dipsticks may be used, but not all components are applicable to avian urine.[166] Chicken urine reportedly contains non-uric acid chromogen.[9] Non-protein chromogens are known to interfere with refractometric and chemical measurement of plasma proteins and also may apply to avian urine sampling.[81]

Few studies even mention test strips used in avian urinalyses. One study evaluated commercial urine dipsticks[a] on normal urine of 35 ostriches.[168] Because ostriches can eliminate urinary waste separate from feces, these values may not apply to most other birds. In the study, 31/35 (89%) and 35/35 (100%) of the urine samples were positive for nitrite and protein, respectively. The urine chemistry strips were negative for glucose, urobilinogen, bilirubin and ketones in all ostriches.[168] No association with renal disease was made. Using the dipsticks, nitrite and protein also were positive in 90% (18/20) and 50% (10/20), respectively, of the ureteral urine samples from pigeons with paratyphus.[87] The same strips identified blood in all samples, which correlated to red blood cells seen in only 45% of urine sediments.[87] If the cells in the urine had been lysed, the strips would be positive and the cytology was negative in this study. Urine strips also may detect undigested hemoglobin found in the excrement of the bird, especially carnivorous species with short digestion times, and give a positive result.[134] Myoglobinuria also may cause positive reactions and can be distinguished from hemoglobinuria only by spectrophotometry.[134] Finally, porphyrinuria, as seen with lead-poisoned Amazon parrots (*Amazona* spp.), may result in red-colored urine visually mimicking hemoglobinuria.[134] Because of the inconsistent results and limited critical studies noted in the literature, difficulty in obtaining ureteral urine and clinical experience, it is the author's opinion that the currently available chemistry strips have limited value in an avian urinalysis.

Urine electrolytes and chemistries can be collected, but there is limited information on their interpretation. It has been suggested that because renal intracellular enzymes are likely voided in the urine, urinary chemistries might be useful in detecting kidney damage.[141] Urine sodium and potassium were measured, and insignificantly changed, in house sparrows undergoing trials with the antidiuretic arginine vasotocin.[89] One study noted that in normal and dehydrated starlings (*Sturnus vulgaris*), cloacal urine contained significantly higher concentrations of magnesium, phosphate, potassium and total osmolality than found in ureteral samples.[204] This study supports the recommendation that ureteral samples must be collected to obtain a "true" evaluation of avian urine, again making urinary chemistry evaluation impractical in a clinical setting.

One renal enzyme, N-acetyl-ß-D-glucosaminidase (NAG), has been successfully evaluated in the urine of chickens as a marker for kidney damage.[74] In mammals and chickens, NAG is a renal tubular enzyme. In humans, urinary NAG has been suggested for use as an early predictor of renal tubular damage and may be a good non-invasive indicator of disease progression.[49] Elevated urinary (ureteral urine), but not plasma, NAG was noted at 40 days of excessive vitamin D_3 supplementation in chickens.[74] Although the information is limited, further studies may show that NAG, and possibly other urinary enzymes, may become useful as early markers of renal disease in birds.

Osmolality and Specific Gravity

Avian urine is typically isosmotic because the predominant reptilian-type nephrons cannot concentrate urine beyond plasma osmolality.[141] In normal birds, urine osmolality can maximally be increased to 2.0 to 2.5 times that of plasma osmolality.[27,28,40,141] Even this number is high for some species, as emus (*Dromiceius novaehollandiae*) are reported to have maximal urine to plasma osmotic ratio of only 1.4 to 1.5.[216] This is minimal in comparison to some mammals that can concentrate urine osmolality 25 to 30 times that of plasma.[27,28,40]

There is limited information on urine specific gravity or osmolality in avian health or disease. The reported average (refractometrically determined) urine specific gravity of ostriches (*Struthio camelus*) is 1.02 with a range of 1.01 to 1.05.[168] Consistent polyuria and hyposthenuria (60% had specific gravity below 1.007) was noted in *Salmonella typhimurium*-infected pigeons, many of which had interstitial nephritis.[87] In a separate evaluation, urine osmolality significantly increased up to 3 times control levels in postflight and dehydrated pigeons.[88] The author has used urine specific gravity diagnostically as discussed below under Water Deprivation Testing.

Urine pH

Urine pH is highly variable in birds. The urine pH may be acid (down to 4.7) in egg-laying female birds during calcium deposition.[77] Once the egg is laid or calcium is no longer being deposited, urinary pH may climb to 8.0. Male birds have an approximate urine pH of 6.4. Hypoxia, as noted in diving ducks, may drop urine pH to 4.7.[77] Normal ostriches have a urine pH range of 6.1 to 9.1, with a mean of 7.6.[168]

ELECTROPHORESIS

Plasma Protein Electrophoresis

Properly determined hypoalbuminemia (via plasma electrophoresis) is not reported in confirmed active cases of avian renal disease. However, it is possible that birds may develop low albumin/protein with some kidney disorders. Biochemically determined hypoalbuminemia has been noted in some active avian renal disease cases.[64,65,185]

The literature states that as the currently available biochemical tests likely do not accurately report avian albumin levels, serum/plasma protein electrophoresis is necessary to properly quantitate blood proteins and should be performed if hypoalbuminemia is suspected.[81,139,142] Decreased albumin and elevated betaglobulins and alpha$_2$ macroglobulin, as recorded with serum electrophoresis, have been reported with avian nephritis.[47,51] However, there are no controlled studies to support the above statements that correlate protein electrophoresis abnormalities with any renal pathology in birds.

With the above stated, one study showed that an analyzer using the biuret and bromocresol green dye-binding methodologies for total protein and albumin determination, respectively, had good agreement between whole blood and plasma samples.[115] On the contrary, there was poor correlation between the results from the studied analyzer and samples evaluated via electrophoresis used at two major reference laboratories. Due to the discrepancies, the authors concluded that neither reference laboratory using electrophoresis served as the "gold standard" for total protein and albumin determination.[115]

These very limited studies suggest inconsistencies in the "gold standard" method of serum/plasma total protein and albumin determination, and question the true value of these diagnostics in birds with renal disease. Regardless, it is the author's opinion that monitoring serum and/or plasma protein levels has diagnostic value in birds, even if not necessarily used in renal disease cases. The author recommends consistently using one of the common biochemical methods of protein determination and comparing those results to electrophoresis, the goal being to become familiar with test results from one or two diagnostic methods and correlating those results to (histologically) confirmed disease.

Urinary Protein Electrophoresis

In mammals, proteinuria is broken down into preglomerular, glomerular and postglomerular urinary protein loss. Preglomerular proteinuria occurs when large amounts of small molecular weight proteins (immunoglobulin fragments, hemoglobin and myoglobin) that readily pass through normal glomerular walls are lost in the urine.[137] Glomerular proteinuria occurs when diseased glomerular membranes allow large proteins (albumin, immunoglobulins, some coagulation proteins/antithrombin III) to pass.[137,245] Postglomerular proteinuria results from normal genital secretions as well as urogenital infections, trauma and neoplasia.[137] Although uncommon in mammals, defects resulting in proximal renal tubular protein resorption result in (postglomerular) tubular proteinuria.[137,245]

Avian urine normally contains a large amount of protein (average of 5 mg/ml up to 15 mg/ml), especially when compared to that of mammals (<0.09 mg/ml in dogs and humans).[27,111] Amino acids are freely filtered at the glomerulus, but normally are almost completely reabsorbed by the renal tubules in birds.[60] Because uric acid is poorly water soluble, very little avian ureteral urine is required to eliminate this protein waste. Instead, proteinuria is likely necessary to maintain the excreted uric acid-containing spheres in a colloidal suspension, preventing aggregation and renal tubular blockage.[28,111] Within the proximal tubule, uric acid is bound to a protein to solubilize the waste product and prevent crystal formation.[215] The reflux of urine into the cloaca may be a mechanism to recover some of the urinary protein, as cloacally voided fluid contains very little protein compared to ureteral samples.[28]

Serum albumin, among other proteins, is found in both the liquid urine and uric acid spheres in chickens.[111] In the normal junglefowl (*Gallus gallus*), the urinary pro-

teins (averaged 2.01 mg/ml urine) identified closely matched the plasma proteins. This led to the conclusion that protein is passed through a glomerular filtration barrier differently than occurs with most mammals.[111] There are, however, differences in concentrations of plasma and urinary proteins suggesting differential filtration and/or absorption of some proteins by renal tubules.[111]

Pathologic proteinuria is poorly described in birds. In one study, control chickens and those with experimentally induced autoimmune glomerulonephritis produced urinary protein (measured via 3% sulfosalicylic acid with a bovine serum albumin standard) at 5 mg/24 h.[21] Test birds developed no abnormal proteinuria, but were considered moderately proteinuric after given IV colloidal carbon (3 to 8 times increase in proteinuria). Colloidal carbon induces proteinuria in other species, but the mechanism is not clear.[21] As discussed under Part 1: General Renal Disease Categories, Glomerulopathies, birds may not be capable of developing pathologic proteinuria with glomerular disease as is recognized in mammals. However, it is possible that pathologic proteinuria develops more slowly in birds compared with mammals, and as a result has not been frequently discussed or evaluated in clinical cases.[86] If pathologic proteinuria is suspected, urine protein electrophoresis should be used to differentiate protein type and size.[94,245] If performed, it would be beneficial to compare urinary protein levels from a sick patient with samples from a healthy member of the same species. Finally, ureteral urine should be collected to rule out any effects from protein absorption or from other proteins present in the lower intestine. In a normal clinical setting, these collection requirements and limited studies make meaningful urinary protein interpretation in birds impractical.

IMAGING

Radiography

Plain and contrast radiography, nuclear scintigraphy, ultrasound, magnetic resonance imaging and computed tomography can be used to "image" the avian kidneys.[108,134,151,166,181,206] The avian kidney lies in a fossae created by the ventral surface of the synsacrum.[79,152] With bone dorsal and air sacs surrounding ventrally, imaging of the avian renal system is difficult with some techniques. Indirect methods such as positive contrast radiography of the alimentary tract may be helpful in outlining renal masses.[141]

A lateral view is the best method to radiographically view the kidneys[141] (Fig 16.12). As viewed with a lateral radiograph, the absence of the normal dorsal diverticulum of the abdominal air sac (dorsal to the kidney and ventral to the synsacrum) may indicate renal enlargement.[166,187] Improper positioning can artifactually change the appearance of this air-filled diverticulum.[166] Because the renal silhouettes are superimposed on a lateral view of the abdomen, an oblique view also may be used to distinguish each kidney.[79] Renal density and gross size changes may indicate renal disease.[166,181] Radiographically visible renomegaly was noted in a salmon-crested cockatoo with chronic interstitial nephritis and calcification as the result of hypervitaminosis D_3.[211] Nephrocalcinosis was detected radiographically in ostriches and appeared as multiple radio-opacities throughout the renal parenchyma.[162]

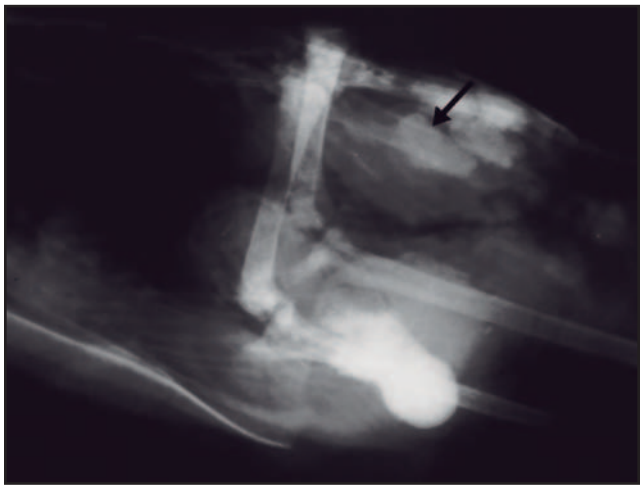

Fig 16.12 | Lateral radiograph of an adult domestic goose with renal fibrosis and mineralization. Note the mineralized kidney tissue (arrow).

Ultrasound

Due to the presence of surrounding air sacs (ventrally) and bone (dorsally and laterally), ultrasonographic imaging of normal avian kidneys is difficult.[108] In one study of 386 mixed bird species that underwent ultrasonographic evaluation of the urogenital tract, abnormalities such as renal cysts (6), cancer (12) and inflammatory nephromegaly (11) were identified in only 29 patients. The authors concluded that sonographic imaging of the normal kidney was not possible.[108] Some disease conditions that either obliterate the air sacs or result in fluid accumulation in the coelomic cavity may actually improve renal ultrasonographic imaging.[152] In these abnormal situations, ultrasonography can serve as a non-invasive and safe means to evaluate coelomic structures such as the kidneys.

Intravenous Excretory Urography

Intravenous excretory urography has been described in birds as a method to gain information on kidney size, shape and function.[141] Use of organic iodine compounds given IV in the basilic vein has been reported. The

organic iodine can be visualized radiographically in the heart and pulmonary artery within 10 seconds, and outlining the kidneys and ureters 20 to 50 seconds later. After 2 to 5 minutes, the cloaca will be outlined. This technique should not be used in birds with severe renal compromise.[141]

It is the author's opinion that intravenous excretory urography may have some limited uses in a clinical setting as demonstrated in the case report below. A water-soluble iodinated contrast agent[b] was successfully used to evaluate the ureters post-ureterotomy in a double-yellow headed Amazon parrot (*Amazona ochrocephala*).[56] The agent was dosed at 400 mg/kg and given in the right medial metatarsal vein. Radiographic images were taken at 1, 2, 7 and 10 minutes postinjection. Ureter peristaltic movement and size were successfully evaluated using this technique.[56]

Renal Scintigraphy

Avian renal scintigraphy has been described.[150] The radioisotopes ^{99m}Tc-dimercaptosuccinic acid (^{99m}Tc-DMSA) and ^{99m}Tc-diethylenetriamine pentaacetic acid (^{99m}Tc-DTPA) were used in domestic pigeons. The tested birds were given nephrotoxic doses of gentamicin at 15 mg/kg IM q 12 h for 6 days. The birds were divided into two groups and renal scintigraphy using a mean of 41.8 MBq of intraosseous ^{99m}Tc-DMSA or 42.8 MBq of intraosseous ^{99m}Tc-DTPA was performed on the last day of gentamicin toxicosis and again 2 days later. Pre and post-gentamicin-treated kidneys were biopsied and confirmed normal histology pre-treatment and significant renal damage post-treatment. Uric acid was measured and interestingly did not significantly correlate with renal histology or scintigraphy findings. The authors reported 'decreased renal radiopharmaceutical uptake for ^{99m}Tc-DMSA and ^{99m}Tc-DTPA indicated nephrotoxicosis'. More specifically, scintigraphy using ^{99m}Tc-DTPA correlated well with renal histologic grades. While scintigraphy using ^{99m}Tc-DMSA did not correlate well with renal histologic grades it may be used to demarcate neoplasms, cysts and other physical alterations to the renal parenchyma. While renal scintigraphy can be performed at facilities that routinely provide nuclear medicine procedures, obvious drawbacks include cost and the need to confine birds for 12 to 24 hours until the radiopharmaceutical used has degraded.[150]

WATER DEPRIVATION TESTING

Water deprivation testing is considered when attempting to rule out unknown causes of polyuria/polydipsia (PU/PD) including central and nephrogenic diabetes insipidus and psychogenic polydipsia. There are numerous causes of PU/PD in birds that first must be ruled out using a complete historical, physical and laboratory evaluation. Some of the many causes of PU/PD in birds include organic (liver, kidney, intestine and cardiac), endocrine (diabetes mellitus) and metabolic (hypercalcemia) diseases.

A water deprivation test is carefully performed using a simple cage. The bird is weighed and blood and urine are collected. Evaluate the packed cell volume (PCV), total solids and osmolality of blood, and specific gravity and osmolality of urine. In one report of an African grey parrot (*Psittacus erithacus erithacus*) undergoing a water deprivation test, the authors evaluated plasma sodium, potassium and osmolality in addition to the above listed urine parameters.[144]

Place the avian patient in a cage with no food or water for the duration of the test. Evaluate both blood and urine parameters every 3 to 24 hours for 12 to 48 hours, depending on the species and physical condition of the bird. The reported African grey parrot was evaluated every 24 hours.[144] As a normal response some birds such as European starlings may become distressed within 24 hours of water deprivation, which should be considered when interpreting the results.[204] On the other hand, pigeons deprived of water for 36 hours had little change in plasma osmolality, demonstrating the variable responses to dehydration in differing species.[88] As a general rule, smaller birds should be evaluated more frequently.

The bird's behavior and laboratory results give a presumptive diagnosis. Birds with psychogenic polydipsia should tolerate this test well and develop more concentrated urine (increased osmolality and specific gravity) and an increase in PCV, total solids and plasma osmolality, all consistent with dehydration. This was the pattern seen in the African grey parrot and subsequent treatment with water restriction proved curative.[144] These individual values should all be carefully interpreted as noted in a study of dehydrated starlings where the hematocrit remained unchanged (compared with hydrated birds) and was not a reliable indicator of hydration.[204]

Birds with central (lack of production of arginine vasotocin [AVT]) or nephrogenic (inadequate response to AVT) diabetes insipidus should have different results than those with psychogenic causes. Birds with diabetes insipidus become dehydrated (as supported by plasma variables) but maintain dilute urine (low specific gravity and osmolality). Normal house sparrows given arginine vasotocin (0.4 ng/kg per minute to 1.6 ng/kg per minute) had a significant drop in urine flow rate (50.2 to 28.9% of normal, respectively) and increased urine osmolality (150.1 to 196% of normal, respectively).[89] A similar response would be expected in other normal birds of different species.

A strain of chickens with hereditary diabetes insipidus has been described.[33] These polyuric chickens produced low osmolality urine and maintained high circulating levels of AVT. The vital functions of these chickens became impaired after 48 hours of water deprivation. When given AVT, additional to their high circulating levels, these birds had minimal response. Either the birds had improperly responding kidneys or the AVT was defective.[33]

In the author's experience with one male canary-winged parakeet (*Brotogeris versicolorus*) with suspected diabetes insipidus, the bird became panicked within 4 hours as he became rapidly dehydrated, but maintained excessive production of dilute urine. The canary-winged parakeet had normal plasma biochemistries, complete blood count, screening radiographs and renal biopsy (light microscopy), and had a history of severe PU/PD since weaning. A diagnosis beyond presumptive diabetes insipidus was not made, since AVT levels were not evaluated.

IDENTIFYING URIC ACID CRYSTALS

Gout results when uric acid precipitates out as a solid, chalky substance in joints (articular) or on tissue surfaces (visceral). Articular gout material may be recovered using fine needle aspiration. Uric acid crystals are easily confirmed using microscopy or the murexide test. Cytologically, "gouty" material typically presents as uric acid crystals surrounded by a pyogranulomatous infiltrate, usually without organisms. The needle-shaped crystals are easy to identify on direct and stained smears. To perform the murexide test, place a small amount of the suspect material on a slide and mix with nitric acid.[141] Use a flame to evaporate and/or dry the mixture. Once cool, add one drop of concentrated ammonia. If urates are present, a mauve color will appear.[141] Due to their water-soluble nature, urates will dissolve in formalin and, therefore, the crystalline form will not be seen on conventionally fixed tissue. However, urates can be seen in alcohol-fixed tissue using Gomori's methenamine silver impregnation technique.[141]

EVALUATING GLOMERULAR FILTRATION RATE

Glomerular filtration rate has been studied in chickens as a method to evaluate renal function. Glomerular filtration rate is considered the most reliable quantitative index of renal function, and is an important tool for the diagnosis and management of kidney disease of mammals.[156] Most methods of measuring glomerular filtration rate and effective renal plasma flow are difficult and time consuming.[197] As a result, determining glomerular filtration rate in birds is often limited to research situations.

In general, urine flow rate (UFR) is first calculated as the volume (of ureteral urine) collected per kilogram of body weight per minute. The urine to plasma concentration ratio of a (usually parenterally administered) marker substance such as inulin is multiplied by the urine flow rate. Glomerular filtration rate (milliliters per kilogram body weight per minute) can then be calculated by measuring the clearance of the marker substance.[73] The basic formula is as follows:

$$\text{Glomerular filtration rate} = \frac{\text{UFR} \times \text{urine marker substance concentration (inulin)}}{\text{plasma marker substance concentration (inulin)}}$$

The single injection, double isotope method, utilizing ^{3}H-inulin ([methoxy-^{3}H]-inulin) and ^{14}C-PAH (para-[glycyl-1-^{14}C]-aminohippuric acid), has been shown to be a simple, reliable and rapid method for evaluating renal function in chickens.[197] If needed, the specific procedures of evaluating glomerular filtration in birds can be reviewed in the literature.[73,88,90,131,197,204,249,250]

BIOPSY

When history, physical examination and/or laboratory abnormalities support the presence of renal disease, consider biopsy. Currently, the only way to definitively diagnose avian renal disease and specific pathologic patterns is with a kidney biopsy and histopathologic evaluation.[141] A renal biopsy is most frequently performed during endoscopic examination of the coelomic cavity and, specifically, the kidneys. Before a renal biopsy is performed, the cost:benefit of the surgical procedure versus conservative therapy must be considered, as many birds have compromised health, especially if they have kidney disease.

Several methods of renal biopsy, primarily via endoscopy, and detailed accounts of avian kidney anatomy and physiology have been previously discussed[78,134,165,167,181,227,229,233,234] (Figs 16.13-16.18). For the most part, renal tissues can be stored in 10% formalin for light microscopy. If available, additional tissue may be stored in glutaraldehyde (electron microscopy), culture media (organism recovery) and alcohol (visualizing uric acid crystals), or frozen (PCR studies).

Renal histologic lesions are rarely pathognomonic for a specific disease process. Many different diseases cause similar renal lesions. Additionally, different pathologists may make differing morphologic diagnoses on the same renal tissue.[239] The author encourages veterinarians to work with a pathologist familiar with normal and abnormal avian histology. Oftentimes, it is the pathologist's interpretation of a renal biopsy combined with the attending veterinarian's case familiarity that enables both parties to make a definitive diagnosis or build a reasonable differential diagnoses list compatible with the kidney lesions noted. This approach has a key role in the

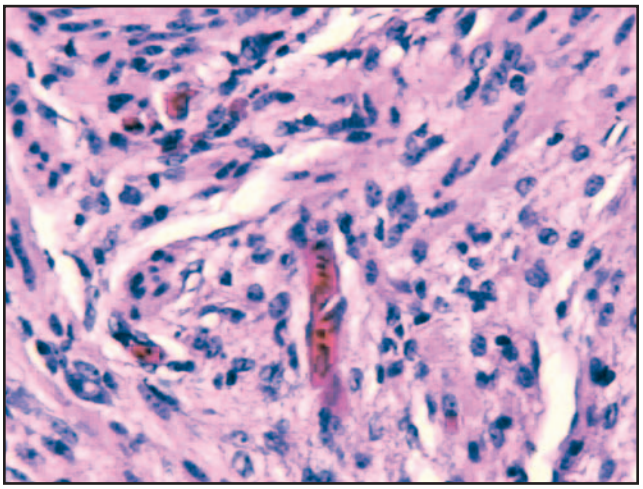

Fig 16.13 | An adult domestic goose with undifferentiated renal sarcoma. The renal architecture is destroyed and has been replaced by neoplastic spindle cells.

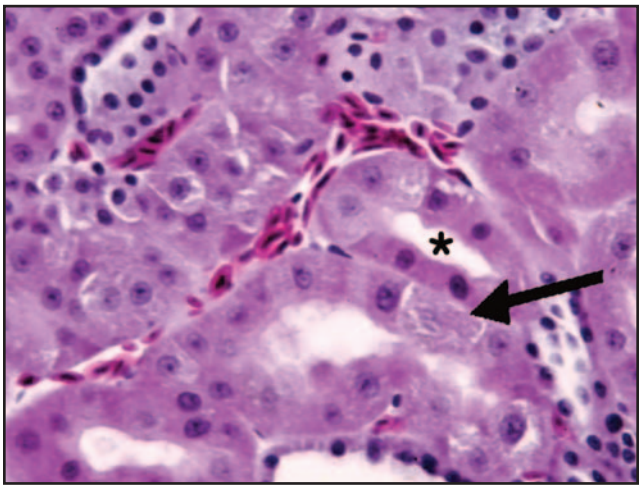

Fig 16.14 | Histologically normal renal tissue from an adult hyacinth macaw (*Anodorhynchus hyacinthinus*). Note the well-organized renal tubules, normal tubular lumen size (*) and lack of inflammatory cells. One tubular epithelial cell is undergoing degeneration (arrow), but the cells appear healthy otherwise.

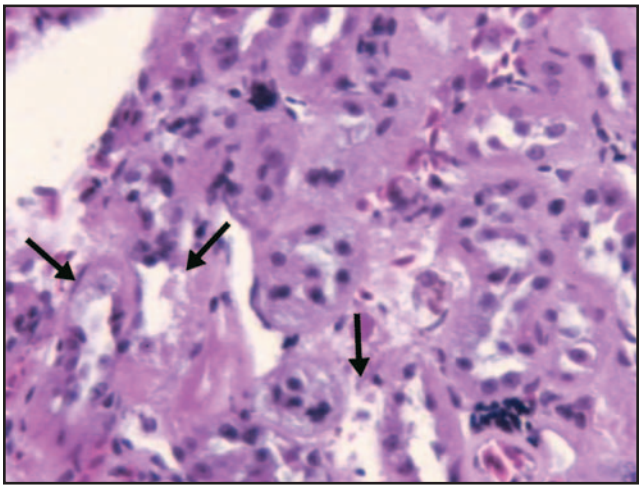

Fig 16.15 | A mitred conure (*Aratinga mitrata*) with mild nephrosis. Note the cellular disorganization and loss of tubular epithelial cell structure or degeneration (arrows).

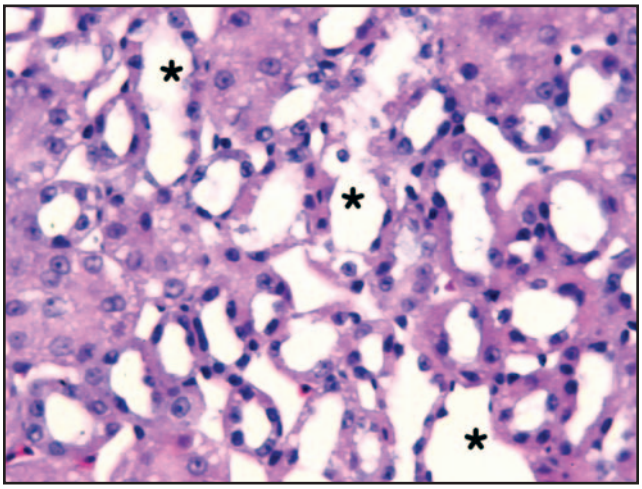

Fig 16.16 | An adult hyacinth macaw (*Anodorhynchus hyacinthinus*) with mild tubular dilatation 6 weeks post-treatment for histologically suspected bacterial nephritis. Note the multiple dilated renal tubules (*). Although there is no evidence of inflammation, tubular dilatation can be seen with bacterial infections and other diseases, and suggests that complete resolution has not been obtained.

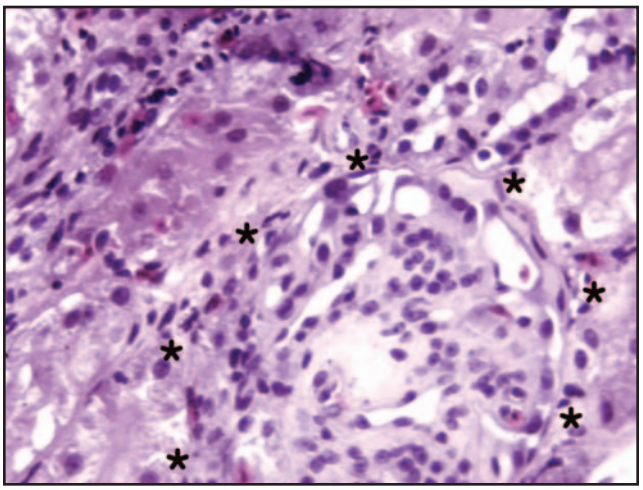

Fig 16.17 | A citron crested cockatoo (*Cacatua sulphurea* sp.) with membranous glomerulopathy of unknown etiology. Due to the significant mesangial enlargement, the mesangium has been pushed to the periphery of the glomerulus. The round glomerulus is outlined (*).

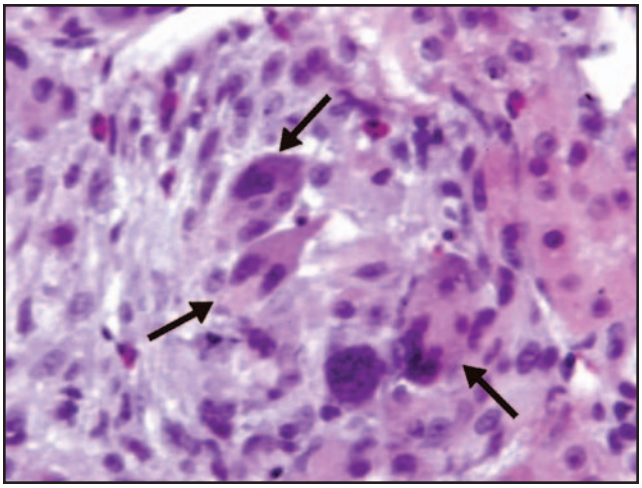

Fig 16.18 | An umbrella cockatoo (*Cacatua alba*) with granulomatous nephritis. Note the multinucleate giant cells within the renal interstitium (arrows).

formation of a viable therapeutic plan for the patient.

Treatment

THERAPEUTIC CONSIDERATIONS

Treatment options for renal disorders in birds depend upon the cause and type of kidney disease and secondary complications present. Most renal disease patients are medically managed, as kidney surgery is difficult and often not needed. Tables 16.4 and 16.5 list medications, and their possible indications, commonly used in renal disease patients.

Because of the location within the renal fossae, avian kidneys are difficult to surgically remove. The close associations with the lumbar and sacral plexuses and extensive vascular network surrounding the kidneys lead to the high probability of significant hemorrhage expected during surgery, and possible neurologic damage.[79] With that stated, focal therapeutic surgery (including endoscopic biopsy) for superficial renal lesions and the ureters may be useful in some cases. Given the concern of serious hemorrhage, most surgical renal disease cases are managed medically.

A few accounts of therapeutic renal surgery exist. Post-renal failure due to urolithiasis or some other obstruction of the ureters or cloaca may be noted. Cloacaliths and other masses within the cloaca may be easily removed, relieving a potential ureteral obstruction. Wideman and Laverty describe the effects of renal vein and ureter ligation on kidney function in domestic fowl.[250] Except for a small island of tissue adjacent to the testes and cranial renal artery, the cranial, and portions of the middle, renal divisions atrophied significantly without compromising overall kidney function.[250] Such a study is worth reviewing if considering renal division ablation or other similar radical procedures. Renal stones were successfully removed via extracorporeal shock wave lithotripsy in a Magellanic penguin (*Spheniscus magellanicus*).[146] Although multiple anesthetic procedures were required, ureteral stones were successfully removed from a 21-year-old male double-yellow headed Amazon parrot (*Amazona ochrocephala*).[56]

The author also has used minor surgery in articular gout cases. In effort to speed the removal of (stabilized) articular gout, make small incisions over the gouty lesions, which are often on the feet. Express the thick material out. Anesthesia is ideal as this can be quite painful. Also, this procedure tends to be bloody, and the feet often require minor bandaging to help prevent continued bleeding and secondary infection.

Another poorly explored area is renal cancer therapy. Clearly, as treatment options advance and are tested in avian species, renal cancer therapy will likely become more prevalent. For example, carboplatin at 5 mg/kg IV q 1 month was used to manage a renal adenocarcinoma (diagnosed at necropsy) in a budgerigar. The bird died approximately 3 months after initiating treatment, but temporarily did show improvement of clinical signs (decreased grip in one foot and lameness changed to almost normal perching, 1 month after starting therapy).[147] It was concluded that while carboplatin may be nephrotoxic in birds, this drug could possibly be useful in treating early renal tumors that have not progressed to renal failure.[147]

As a general note in any bird with organ dysfunction, patients should be monitored with routine physical and laboratory evaluation, especially when taking any medication(s) chronically. The intervals between recheck examinations will vary on the patient's condition and clinician's experience in handling the given case.

DIURESIS AND FLUID THERAPY

As in other animals with renal disease, maintaining hydration is important in birds with most kidney disorders. Acid-base and electrolyte disorders may likely be present in birds with renal disease. At this time, only general statements concerning diuresis and fluid therapy can be made.

Anuric and oliguric patients should be diuresed. Although mannitol and furosemide have been recommended to induce diuresis in birds, these drugs are poorly studied in avian species.[141,181] Mannitol (added to a solution containing inulin and para-amino hippuric acid) was used to induce diuresis in chickens at a dose of 2.5% given at a rate of 0.2 ml/kg per minute.[251] Furosemide given IV (1 mg/kg BID) along with SQ saline for 72 hours was used to successfully treat a red-tailed hawk (*Buteo jamaicensis*) with acute obstructive uric acid nephropathy.[141] Some birds, especially lories, may be sensitive to the effects of furosemide and its use should be judicious.[203] Furosemide also may cause increased urinary excretion of Na^+, K^+ and Cl^-.[248] If furosemide is used, electrolyte replacement may be needed. Clinically, providing parenteral fluids often induces diuresis in birds, even with most forms of renal disease.

Until acid-base and electrolyte disorders are better evaluated in birds with renal disease, balanced electrolyte solutions should be used to maintain hydration, replace fluid losses and/or induce diuresis as needed. The estimated daily fluid requirement for most birds is 40 to 60 ml/kg per day.[52,223] It has been recommended that 10% of the bird's body weight should be given in fluids when

Table 16.4 | Treatment Guide for Stable Avian Patients with Renal Disease

	Surgery	Fluid Therapy	Antibiotics	Allopurinol	Colchicine	Dietary Modification	Omega-3 Fatty Acids	Parenteral Vitamin A	Low-dose NSAIDs
Nondescript nephritis			+			+	+	+	+
Glomerulopathy							+++		++
Bacterial nephritis			+++				+		
Parasitic nephritis							+		
Nephrosis						++	++	+	
Fatty nephropathy						+++			
Neoplasia	+						++		
Urolithiasis	++					+	++	+	
Amyloidosis					+		+		
Renal fibrosis					+++		+		
Renal (visceral) gout		+++		+++	+++	+	++	+	
Articular gout	+	++		+++	+++	+	++	+	

Note: Most birds with visceral gout are likely in renal failure and usually require immediate medical attention. Fluid therapy, nutritional support and other appropriate supportive care may be required for any bird in poor condition, and treatment choices are based on the bird's health and attending clinician's experience.

NSAIDs = non-steroidal anti-inflammatory drugs
+ = occasionally indicated
++ = occasionally to often indicated
+++ = often indicated

Table 16.5 | Doses and Durations of Drugs Commonly Used in Psittacine Renal Disease Patients
(M.S. Echols, unpublished data)[37,78]

	Dose	Route	Duration	Potential Side Effects
Ceftazidime*	75-200 mg/kg BID-QID	IM, IV	4-6 weeks + for bacterial nephritis	—
Ceftiofur*	100 mg/kg TID	IM	4-6 weeks + for bacterial nephritis	—
Ciprofloxacin*	20-40 mg/kg BID	PO	4-6 weeks + for bacterial nephritis	—
Enrofloxacin*	10-30 mg/kg SID-BID	PO, IM	4-6 weeks + for bacterial nephritis	Muscle/tissue necrosis/irritation upon injection.
Piperacillin*	100-200 mg/kg BID-TID	IM, IV	6 weeks + for bacterial nephritis	—
TMP Sulfa*	16-100 mg/kg BID-TID	PO	6 weeks + for bacterial nephritis. Use lower dose for birds over 300 g.	May cause regurgitation. Use cautiously with dehydrated birds.
Allopurinol	10-30 mg/kg BID	PO	Use until hyperuricemia and/or physical signs of gout normalize. Use higher dose short-term (<4 weeks).	Renal toxicity noted in red-tailed hawks, but not psittacines.
Colchicine	0.04 mg/kg SID-BID	PO	Use until signs of hyperuricemia and/or histologic fibrosis normalize. Can be used with allopurinol and for 6-12 months.	—
Omega(Ω)-3 fatty acids	0.22 ml/kg of a supplement containing <6:1 (Ω-6:Ω-3 fatty acids)	PO	Use at least until laboratory and/or renal histologic abnormalities normalize. Can be given 6-12+ months.	—
Vitamin A	2000-5000 IU/kg once	IM	Use single dose in conjunction with diet modification. Repeat dose in 3 weeks if needed.	May lead to vitamin A toxicity if used chronically.
Aspirin	0.5-1.0 mg/kg SID-BID	PO	Use until evidence of glomerulopathy is gone or lab abnormalities have normalized. Can be given 6-12 months.	May lead to renal disease if overdosed. Do not use in dehydrated or moderate to severely compromised patients.

*Antibiotic choice should be based on culture and sensitivity (C&S) from histologically confirmed or suspected bacterial nephritis. Otherwise, base antibiotic choice on C&S results from a separate infected lesion, septicemic blood or cloacal cultures.

BID = twice daily
IM = intramuscular
IV = intravenously
PO = orally
SID = once daily
TID = three time daily
TMP = trimethoprim-sulfamethoxazole

For more complete dosing schedules in other species, see Chapter 9, Therapeutic Agents.

the patient is in renal failure.[141] Once a dose has been determined, warmed fluids are given with food (tube/syringe-fed), SQ, IV or IO. The IV and IO routes are most appropriate for critically ill patients.[223] While appropriate in many cases, subcutaneous fluids are not adequate to rehydrate patients with severe dehydration, shock or hypothermia.[223] Oral fluids are reserved for stable patients with mild dehydration that have normal gastrointestinal function, and are contraindicated in critically ill birds.[112]

Fluid therapy for critically ill birds should ideally be tailored to the bird's electrolyte status and/or overall condition and is ultimately decided by the attending clinician. The author typically diureses ill and severely hyperuricemic renal disease patients. While the definition is debatable, the author generally considers severe hyperuricemia to be present when one or more of the following conditions are met in clinically ill non-carnivorous and appropriately fasted carnivorous birds:

1. Uric acid levels exceed 30 mg/dl.

2. Uric acid levels are elevated (>10 mg/dl for most species) and rising over a period of several days (even if below 30 mg/dl).
3. There is evidence of rapidly progressive articular or visceral gout.

Depending on the patient's condition, the author will typically give 50 to 100 ml/kg of fluid BID via SQ, IV, IO or combination routes. Fluid therapy (combined with other medications if needed) is generally continued until the blood uric acid level drops to either normal or mildly elevated levels (10-20 mg/dl) and the bird is showing signs of improvement (eg, eating, more active). Lower amounts of parenteral fluids are given if overhydration is either suspected or a concern.

ANTIBIOTICS

Antibiotics are indicated in patients with known or suspected bacterial nephritis. Bacterial renal infections in birds may result from an ascending ureteritis, extension from local tissues (eg, peritonitis, oophoritis, salpingitis) and hematogenously.[187] Because of the renal portal system and possible shunting of blood from the intestines directly to the kidneys, alimentary tract organisms may contribute to kidney disease and should be considered when using antimicrobial therapy. Drug choices are based on an isolated renal organism (ie, identified during kidney biopsy sampling) or a suspected infectious agent (blood, ovarian, salpinx, or cloacal/fecal cultures and/or supportive histopathology). Clinical consideration regarding potential antimicrobial-induced toxicities is important.

The distribution, elimination and toxicities of many antimicrobials are poorly defined in most bird species, although an excellent review of antimicrobial use in birds with specific consideration toward the renal system is available.[78] Although mammalian literature warns of potential nephrotoxicity with amphotericin B, cephalosporin, fluoroquinolone, trimethoprim/sulfonamide and tetracycline use, only aminoglycosides have been consistently and definitively associated with renal disease in birds.[71,78,117,166] Those drugs with known potential nephrotoxicity should be cautiously used in birds with renal impairment. Until additional studies are completed in birds, antimicrobials that reach high concentrations in the renal tissue and urine without inducing toxicity should be chosen and cautiously used in kidney disease patients.

The ideal duration recommendable for treating renal infections has not been established in birds. In cats and dogs, greater than 4 to 6 weeks of antimicrobial use is generally recommended for treating bacterial kidney infections.[136] The author's clinical experience with bacterial nephritis suggests that response is best when a minimum of 6 weeks of antibiotic therapy is administered. These suggested guidelines are based on renal histopathologic evaluation supporting the presence of infectious nephritis, post-treatment resolution of clinical pathology abnormalities and improved follow-up kidney biopsy and histopathology in a small number of avian renal disease cases.[64,65] There are no controlled studies evaluating antibiotic therapy in active bacterial nephritis cases in birds.[64] Additionally, the author will generally treat concurrent colitis (based on culture and sensitivity results of fecal and/or cloacal cultures) for 5 to 7 days, or until signs abate, in renal disease patients.

MANAGING HYPERURICEMIA, RENAL FIBROSIS AND AMYLOIDOSIS

Allopurinol

Allopurinol's main action is to decrease uric acid production. Specifically, allopurinol inhibits xanthine oxidase, which is required to convert hypoxanthine to xanthine and subsequently to uric acid.[35,53,132,195] In chickens, xanthine dehydrogenase, closely related to xanthine oxidase, is the actual enzyme used in this pathway.[35,46,195] Allopurinol has been specifically shown to prevent renal synthesis of urates and allow the excretion of unchanged xanthine.[195] Regardless, both clinical and experimental data show decreased plasma/serum and/or urinary uric acid levels in birds treated with allopurinol.[46,53,68,132,215] Interestingly, allopurinol does not appear to affect pancreatic xanthine dehydrogenase activity, suggesting differing mechanisms of uric acid metabolism in the pancreas and kidney.[132]

Specifically in red-tailed hawks (*Buteo jamaicensis*), allopurinol has been shown to be toxic at 50 mg/kg PO SID with clinical signs of vomiting and laboratory-supported significant hyperuricemia and a renal function disorder.[145] The renal toxicity was even worse and included visceral gout when red-tailed hawks were given 100 mg/kg followed by 50 mg/kg of allopurinol. The toxic signs were attributed to oxypurinol, the active metabolite of allopurinol.[145] Allopurinol given at 25 mg/kg SID PO to red-tailed hawks was shown to be safe, but had no significant effect on plasma uric acid concentrations.[191c] The authors concluded that allopurinol has a very low therapeutic ratio, at best, in red-tailed hawks and that other means of controlling hyperuricemia, such as urate oxidase, in this species should be considered.[191c] With the exception of red-tailed hawks, allopurinol use is reported to be nontoxic in birds (in studied chickens), including chicks.[132,181,246] Although the long-term effects are not clear, allopurinol given to chickens increases oxidative activity by lowering plasma uric acid, an important avian antioxidant.[215]

The author uses allopurinol as a first-line drug to lower

uric acid when fluid therapy and diet modification alone are not sufficient or when hyperuricemia is severe. Clinical experiences suggest that allopurinol is safe to use at published doses in Psittaciformes and Columbiformes, even when used chronically (3-6+ months). Because of the noted toxicities in red-tailed hawks and until further studies are conducted, it is reasonable to assume that allopurinol should be used judiciously, if at all, in birds of prey.

Colchicine

Theoretically, colchicine can reduce serum uric acid levels in birds and be used to control hyperuricemia. In chicken livers, colchicine reversibly inhibits xanthine dehydrogenase (compared to a "pseudo-reversal" with allopurinol).[67,68] Colchicine prevents the progression of renal disease in humans with familial Mediterranean fever, a disease of recurring fever often complicated by amyloidosis.[179] In humans, colchicine is best known for its antigout activity.[191] In small animals, colchicine blocks the synthesis and secretion of serum amyloid A, and decreases the formation and increases the breakdown of collagen. For these reasons, colchicine has been used to treat amyloidosis and hepatic fibrosis, respectively.[191]

Clinical use of colchicine suggests possible benefit in reducing hyperuricemia in birds with renal disease.[64,65] The author also has used colchicine to reduce renal (and hepatic) fibrosis in birds, and has had good success based on pre- and post-treatment tissue biopsies (M.S. Echols, unpublished data). As such, the author uses colchicine as a second-line drug to reduce hyperuricemia and a primary medication for histologically confirmed tissue fibrosis. Allopurinol and colchicine are well tolerated when given together in most birds. If diagnosed antemortem, colchicine may be used in birds with amyloidosis. No controlled studies were found using colchicine in birds with renal disease.

Urate Oxidase

Urate oxidase also has been recently discussed as an alternative method to manage hyperuricemia in birds.[191b] At least in humans, urate oxidase is reported to degrade the excess of uric acid to allantoin, which the kidneys can clear more easily than uric acid. Urate oxidase also is very specific for urates and uric acid and does not interfere with the metabolism of purines as does allopurinol. In one study, urate oxidase was given (200 and 600 U/kg and 100 and 200 U/kg IM) to pigeons and red-tailed hawks, respectively. When compared to controls, all dosing regimens caused a significant decrease in plasma uric acid concentrations within 2 days of the first dose. The authors concluded that "urate oxidase is much more effective compared with allopurinol," but this promising drug needs further evaluation to better understand its use and potential long-term effects.[191b]

DIETARY MODIFICATION

As a general note, birds should be fed diets appropriate for their species. Supportive dietary therapy should always be considered in any anorectic patient. As is true with all sick birds, renal disease patients should be weighed routinely at regular intervals and monitored for weight loss.

Protein

The question of dietary protein restriction in the face of renal disease remains controversial. The current human and veterinary literature cites arguments for and against both restriction and supplementation of protein with renal disease patients.[94,95,137,239] The current human literature cites malnutrition (potentially from protein-restricted diets) as the most potent predictor of death in end-stage renal failure.[179] The resultant recommendation is that patients on protein-restricted diets should be well supervised and provided adequate calories.[179]

Although feeding 20% protein to chicks, including young cockatiels, has been recommended as a general level for normal development, excessive protein intake for birds with renal disease has not been determined.[207] Feeding diets consisting of 60 and 80% protein (2 separate studies) were required to induce articular gout in genetically predisposed chickens.[9] In a study using adult cockatiels, birds fed up to 70% protein for 11 months had no evidence of visceral or articular gout or significant renal lesions. This led the authors to the conclusion that, in cockatiels, high dietary protein levels are not associated with kidney dysfunction.[123] These experimental diets represent unnaturally high protein levels and do not serve as a realistic evaluation of the effect of diet on renal disease and/or gout in birds.

The management of hypoproteinemia also may be important in birds with renal disease. As mentioned under Part 2: Electrophoresis, Plasma Protein Electrophoresis, the identification of hypoproteinemia and association with renal disease in birds is unclear.

Until further research better defines the role of dietary protein needs in relation to renal disease, avian kidney disease patients should be fed a well-balanced diet appropriate for their respective species. If instituted, birds fed protein-restricted diets should be carefully monitored. No current studies evaluate the effect of low or high-protein diets in birds with naturally occurring renal disease were available at the time of writing. A safe recommendation is that birds with hyperuricemia and/or gout should not consume diets with protein levels greater

than what is considered normal for the given species.

NUTRITIONAL SUPPLEMENTATION

Treatment: Omega-3 Fatty Acids

Omega-3 fatty acids (*n*-3 FA) have gained popularity for their anti-inflammatory, lipid-stabilizing and antineoplastic effects, renal protective properties and other potential qualities.[12,190] The *n*-3 FA are polyunsaturated and are designated by their first carbon-carbon double bond occurring at the third carbon from the methyl group.[190] The *n*-3 FA are those rich in eicosapentaenoic (EPA), docosahexaenoic (DHA) and/or linolenic acid.[4,31] Flax seed and menhaden (cold-water plankton-feeding fish) oils contain predominately linolenic acid, and EPA and DHA, respectively, and therefore have different *n*-3 FA compositions.[4] DHA and EPA are more readily incorporated into biological tissues, but also carry greater potential to create metabolic oxidative stress than linolenic acid.[4] The clinical impact of the differences of the various *n*-3 FA has not been clearly defined.

Studies evaluating *n*-3 FA in mammals serve as the basis for potential treatment value in birds with selected renal disease. At this time, only anecdotal information exists regarding use of *n*-3 FA in birds with renal disease.

In mammals, *n*-3 FA can significantly reduce thromboxane A_2 (TXA) synthesis in platelets and glomerular cells, and increase production of vasodilatory prostaglandins.[95] *n*-3 FA partially substitute EPA and DHA for arachidonic acid in membrane phospholipid.[31,104,159] This pathway decreases the release of arachidonic acid and, subsequently, the cyclooxygenase-mediated synthesis of TXA.[31,95,190] In contrast, most animals readily convert omega-6 fatty acids (*n*-6 FA) to arachidonic acid and, subsequently, eicosanoids (prostaglandins, TXA).[31] As with arachidonic acid, EPA also serves as a substrate for the formation of vasodilatory prostaglandin/cyclins (PGI/PGE) and their respective products (PGI_2 /PGE_2 and PGI_3 /PGE_3), all of which have similar biologic potency.[95,190] These vasodilatory prostaglandin/cyclins increase renal blood flow and single nephron GFR.[31,190]

In humans and rats supplemented with *n*-3 FA for at least 4 to 6 weeks, single nephron GFR, plasma flow and renal blood flow increased and/or decreased renal vascular resistance occurred.[95] In a separate evaluation, dogs on a low-fat diet supplemented with *n*-3 FA had preserved renal function and structure when induced with renal disease.[31] Another study found that *n*-3 FA supplementation reduced glomerular capillary pressure and prevented deterioration of GFR in dogs with renal disease.[32] Compared with controls and thromboxane synthetase inhibitor-treated dogs, beagles supplemented with *n*-3 FA demonstrated increased renal production and excretion of PGE_2 and PGE_3, which was believed to have stabilized renal tubular lysosomal membranes.[95] These *n*-3 FA-supplemented dogs had decreased gentamicin-induced proximal tubular necrosis when compared to controls.[95]

Specific toxicities associated with *n*-3 FA supplementation are poorly described, but some potential adverse effects may occur. Chickens fed diets high in *n*-3 FA had reduced plasma and tissue vitamin E (the body's primary antioxidant) and plasma carotenoid levels due to lipid peroxidation.[4,5,230] Therefore, supplementing the diet with *n*-3 FA increases the requirements for dietary vitamin E.[4,45] As supported by clinical investigations, vitamin E supplementation should be considered with use of *n*-3 FA or any other polyunsaturated fatty acids.[182,230] Specifically, 160 mg/kg of vitamin E (dl-α-tocopherol acetate) was shown to prevent loss of α-tocopherol in tissues, and normalize or increase resistance to lipid peroxidation in chickens fed a commercial diet supplemented with 3% tuna oil (*n*-3 FA).[230]

Other potential side effects may be noted with *n*-3 FA supplementation in birds. Menhaden oil supplementation in laying chickens has been shown to contribute to hepatic lipidosis, likely via enhancing the lipogenic activity (along with estradiol) of the liver.[240] This study cautions the use of *n*-3 FA in reproductively active hens. In another study, chickens fed diets high in *n*-3 FA had no alteration in primary or secondary humoral response, but experienced a 50% reduction in antibody-dependent cell cytotoxicity (ADCC).[80] The concern presented therein was that reduction in ADCC-related immune functions might increase a patient's susceptibility to certain disease (Marek's).[80] The *n*-3 FA supplementation also may affect the ability of antigen-presenting cells to present antigen, again suggesting the potential for immune system alteration.[103] An increased incidence of infectious disease in birds has not definitively been associated with *n*-3 FA supplementation.

Although specific doses have not been established, some believe that the appropriate *n*-6 to *n*-3 FA ratio is more important to inhibiting eicosanoid synthesis from arachidonic acid than is the absolute amount of *n*-3 FA.[95] A dietary *n*-6 FA:*n*-3 FA ranging from 5:1 to 15:1 has been proposed as desirable for dogs and cats with renal disease.[31] Using the above dietary guideline, 2 to 4 weeks are required to see any initial effects of the dietary change in dogs and cats.[31] One study in chickens showed that maximal *n*-3 FA tissue (egg yolk) levels were obtained after 3 to 4 weeks of supplementation.[240] Long-term supplementation (3 to 6 months or more) is likely appropriate if *n*-3 FA are to be used.

The author has successfully used supplements containing

n-6 FA:*n*-3 FA of 4-5:1 to 1:3 combined with low-dose aspirin (0.5-1.0 mg/kg PO q 12 h) to manage histologically confirmed glomerulopathies in avian patients (M.S. Echols, unpublished data). Success was gauged on normalized hyperuricemia (4/4), improved clinical appearance (3/4) and repeat renal biopsy showing normal glomerular light microscopic histology (1/1) in an African grey parrot (*Psittacus erithacus erithacus*), citron-crested cockatoo (*Cacatua sulphurea citrinocristata*), red-lored Amazon parrot (*Amazona autumnalis*) and a ring-neck dove (*Streptopelia risoria*) (M.S. Echols, unpublished data). The author also has used a supplement[e] containing *n*-6 FA:*n*-3 FA of 1:3 (0.22 ml/kg body weight, PO, SID) alone to manage various forms of renal disease in mixed avian species with no recognized adverse side effects. Unfortunately, no clinical trials using fatty acids in avian renal disease were found, only anecdotal reports such as noted here.

Vitamin A

Parenteral vitamin A has been recommended in birds with renal disease.[141] Hypovitaminosis A is a reported cause of renal failure and results from metaplasia of the ureters leading to hyperkeratinization, decreased mucin production and impaction.[116,214] Vitamin A deficiency is discussed in more detail in Chapter 4, Nutritional Considerations. In birds with suspected hypovitaminosis A and renal disease, appropriate diet modification and short-term parenteral vitamin A are logical components of therapy. In such situations, the author gives a single IM vitamin A injection at the beginning of the therapy and recommends correcting the patient's diet to improve long-term nutritional status. The diet must be evaluated and the potential of hypervitaminosis A must be ruled out prior to parenteral vitamin A administration. See Chapter 4, Nutritional Considerations: Section II, Nutritional Disorders for more about hypervitaminosis A.

NON-STEROIDAL ANTI-INFLAMMATORY DRUGS

Non-steroidal anti-inflammatory drugs (NSAIDs) are frequently discussed for use in human and animal renal disease patients.[92,94,95,135,179] In general, NSAIDs such as aspirin and ibuprofen are non-specific cyclooxygenase inhibitors. Low doses of aspirin may actually inhibit platelet cyclooxygenase production, but allow beneficial (vasodilatory) prostacyclin formation and may be safe.[94] Consequently, low-dose aspirin therapy has been suggested to reduce platelet aggregation and subsequent thromboembolism, and to minimize glomerular inflammation for mammalian patients with some glomerulopathies.[94,137] More specific NSAIDs such as thromboxane synthetase inhibitors have been shown to attenuate renal dysfunction/damage as noted by one or more of the following: decreased proteinuria, enzymuria and tubular necrosis, and preserved renal blood flow and GFR in various animals with a variety of renal diseases.[92,94,95,135] Unfortunately, the beneficial effects of low-dose or specific NSAID therapy have not been studied in birds with renal disease.

Although there are limited avian studies, most NSAIDs are eliminated by renal clearance and should be used with caution, as they have been associated with a variety of renal lesions in birds and mammals.[6,120,137,179,196] Flunixin meglumine[d]-induced glomerular lesions in bobwhite quail (*Colinus virginianus*) that increased in severity proportionally with the dose. In this short study, no biochemical or electrolyte parameters were altered, but uric acid was not measured.[120] Aspirin has been associated with significant inhibition of prostaglandin synthesis (specifically prostaglandin $F_{2\alpha}$) in Japanese quail.[164] In this same experiment, aspirin was shown to induce liver enlargement resulting from hepatic lipid accumulation in *n*-6 FA-deficient Japanese quail.[164] Acetylsalicylic acid (aspirin) injected IV into Pekin ducks induced temporary diuresis lasting 30 minutes, which is in contrast to the antidiuretic effect seen in mammals, and had no effect on GFR or peripheral blood pressure.[97] Several *Gyps* spp. of vultures have died with renal failure and gout as a direct result of consuming diclofenac-treated livestock.[175b] The veterinary use of diclofenac has been specifically implicated in the decline of the critically endangered Oriental white-backed vulture (*Gyps bengalensis*) in Pakistan.[175b] These scattered studies serve only to point out potential varied effects of NSAIDs in birds.

Even with the noted toxicities and lack of therapeutic studies in birds, the author feels that low-dose aspirin, and possibly other NSAIDs, use can be beneficial in avian kidney disease patients. In the author's experience, low-dose aspirin (0.5-1.0 mg/kg PO q 12 h) combined with *n*-3 FA supplementation is safe and may be effective at reducing the severity of some forms of avian renal disease, especially glomerular disorders (M.S. Echols, unpublished data). Aspirin (and *n*-3 FA) therapy can be used chronically, and the author discontinues use once evidence of renal disease is gone or the disorder is satisfactorily managed.

TREATMENT SUMMARY

Treatments of avian renal disease should be individualized according to the patient's needs, accurate renal histologic diagnosis (if available), concurrent disorders and client considerations. Identified parasites are treated appropriately. If ova are identified in the urine, consider whether or not the eggs were actually released in the

intestines. Treatment of bacterial nephritis with appropriate antibiotics should be based, in part, on culture and sensitivity results when available. Otherwise, suspected bacterial-induced nephritis should be treated with broad-spectrum bacteriocidal antibiotics that reach high kidney concentrations and which are non-nephrotoxic. Antibacterials also should be considered when concurrent colitis is present. Removing known nephrotoxins and addressing secondary complications may best manage nephrosis. Such secondary complication of any renal disease may include dehydration, hyperuricemia, fibrosis, infectious diseases and anorexia. Dietary-induced renal diseases can be managed with diet change or supplementation, depending on the etiology. Antineoplastic treatment of certain avian renal tumors may be indicated and should be considered. Specifically identifying and managing underlying diseases that may be concurrently present may best control glomerulopathies. Confirmed glomerular disorders in birds without an obvious underlying disease may be managed in some cases with low-dose aspirin and *N*-3 FA supplementation. Nutritional management such as weight loss, providing a balanced diet and vitamin A supplementation also may be indicated.

Table 16.6 represents a quick treatment summary of some of the more common renal disease classifications.

Table 16.6 | Avian Renal Disease Treatment Summary

- **Nephrosis:** Parenteral vitamin A. Remove exposure to toxins if known. Consider *n*-3 FA supplementation.
- **Glomerulopathy:** If identifiable, remove/control any source of infection/inflammation. Give *n*-3 FA and low-dose aspirin until all signs of renal disease (hyperuricemia, histologic changes, etc) are gone. *n*-3 FA can be given chronically if needed.
- **Bacterial Nephritis:** Antibiotics for a minimum of 4 to 6 weeks.
- **"Diet-induced Renal Disease of Color Variety Psittacine Birds":** Discontinue pellets and change diet over to whole grains, seeds, fruits and vegetables as is appropriate for the species. If after 3 to 6 months all signs of renal disease are gone, pellets (<50% of total diet) can be cautiously added to the diet.
- **Renal Fibrosis:** Use colchicine until histologic fibrosis resolves. Otherwise, use colchicine for 6 to 12 months or until laboratory abnormalities normalize. The *n*-3 FA also may be beneficial.
- **Articular Gout:** Use colchicine and allopurinol together until all signs of gout and hyperuricemia have resolved. Consider diagnosing the cause of probable underlying renal disease and manage appropriately. Give vitamin A if hypovitaminosis A is suspected. Articular gout lesions also may be surgically opened and expressed to speed removal of uric acid crystal accumulation. *n*-3 FA may be beneficial. Use aggressive fluid therapy if articular or visceral gout is accumulating rapidly. See Chapter 4, Nutritional Considerations: Section 2, Nutritional Disorders.

Articular gout, although not a renal disease, also is included. With the possible exception of "diet-induced renal disease of color variety psittacine birds," the patient's diet should be modified as is appropriate for that avian species. Secondary infections, dehydration, unacceptable weight loss, etc, should be managed as needed. Combination therapy should be considered when two or more histologic renal lesions are present.

Prognosis

The World Health Organization classification of renal disease is based on distinct glomerular pathological findings and is used for prognosis, treatment and outcome.[109] Presently, no such classification system exists in avian medicine. In fact, there are limited studies that estimate the outcome of selected avian renal disorders. One such review noted that most birds live less than 3 months following a diagnosis of a renal neoplasm.[79] This may seem to offer a poor prognosis, but represents only one form of renal disease that is usually diagnosed late and with which there are few treatment options. Based on the author's experience, several forms of renal disease can be successfully managed and some resolved, giving a good prognosis for long-term health to the individual patient.

Clinicians are encouraged to thoroughly evaluate each avian renal disease patient individually from diagnosis through to management or completion of treatment. Consider renal biopsy as a viable tool for diagnosing and managing disease. Dr. Robert Schmidt states, "The problem is that clinical lab tests may indicate renal disease in birds, but several kidney disorders cause similar (lab) abnormalities. If you want a definitive diagnosis, biopsy the kidney" (R. Schmidt, personal communication, 2003). Treatment completion may have to be defined, in some cases, as return to normal renal histology by follow-up biopsy. Until renal diseases of birds are better understood, classified and treated, the short- and long-term prognoses can be estimated based only on the severity of kidney lesions at that time and secondary disorders of the patient.

Products Mentioned in the Text

a. Combur-9 Stix, Boehringer Mannheim www.burnsvet.com/home/default.asp

b. Renografin-76, Squib Diagnostics, Princeton, NJ

c. Optomega, USANA Health Sciences, Salt Lake City, UT, www.unitoday.net/USPSupplements

d. Banamine, Schering-Plough Animal Health, www.spah.com

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