UROGENITAL TRACT DISEASES OF REPTILES

Drury R. Reavill, DVM, Dipl ABVP [Avian.] Dipl ACVP* and Robert E. Schmidt, DVM, Dipl ACVP, PhD

Zoo/Exotic Pathology Service, 2825 KOVR Drive, West Sacramento, CA 95605 USA


ABSTRACT

This paper will cover the diseases of the urogenital system of reptiles. It is not a comprehensive review. More in-depth disease descriptions can be found in the articles, website, and reference books listed in the literature cited.

The paper is divided by etiologic disease categories involving the urogenital system. A short discussion of the disease conditions is found in each section. For the purposes of this paper, chelonian will refer to all of the shelled reptiles. The term “tortoise” will be used to describe the large land animals that have stout elephantine feet.

Kidney

Abnormalities of Development

There are some described congenital abnormalities of snake kidneys in the literature. These include rare cases of agenesis of parts or a whole kidney in snakes as well as an extra kidney in an anaconda (Eunectus murinus).67

Renal Cysts

Renal cysts are characterized by variable cystic formations within the renal parenchyma.67 Some cysts are derived from greatly dilated renal tubules; however, glomeruli can also develop dilated cystic Bowman spaces. The cysts may be identified throughout one or both kidneys. Some cases of renal cyst development may be due to underlying chronic inflammatory diseases. Tubules may become markedly dilated if there is interstitial fibrosis and inflammation. Gout tophi may also form in these cases.22 There has been a reported case of a possible congenital renal and hepatic cyst development in a giant tegu (Tupinambis merianae). This congenital condition (polycystic disease) is similar to the described lesions reported in mammalian species.67
Hermaphroditism has been reported in a phenotypic male common green iguana (*Iguana iguana*).  

**Deposition Disorders**

**Nephrocalcinosis**

Nephrocalcinosis is due to the deposit of calcium salts (mineral) into the soft tissues and is a common finding in reptiles.  This deposition may be identified within the glomerular mesangium or basement membranes in both the glomeruli as well as the renal tubules. Calcium deposits may be recognized within the interstitium as well as involving the vascular structures. There are two general mechanisms of tissue mineralization; dystrophic and metastatic. Dystrophic calcification occurs in nonviable or dying tissues. Dystrophic is not associated with hypercalcemia or other disturbances of calcium homeostasis. It occurs in cells injured in a variety of ways, including vascular, toxic, metabolic, or inflammatory diseases. Metastatic calcification results in the deposition of calcium in vital tissues and reflects some disturbance in calcium metabolism. In renal disease, it is difficult to differentiate dystrophic (degenerative lesions of uremia) from metastatic calcification (secondary hyperparathyroidism). Histologically calcification is characterized by irregular foci of dense basophilic [blue] material that can be identified by special stains. Additional sites of mineral deposition include the great vessels, heart, lung, intestines and skin.

**Renal Gout**

Renal gout is a deposition of uric acid in the soft tissues; another common lesion in reptiles. There is a variable percentage of uric acid that comprises the end product of protein excretion from the body in across reptile species. In general, the percentage excreted as uric acid is most likely related to the animal’s natural habitat (e.g., desert tortoises (*Gopherus agassizii*) convert the majority of their protein wastes to the insoluble salts of uric acid. The cause of tissue urate deposition is renal dysfunction. Early gout lesions will have uric acid crystals deposited within the tubular epithelial cells with gradually more crystals accumulating around these centers. As the disease progresses, these will break through the basement membrane of the tubule, forming the typical gout tophi. The gout tophi has radiating uric acid crystals surrounded by variable numbers of inflammatory cells. In more acute cases, these inflammatory cells may be degenerate heterophils and, as the lesions become more chronic, there will be macrophages and multinucleate giant cells. Gout tophi are most commonly identified associated with the tubules, although they may also be found within the interstitium as well as within the glomerular mesangium.

It is suspected that gout may be induced by dietary factors. One example is of inappropriate diet fed to herbivorous reptiles, e.g. green iguanas fed high-protein dog and cat foods. In crocodiles (*Crocodylus johnstoni* and *C. porosus*), gout was associated with suspected dietary hypovitaminosis A. There has also been a suggestion that chronic low-grade dehydration can
impair renal function and lead to gout. Renal toxins (described below) are linked to gout formation within the kidney.

Oxalates

Oxalate crystals within the renal tubules as well as present in the colloid of the thyroid gland have been recognized as an incidental finding in wild desert tortoises (Gopherus agassizii). It is suspected the oxalates are of plant origin. In green sea turtles (Chelonia mydas) the calcium oxalate deposition in the renal tubules was associated with granuloma formation.

Pigment Deposition

Pigments identified as granular golden-yellow to brownish material are not uncommonly identified in the cytoplasm of the renal tubular epithelial cells. The identity of this pigment is not always definitively determined. These can be from lipofuscin, hemosiderin, or bile pigments and special stains may be helpful in determining the classification. Lipofuscin is an intralysosomal pigment formed by peroxidation and polymerization of unsaturated fatty acids. While not injurious to the cell, this pigment is a sign of free radical injury and lipid peroxidation. This occurs with loss of antioxidant defense mechanisms such as hypovitaminosis E. It is also associated with aging, severe malnutrition, and cancer cachexia. Inexperienced pathologists could possibly confuse these intracytoplasmic pigments with the cytoplasmic inclusions of Inclusion Body Disease (IBD) which is discussed below.

Amyloid

Amyloid deposition has been poorly documented, but there are small numbers of reports in reptiles. These describe deposition of material consistent with amyloid in a Central American boa (Boa constrictor imperator) and a rainbow water snake (Enhydris enhydris). An amyloid-type material has also been identified in the renal interstitium and mesangium of the glomeruli in four Komodo dragons (Varanus komodoensis). Amyloid is an insoluble pathologic proteinaceous substance, deposited between cells in various tissues and organs of the body. This amorphous, eosinophilic hyaline extracellular substance encroaches on and results in pressure atrophy of adjacent cells. Special stains and electron microscopy can be helpful in further classifying these rare deposits.

Cholesterol

A deposition of cholesterol crystals and associated inflammation has been described in round island geckos (Phelsuma geuntheri). In these geckos, the primary lesion was of a lipodosis involving the liver as well as the spleen. The cholesterol crystals (acicular clefts) were associated with acute and chronic inflammation (xanthomas) and identified in the kidney and liver. In another report of several gecko species (Naultinus grayi, Uroplatus henkelii, U. sikorae, U. fimbriatus), these systemic xanthomatous changes were not identified in the kidney.
Nutrition-related Disorders

Hypovitaminosis A can lead to squamous metaplasia of mucosal epithelium. This metaplasia can involve the renal collecting ducts, and the accumulation of desquamated cornified cells may result in a partial blockage. This can result in the formation of cystic dilations of the ducts. Concurrent and/or subsequent uric acid deposition has also been described in crocodiles with hypovitaminosis A. This metaplasia and hyperkeratosis of the renal tubules will decrease the renal clearance of the urates. With a hyperuricemia, there will be a precipitation of uric acid crystals and the development of gout tophi in multiple organs.

Toxins

Gentamicin has been demonstrated to be nephrotoxic, particularly in snakes. The lesions progress from a cloudy swelling of the proximal tubules to hydropic degeneration and finally to tubular necrosis in one study. The snakes in the high-dose group developed visceral gout and also had extensive tubular necrosis. The tophi were identified on the pericardium, the serosal membranes and parenchyma of the kidney, liver, spleen, and lungs. A similar lesion has also been described in snakes and a South African monitor (Varanus exanthematicus) that were exposed to the insecticide azinphos-methyl.

Agents of Disease

Metazoan Parasites

Trematodes identified as Stylphodora renalis and Stylphodora horrida have been described in the boa and python. Ureters were dilated and filled with the parasites as well as urates, cellular debris, and small amounts of calcium. In the boa constrictor, the trematodes Stylphodora horrida were found in the kidney. Trematodes have also been reported in king snakes (Lampropeltis species), cottonmouth (Agkistrodon species), indigo snakes (Drymarchon species), tropical rat snakes (Liophis species), black stripe snakes (Simoselaps calonotus), bushmasters (Lachesis species), as well as boas (Boidae, genus unspecified).

Spirochid trematodes (blood flukes) have been identified in the ureters of painted turtles (Chrysemys picta) and red-eared slider turtles (Trachemys scripta elegans) which also had ureteroliths. The lesions are due to microgranulomas forming around the ova lodged within the blood vessels.

Strongyloids, which have an alternating free living and parasitic life cycle were recognized in one case of a Burmese python (Python molurus bivitattus). These nematodes were identified in the ureters, kidneys, as well as the small intestine. They were associated with a ureteritis as well as an enteritis. The ureters were bilaterally obstructed. It is felt that these Strongyloides had possibly migrated from the cloaca.

Microfilaria has also been reported in the cardiac great vessels or in the renal vein of reptiles. These have not been associated with significant pathology.
Protozoan Parasites

Coccidia

Intranuclear coccidial protozoa is described in several species of captive tortoises in the United States. The species include: captive-bred juvenile radiated tortoises (*Geochelone radiata*), adult radiated tortoises, wild caught adult impressed tortoise (*Manouria impressa*), captive-bred juvenile leopard tortoise (*Geochelone pardalis*), Travancore tortoises (*Indotestudo forstenii*) and young adult radiated tortoises. All tortoises had intranuclear coccidial parasites in a variety of epithelial tissues. Inflammation of the lung was noted in five tortoises and one had a proliferative pneumonia.\(^{12,28,52}\)

Disseminated visceral coccidiosis by two species of *Eimeria* was found in wild caught indogangetic flap-shelled turtles (*Lissemys punctate andersonii*). The intracellular coccidian was recognized in the melanomacrophages of the liver and spleen, interstitium of the auditory canal, nasal mucosa, pharynx, lung, intestine, and the renal interstitium and epithelial cells of the renal tubules in the kidney. A compromised immune system was felt to be responsible for the disseminated infection.\(^{18}\)

A similar coccidian has also been described in the collecting ducts and ureters of the boa constrictor. The exact classification is currently unresolved but may be *Klossiella boae* or *Tyzzeria boae*. The infected epithelial cells are enlarged but appeared to result in little pathology.\(^{67,68}\)

Cryptosporidia

Rarely cryptosporidia has involved the urinary system. A cystitis and colitis due to cryptosporidia has been reported in green iguanas.\(^{35}\)

*Entamoeba invadens*

*Entamoeba invadens* can cause high morbidity and mortality among some snakes and chelonians\(^{10,30,58,36,39}\) and rarely in lizards.\(^{10}\) *Entamoeba invadens* is a member of the *Entamoeba histolytica* group of amoebae. This protozoa is an important obligate parasite that has a direct life cycle. It is common to see secondary bacterial infections associated with these organisms. In snakes and chelonians, the infections start primarily within the colon. From here, they will be found, by the portal circulation, in the liver and other organs including the kidney.\(^{21,24,67}\) The lesions are of extensive necrosis with inflammation caused by macrophages, heterophils, and lymphocytes. The protozoa are approximately 10-15 µm in diameter, round, and stain poorly on hematoxylin and eosin (H&E) sections.

Microsporidia

Microsporidia are small, intracellular protozoans. They form an infective thick-walled spore containing the sporoplasm which once ingested, is discharged and migrates to its target organ.
Microsporidian protozoa include *Encephalitozoon* sp., *Pleistophora* sp., *Nosema* sp. and other species. The reports in reptiles are primarily of systemic fatal infections in bearded dragons (*Pogona vitticeps*). The lesion is a severe hepatic necrosis with clusters of light basophilic intracytoplasmic microorganisms packed within distended hepatocytes as well as being free in areas of necrosis. Similar microorganisms can be found in cytoplasmic vacuoles of renal epithelial cells, pulmonary epithelial cells, gastric mucosal epithelial cells, enterocytes, capillary endothelial cells, ventricular ependymal cells in the brain, and in macrophages within granulomatous inflammation of the colon, adrenal glands, and ovaries. They are oval, approximately 1µm in length, and stain faintly on H&E sections. The spores are acid-fast positive and stain variably gram positive.

**Renal Flagellates**

There are many flagellate protozoa found in reptiles. Most reside in the lumen of the intestines; however, there are flagellates associated with disease found in the urogenital system of reptiles. These are of the genus *Spiroplastus* and have been recognized as a cause of disease in chelonians and snakes. Cases in chelonians are subacute and the infections can be persistent. Tubulointerstitial nephritis and necrosis are the common renal lesions with the protozoa accumulating within the lumen of the tubules. The majority of cases seen by the authors have been in box turtles (genus and species not provided), a water dragon, and geckos (species not provided). The life cycle is direct with transmission by ingestion of food contaminated with affected urine or feces. They can be identified on fresh urine or fecal direct smears. The trophozoites are pyriform in shape and have multiple flagella.

**Myxosporidia**

Myxosporidia (protozoa of the class Myxosporea and phylum Myxozoa) are common parasites of fish, and uncommon parasites of reptiles. The genus *Myxidium* is best described in the urinary system of chelonians; however, they have not typically been associated with significant pathology. Recent reports indicate this protozoa can be a cause of renal disease in chelonians, primarily turtles (Indo-Gangetic flap-shelled turtles [*Lissemys punctata andersonii*] and Crowned River turtles [*Hardellathurii*]). Histologically, renal intratubular myxozoan spores were associated with renal tubular necrosis, tubular mineralization, and chronic interstitial nephritis, with membranoproliferative glomerulopathy. Specific identification of these protozoa requires electron microscopy and genomic analysis.

**Chromomycosis**

Chromomycosis is a systemic fungal infection by pigmented fungi of the family Dematiaceae. These fungi are saprophytes that live in soil and decaying vegetable matter, predominantly in warmer climates of tropical and subtropical countries. Some identified members include *Cladosporium herbarum*, *Scolecobasidium humicola*, *Fonsecaea* spp., *Phialophora* spp., *Rhinocladiella* spp., *Hormodendrum* spp., *Curvularia* spp., and *Drechslera* spp. The fungal organisms produce a characteristic amber-brown, thick-walled, septate structures known as sclerotic bodies. Chromomycosis infection is most commonly described in amphibians but has
also been reported in mammals, a radiated tortoise, pythons, boas, and a mangrove snake (*Boiga dendrophila*) with a concomitant fibrosarcoma. Transmission is suspected to be by the alimentary tract and/or skin abrasions. Skin trauma incurred during feeding may be the most likely portal of entry (especially in colonies of animals or with vigorous eaters). The stress of captivity or other debilitating disease processes can also contribute to the development of the disease.

Chromomycosis generally presents first as an ulcerated or granulomatous skin lesion. These lesions can be nodules, grey-black papules and/or irregularly shaped grey-black ulcers. The most common sites for external lesions are the dorsal and ventral skin surfaces. Over a period of time (which can be greater than 6 mo) the animal succumbs to disseminated disease. On gross examination multiple organs may contain multiple coalescing grey-black nodules. These granulomas are commonly described in the liver and kidney, but also occur in the spleen, lung, heart, adrenal, gastrointestinal tract (serosal and mucosal surfaces), bone, and central nervous system. These organisms are zoonotic with human infection resulting from the contaminated environment.64

Bacteria

Any number of bacterial infections can involve the urinary system. The majority of these in reptiles are gram-negative bacteria and often *Pseudomonas* or *Aeromonas* species. With bacterial septicemias, the renal blood vessels within the glomerular capillaries as well as in the interstitium may be blocked by clusters of the bacterial organisms. There may also be a peripheral heterophilia in response to a bacterial infection.

Mycobacterial infections, which are generally systemic diseases, can involve the kidney. Although all reptiles are suspected to be susceptible, the reports are rare. Those reports describing renal involvement include a Kemp's ridley sea turtle (*Lepidochelys kempii*) with systemic *Mycobacterium chelonae* and disseminated mycobacteriosis in freshwater crocodiles (*Crocodylus johnstoni*).3,16 The granulomas typically have central necrosis supporting large numbers of acid-fast rod-shaped bacteria and surrounded by multinucleate giant cells as well as macrophages. There may be a fibrotic capsule, depending on the chronicity of the lesions. *M. chelonae* was identified as a systemic infection in the Mojave (*Crotalus scutulatus*) and Western rattlesnakes (*Crotalus viridis*).53

Virus

*Adenovirus*

The kidney can be involved in systemic adenovirus infections of bearded dragons (*Pogona vitticeps*).46 The large, angular amphophilic intranuclear viral inclusions are present within the epithelium of the renal tubules as well as hepatocytes and biliary epithelium. These are associated with a non-suppurative interstitial nephritis and hepatitis.
Inclusion Body Disease (IBD)

The eosinophilic glomerular intracytoplasmic inclusion bodies within the epithelial cells of many tissues is the lesion associated with inclusion body disease (IBD) of boid snakes and Palm vipers (Bothriechis marchi). This disease can be responsible for clinical signs including chronic regurgitation, incoordination, loss of righting reflexes, paresis, and an increased incidence of secondary infections such as stomatitis and pneumonia. Clinical signs referable to the central nervous system are more prominent in the Pythoninae subfamily. Antemortem diagnostics include CBC’s and biopsies of the esophagus (especially of lymphocytic stromal aggregates or “tonsils”), gastric mucosa, and liver. The etiologic agent of IBD in boids is an arenavirus. At this time the mode of transmission is unknown; however, consider fecal/oral contamination, airborne via respiratory discharges, or by the snake mite (Ophionyssus natricis) as a vector.

Chronic Renal Disease

The majority of reptiles that have renal disease generally have chronic changes in which the etiology can no longer be determined. These chronic changes include variable degeneration and/or necrosis of glomeruli and/or tubules. Interstitial and glomerular fibrosis may be prominent. There can be variable dilation of tubules and, in some cases, calcification as well as gout tophus formation. These types of lesions are more common in the common green iguana and other large lizards, and are suspected to be of multifactorial etiology, including poor nutrition such as extremes in protein, chronic dehydration, and imbalanced vitamin and/or mineral supplements.

Renal Tumors

The primary renal tumors reported in reptiles are adenocarcinoma, adenoma, and nephroblastoma. These tumors have been described in lizards, snakes, and chelonians. Several references list tumors affecting the kidney, including the primary renal tumors. In lizards, renal tumors present as firm swellings in the caudal coelom and can occasionally be palpated extending cranially past the rim of the pelvis. In snakes, swelling in the caudal third of the body cavity is typical. Grossly one or both kidneys may have irregular masses within the parenchyma.

Differential diagnoses for these lesions include acute and chronic renal disease in lizards and impacted eggs in snakes. Occasionally in snakes, renal tumors have been mistaken for impacted eggs and massaged out of the body through the cloaca. Metastasis is unusual but has been reported. Sites include liver, lung, and perirenal abdominal wall. Surgical removal of renal tumors is recommended; however, the tumor can be present bilaterally in the kidneys.

Urinary Bladder

Any microscopic precipitates or polycrystalline concretions found in the urinary tract are classified as urinary calculi. These urinary calculi, uroliths, have been reported in lizards, chelonians, and snakes. Most are located in the bladder of those animals with a urinary
bladder, and uncommonly some cases are described in the ureters and cloaca.\textsuperscript{23} For species without urinary bladders, such as snakes, the concretions may be found in the distal ureters where urine is frequently stored. The cause of the calculi formation is unknown. Some proposed etiologies include nutritional deficiencies, such as of vitamin A and D. Excessive dietary protein, oxalates, as well as bacterial infections and suture remnants have been reported as causes. Some of these factors contribute to or form a nidus on which concentric layers of material are laid. A common clinical finding with calculi formation is dehydration. In tortoises, a phenomenon recognized in females is of fully developed eggs being retropulsed into the urinary bladder. They apparently are unable to be passed back out and will develop into a calculus.\textsuperscript{44,61}

The majority of small calculi generally will not result in significant lesions or clinical signs. If there are clinical signs they are of anorexia, constipation, egg binding, dysuria, and poor growth.\textsuperscript{37,40} Calculi with rough surfaces or increasing sizes may irritate the lining of the urinary bladder, resulting in hematuria as well as hypertrophy of the bladder wall and hyperplasia of the lining epithelial mucosa. Pressure necrosis to the bladder wall as well as internal viscera have been reported, particularly with large stones.\textsuperscript{32,38,40} Uroliths of reptiles all appear to be composed of a type of urate salt. This urate salt may be complexed with calcium and phosphates.\textsuperscript{38,41} Rarely cystic calculi primarily composed of apatite (calcium phosphate) are reported.\textsuperscript{41}

The authors have identified transitional cell carcinomas in the bladder of common iguanas.

Reproductive System

\textit{Scent Gland and Hemipene Impactions}

These conditions are primarily identified in the common green iguana as well as some commonly kept snakes. There will be casts of the inspissated exudate that accumulates around the hemipene and occasionally involves the scent gland.\textsuperscript{32} This will be composed of keratin and other secretory material commonly supporting secondary bacterial and fungal infections.

\textit{Hemipene or Penile Prolapse}

The majority of these conditions are due to trauma during eversion of the copulatory organ in breeding season. The trauma results in extensive swelling, preventing retraction and leads to further trauma. Secondary infections are common.

\textit{Salpingitis and Yolk Retention in Reptiles}

Inflammation of the oviduct/uterus can be due to infectious agents, or secondary to retained yolk with impaction. The inflammation in the latter case is secondary to irritant tissue effects of the yolk protein.

A study was conducted to compare thiamine concentrations in American alligators (\textit{Alligator mississippiensis}) and Florida largemouth bass (\textit{Micropterus salmoides floridanus}). Results
suggest that thiamine deficiency might be playing an important role in alligator embryo survival. These results suggest that thiamine deficiency might be playing an important role in alligator embryo survival but not in reproductive failure and recruitment of largemouth bass. The cause(s) of this thiamine deficiency are unknown but might be related to differences in the nutritional value of prey items across the sites studied and/or to the presence of high concentration of contaminants in eggs.55

Tumors

Teratoma

Teratomas are composed of tissues derived from at least two of the three embryonic germ layers (endoderm, mesoderm, and ectoderm). Typically, they arise from the gonads. The ovaries are common sites for teratoma development in the common green iguana (Iguana iguana)1 and other unspecified saurians29, as well as a chelonian.48 Clinical signs are the result of a space-occupying mass and may include digestive and respiratory dysfunction as well as coelomic cavity distention. Differentials in females include neoplasia or granuloma of the ovary or oviduct, cystic ovary, segmental pyosalpinx, and neoplasm or granuloma of the adrenal gland or spleen. In the few described cases the tumors had a rapid growth rate and a potential for malignancy. Early surgical removal is recommended.

On the basis of the morphologic and immunohistochemical results, a diagnosis of ovarian undifferentiated carcinoma was made in a corn snake (Pantherophis guttatus guttatus). Histologic specimens consisted of a highly cellular mass composed of pleomorphic, spindle-shaped cells and, occasionally, round to polygonal cells arranged in irregular fascicles. The neoplastic cells were immunoreactive for cytokeratin (AE1/AE3), smooth muscle actin, and skeletal muscle actin, but did not stain for vimentin or desmin.50

LITERATURE CITED

45. Montali RJ, Bush M, Smeller JM. 1979. The pathology of nephrotoxicity of gentamicin


