UROGENITAL TRACT DISEASES OF REPTILES AND AMPHIBIANS

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ABSTRACT

This paper covers the diseases of the urogenital system in both reptiles and amphibians. 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.

After a brief summary of the normal gross appearance, the paper is divided by etiologic disease categories involving the urogenital system. A short discussion of the disease conditions of reptiles and amphibians are 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. Few references to marine turtles, caecilian, and crocodilian species are included, as these are uncommonly seen in most clinical practices.

Normal Gross Anatomy

It will be important to recognize the normal gross appearance of the urogenital tract in order to determine if there are abnormalities that require further examination, either by surgical biopsies or histologic examination during a necropsy procedure.

The kidneys in lizards are located in the caudal dorsal coelom, lateral to the lumbar spine. Most lizards, particularly the iguanids, will have the kidneys within the pelvic canal. Monitor species have the kidneys located approximately mid-caudal coelom. The kidneys are paired, symmetric, elongated, and slightly lobulated. In many lizard species, the caudal aspect of the kidneys may be closely apposed or fused. The ureter leads from each kidney to the urodeum. A thin-walled urinary bladder is present in most species and it connects with the urodeum.[82] Males of some lizard species, such as the geckos, skinks, chameleons, and iguanids, possess a sexual segment of the renal tubule. The sexual segment can give a portion of the kidneys a more swollen appearance. In chameleons, these sexual segments are generally located in clusters situated throughout the kidneys. The clusters are typically wedge shaped and may be confused with disseminated disease.[116] The sexual segment of lizards and snakes is anatomically the last part of the nephron before it enters the collecting duct.[6]

Reproductive organs in lizards are paired and located craniomedial to the kidneys. The oval testes are yellow to off-white, and the ovaries are clusters of variably developed follicles that are yellow to pink. Males have paired hemipenes that are inverted in the ventral tail distal to the vent. These blind-ended organs mechanically transfer sperm via the seminal groove and are used for reproduction, not urination.[37]

The kidneys of snakes are elongated and located in the caudal third of the body. They are brown, paired, and flattened organs that have prominent segmental lobules. Generally, the right kidney is located cranial to the left. Males of many species have a sexual segment that when they are reproductively active, will result in enlargement of the kidney. The ureters connect the kidney to the urodeum, and a urinary bladder is not present in snakes. The ureters enter the cloaca dorsally, where they are separate from the vas deferens or oviduct.[81]

The sexual segment of the kidney in male snakes will produce a secretion rich in proteins and lipids, which is used as a copulatory plug.[81] In snakes, the sexual segments are typically situated at the surface of the kidneys. Histologically these segments are comprised of enlarged tubular epithelial cells that contain abundant eosinophilic granules. When they are active, producing the secretions, they can be grossly confused with tubules dilated with urates or even gout.[6]

The testes in snakes are elongated, lightly colored, and located between the pancreas and the kidneys. They will enlarge during breeding season as do the testes of any of the reptilian and amphibian species. The ovaries are located near the pancreas. Male snakes have paired hemipenes that are also inverted into the ventral tail base. They have no connection with the urinary system. In snakes there is a cloacal or musk gland that lies parallel to the inverted hemipenes and opens into the dorsal cloaca.[81]

Chelonian kidneys are retroperitoneal and attached to the carapace just dorsal to the hind limbs. These paired structures are generally flattened, lobulated, symmetric, and in close association with the gonads. All chelonians possess a urinary bladder. The ureters connect the kidney to the bladder, where they empty into the neck of the bladder as opposed to entering the urodeum as in other reptiles. The urinary bladder, which is thin-walled, distensible, and, in some species, lobed, and has a short urethra connecting the bladder to the urodeum of the cloaca.[83]

The ovaries and testes of chelonians are paired and are anterior to the kidneys. Male chelonians do not have hemipenes, like other reptiles. They have a dark purple single erectile copulatory organ that lies on the floor of the proctodeum. There is a seminal groove, which aids in sperm transport.[83,91]

There is some variation in the gross anatomy of different amphibian species. In general, the kidneys are just caudal and adjacent to the gonads, positioned in the dorsal caudal coelom. In pregnant females, the follicles/ova will fill the coelomic cavity. The kidneys are normally red-brown in color and cylindric in shape. It may be possible to identify a focal area of color change in the renal parenchyma, which is the adrenal gland.[86] A urinary bladder is present in many amphibians but is easily overlooked during examination. It is a very thin-walled structure ventral to the large intestine and is connected to the cloaca. The urinary bladder in many caecilians is bilobed.[86]

Kidney

Abnormalities of Development

There are a number of described congenital abnormalities of the kidneys. Rarely agenesis of parts or a whole kidney has been reported in snakes as well as an extra kidney in an anaconda (*Eunectus murinus*).[116]

An inherited trait in axolotls (*Ambystoma mexicanum*) results in a lethal renal insufficiency and short toes.[45]

Renal Cysts

Renal cysts are characterized by variable cystic formations within the renal parenchyma. These have been recognized in reptiles as well as amphibians.116, 115 Some cysts are derived from greatly dilated renal tubules. 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.[46] There has been a reported case of a renal and hepatic cyst development in a Giant Tegu (*Tupinambis merianae*). This congenital condition (polycystic disease) has been reported in mammalian species.[116]

Multiple renal cysts are also described in hybrids between Japanese toads (*Bufo japonicus*) and Chinese toads (*Bufo raddei*).[69] With increasing age, these cysts transform to renal carcinomas.[69]

Hermaphrodites

The toads of *Bufo, Pedostibes, Pseudobufo, Atelopus, Leptophryne, Dendrophryiscus*, and some *Nectophryne* have a structure called the Bidder's organ.[26] This is a wedge-shaped band or cap-like mass of pigmented oocytes that are closely associated with the cranial pole of the testes. This is a normal structure for the listed toads; however, the organ can be easily misclassified as the ovotestes of hermaphrodites. Hermaphroditism has been recognized in a Madagascar tomato frog (*Dyscophus antongilii*).[26] This animal had both testes that exhibited active spermatozoa formation as well as masses of heavily pigmented yolked ovarian follicles. Hermaphroditism has also been reported in a phenotypic male common green iguana (*Iguana iguana*).[75]

Deposition Disorders

Nephrocalcinosis

Nephrocalcinosis is due to the deposit of calcium salts (mineral) into the soft tissues and is a common findings in reptiles.[39,55,116] 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: dystropic 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.[90,97]

Renal mineralization is rarely described in amphibians. Extensive mineralization of the kidneys and heart was noted in an Argentine horned frog (*Ceratophrys ornata*).[25] This frog also had coelomic cavity fluid accumulation. The kidneys were enlarged and mottled with yellow-gray foci.

Edible frog tadpoles (*Rana esculenta)*, Solomon Island leaf frogs (*Ceratobatrachus guentheri*), and leopard frog tadpoles (*Rana pipiens*) that are fed diets high in oxalates develop an oxalic calculogenesis.[18,29,99] These may represent dietary imbalances secondary to diets high in oxalates (e.g., spinach). There will be extensive mineralization as well as granulomas forming around crystals consistent with oxalic crystals within the renal tubules. They have been reported as a common incidental finding and occasionally leading to nephrosis.

Renal Gout

Renal gout is a deposition of uric acid in the soft tissues; another common lesion in reptiles.[3,12,39,74,109,110,116] There is a variable percentage of uric acid that comprises the end product of protein excretion from the body in both reptiles and amphibians. In general, the percentage excreted as uric acids is most likely related to the animal's natural habitat (e.g., desert tortoises [*Gopherus agassizii*] convert wastes to the insoluble salts of uric acid).[84] 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. Such factors can be an inappropriate diet fed to herbivorous reptiles (e.g., green iguanas fed high-protein dog and cat foods). In crocodiles, gout was associated with suspected hypovitaminosis A.[3] There has also been a suggestion that chronic low-grade dehydration can impair renal function and lead to gout.[110] Renal toxins are linked to gout formation within the kidney.[76]

This condition is uncommon in amphibians. There are a few reports of renal gout and concurrent bladder stones in painted-belly monkey frogs (*Phyllomedusa sauvagii*).[115]

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 definitively determined; however, one reference suggests that it is lipofuscin.[116] 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. Other materials such as hemosiderin or bile pigments are possible and special stains can be helpful in determining the classification. 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*).[17] An amyloid-type material has also been identified in the renal interstitium and mesangium of the glomeruli in four komodo dragons (*Varanus komodoensis*).[31] 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. No reports of amyloid deposition in amphibians are identified via VIN and PubMed literature searches (DRR 2006).

Cholesterol

A deposition of cholesterol crystals and associated inflammation has been described in round island geckos (*Phelsuma geuntheri*).[16] In these geckos, the primary lesion was of a lipidosis involving the liver as well as the spleen. The cholesterol crystals are acicular clefts associated with chronic and acute inflammation (xanthomas) and identified in the kidney and liver. In another report of different gecko species, these systemic xanthomatous changes were not identified in the kidney.[32]

There are two reports in Cuban tree frogs (*Osteopilus septentrionalis*) of xanthomatosis involving many organs including the kidneys and ovaries.[11,93] The condition is one in captive amphibians having a high serum or plasma cholesterol and concomitant lesions of corneal lipidosis. The underlying cause of this disorder is unknown, but it is likely that a diet high in cholesterol plays a role.

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 spaces.[116] Concurrent and/or subsequent uric acid deposition has also been described in crocodiles.[3] 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.[76] The lesions progress from a cloudy swelling of the proximal tubules to hydropic degeneration and finally to tubular necrosis. 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.[116]

The toxicity of the anti-cancer drug cis-diamminedichloroplatinum (II) (cisplatin), has been studied in the frog, *Rana pipiens*. Major non-nervous system toxicity occurred in the kidney. Renal failure was manifested as anasarca and increasing blood urea nitrogen (BUN). Histopathologic changes included acute tubular necrosis and tubular dilatation, which were more severe at higher doses. Interstitial fibrosis occurred after prolonged survival after a single dose. Ultrastructurally, there was increased electron-dense material in tubular cells, but no specific changes in mitochondria or nuclear structures were seen.[7]

Agents of Disease

Metazoan Parasites

Trematodes identified as *Styphlodora renalis* and *Styphlodora horrida* have been described in the boa and python.[14,59,78] 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 *Styphlodora horrida* were found in the kidney. Trematodes have also been reported in king snakes, cottonmouth, indigo snakes, tropical rat snakes, black stripe snakes, bushmasters, as well as boas.[104]

The metacercariae of echinostomatid trematodes also may affect the kidneys of leopard frogs and green frogs (*Rana clamitans*). Cysts occur predominantly in the renal cortex and some are within the lumen of the Bowman's capsules. Most cysts are enclosed by a fibrous capsule of host origin, or are surrounded by an inflammatory mantel. In heavily infected kidneys the cysts result in the displacement of functional renal tissue which may impair renal function.[68]

Spirorchid trematodes (blood flukes) have also been identified in the ureters of painted turtles (*Chrysemys picta*) and red-eared slider turtles (*Trachemys scripta elegans*) which also had ureteroliths.[47,54] The lesions are due to microgranulomas forming around the ova lodged within the blood vessels.

Strongyloids, which have an alternating free moving 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.[107]

Microfilaria have also been reported in the great vessels or at the renal vein of reptiles. These have not been associated with significant pathology.[116]

Protozoan Parasites

Coccidia

An intranuclear protozoa is reported in several species of captive tortoises in the United States.[30] This has been described in two captive-bred juvenile radiated tortoises (*Geochelone radiata)*, two adult radiated tortoises, one wild caught adult impressed tortoise (*Manouria impressa*), one captive-bred juvenile leopard tortoise (*Geochelone pardalis*), three Travancore tortoises (*Indotestudo forstenii*) and four 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.[30,52,89]

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 appear to result in little pathology.[116,117]

Isospora lieberkuehni has been identified in the kidney of leopard frogs (*Rana pipiens*). The oocytes infect the tadpoles and the meronts and later stages develop after metamorphosis. These are intracytoplasmic merozoites that are associated with few to no lesions.[63]

Entamoeba invadens

Entamoeba invadens can cause high morbidity and mortality among some snakes and chelonians.[20,53,58,60,61,65] and rarely in lizards.[20] *Entamoeba invadens* is a member of the *Entamoeba histolytica* group of amoebae. This protozoon 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.[41,48,116] The lesions are of extensive necrosis with inflammation of macrophages, heterophils, and lymphocytes. The protozoa are approximately 10-15 µm in diameter, round, and stain poorly on hematoxylin and eosin (H&E) sections.

Renal amebiasis has been described in a *Bufo marinus*. This is uncommon in amphibians. In this collection, one animal had, within the tubules, an oval unicellular protozoa with characteristics most consistent with a amoeba protozoa. Most of the amoeba had a single nucleus, but some had up to four. They are approximately 11-32 µm in diameter, staining positive with PAS and Grimelius silver. Specific identification of these amoeba protozoa requires the trophozoite as well as cyst size. In this report the protozoal infection was associated with a lymphohistiocytic interstitial nephritis.[105]

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*).[49] The primary 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 1 µm 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 and amphibians. 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 *Spironucleus* and have been recognized as a cause of disease in chelonians and snakes.[116,118] 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 amphibians and 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[28,38,116] in chelonians, primarily turtles (Indo-Gangetic flap-shelled turtles [*Lissemys punctata andersonii*] and Crowned River turtles [*Hardella thurjii*]). 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.

Renal myxosporidiasis and associated lesions were seen in Asian horned frogs, (*Megaphrys nasuta*) and hyperoliid frogs (*Afrixalus dorsalis, Hyperolius concolor, Hyperolius* sp.). In the horned frogs, the organism was identified as *Chloromyxum* sp. on the basis of histopathology, cytology, and electron microscopy. Histologic changes in the kidneys included varying degrees of renal tubular dilation and necrosis, and mild to severe nonsuppurative tubulointerstitial nephritis associated with vegetative stages of the myxosporidian.[77] The hyperoliid frogs developed a proliferous, polycystic and sometimes fatal kidney disease due to an infection with the myxosporidia *Hoferellus anurae* n. *Myxosporidian plasmodia*, different developmental stages and spores occurred in the kidney, ureter, and urinary bladder and in the intestine of the frogs.[80]

Fungal Agents

Chromomycosis

Chromomycosis is primarily a systemic fungal infection by pigmented fungi of the family Dematiaceae.[102] These fungi are saprophytes that live in soil and decaying vegetable matter, predominantly in warmer climates of tropical and subtropical countries.[73] Some identified members include *Cladosporium herbarum*, *Scolecobasidium humicola*, *Fonsecaea* spp., *Phialophora* spp., *Rhinocladiella* spp., *Hormodendrum* spp., *Curvularia* spp., and *Drechslera* spp.[2,9,15,23,92,103] The fungal organisms produce a characteristic amber-brown, thick-walled, septate structures known as sclerotic bodies.[103] Chromomycosis infection is most commonly described in amphibians but has also been reported in mammals, a radiated tortoise, pythons, boas, and a mangrove snake 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.[94,102]

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.[102] 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.

Exfoliative cytology of the cutaneous lesions may have mononuclear cells surrounding pigmented, septate fungal hyphae.[102] The fungal organisms are not readily isolated by culture, as they are slow growing and temperature sensitive (25–27°C).[19,108]

Histologically the multifocal granulomas are comprised of macrophages, lymphocytes, plasma cells, and multinucleated giant cells. They contain brown-pigmented fungal elements which are spherical, thick-walled sclerotic bodies (8–12 μm in diameter) with equatorial and occasionally vertical septations. Pseudohyphae and, rarely, septate hyphae can be found. The fungal organisms may be found extracellularly as well as within the cytoplasm of multinucleated giant cells. These organisms are zoonotic with human infection resulting from the contaminated environmental.[103]

Bacteria

Any number of bacterial infections can involve the urinary system. The majority of these in both reptiles and amphibians are gram-negative bacteria and primarily *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 bacteremia.

Mycobacterial infections, which are generally systemic diseases, can be identified within the kidney. Although all reptiles are suspected to be susceptible, the reports are rare. Those with renal involvement include a Kemp's ridley sea turtle (*Lepidochelys kempii*) with systemic *Mycobacterium chelonae* and disseminated mycobacteriosis in freshwater crocodiles (*Crocodylus johnstoni*).[4,36] 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.

Mycobacterial species resulting in systemic infections of amphibians include *Mycobacterium ranae* (previously reported as *M. fortuitum*), *Mycobacterium xenopi*, and *Mycobacterium ranicla*.[21,56,57] These infections are generally opportunistic and are present in the environment. They can be cultured from aquariums as well as from the skin of amphibians.[21] *Mycobacteria* spp. generally cause disease opportunistically through skin or mucosal abrasions in debilitated amphibians. Clinical signs and gross lesions include: sluggish behavior and long periods of motionless in water, multiple abscesses on feet with cellulitis extending into the legs and skin, nodular cutaneous lesions that may be ulcerated, splenomegaly and numerous small nodules in subcapsular locations in the liver, kidneys, and spleen. Histologically these nodules are granulomas comprised of macrophages surrounded by a rim of epithelioid cells and several layers of fibroblasts. Nodules may contain numerous pleomorphic acid fast bacilli.

Chlamydophila

Chlamydophila psittaci septicemia of African clawed frogs (*Xenopus tropicalis*) and eyelash leaf frogs (*Ceratobatrachus guentheri*) results in clinical signs similar to bacterially induced "red leg."[42,43,44,111,113] The frogs develop lethargy, skin sloughing, petechiation and cutaneous depigmentation. Respiratory distress, characterized by increased frequency of gulping air, edema and hemorrhage also occurs.[112] Outbreaks are generally epizootics of high morbidity and mortality. On gross examination animals have hepatomegaly, hydrocoelom, subcutaneous edema, cutaneous petechiation, and epidermal ulceration.[113] A pyogranulomatous inflammation is present in multiple organs (liver, spleen, kidney, lung, heart) and basophilic intracytoplasmic inclusions consistent with chlamydial organisms are within sinusoidal lining cells and hepatocytes.[113]

Viruses

IBD

The eosinophilic glomular 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*).[51,88,106] 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 is suspected to be a retrovirus.[51] At this time the mode of transmission is unknown; however, consider fecal/oral contamination, airborne via respiratory discharges, or by the snake mite as a vector.

Iridovirus

Iridovirus has been recognized as systemic infections in both salamanders and frogs.[8,85] Infection in frogs is characterized by increased tadpole mortality and is best described in the tadpoles of the American bullfrog.[114] There will be hemorrhage identified in the skin and muscle as well as stomach. Necrotic foci are recognized in the liver, kidney, and intestines. *Xenopus laevis* has been used as a model to study the amphibian immune system response to iridovirus.[27] A viral epizootic has been recognized in larval and adult tiger salamanders.[8] The primary lesion was a skin lesion with cutaneous ulcers and erosions. These epithelial cells contain large cytoplasmic inclusions. Systemic effects were noted; however, no specific lesions were associated with the direct viral infection.

Herpesvirus

The classic viral renal infection of leopard frogs is Lucke's herpesvirus. This particular herpesvirus will induce bilateral papillary renal adenocarcinomas. It is temperature-dependent and has two phases. In the winter phase (4-9°C), the virus replicates in the renal tubular epithelial cells, resulting in lysis and shedding in the urine. Intranuclear inclusions can be identified at this time. In the summer phase, at temperature 22-25°C, the virus can no longer be identified or isolated. The kidneys will enlarge 3-4 times and will be multinodular with white to tan foci.[24,96]

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 formations. 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. Similar lesion have been seen in amphibians.[115,116]

Renal Tumors

The principal renal tumors reported in reptiles are adenocarcinoma, adenoma, and nephroblastoma. These tumors have been described in lizards, snakes, and chelonians.[5,10,33,50,74] Several references list tumors affecting the kidney, including the primary renal tumors.[13,115,116] 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.

Renal tumors of amphibians are described previously under cystic kidneys and Lucke's viral infection.

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, snakes, and amphibians.[62,67,72] Most are located in the bladder of those animals with a urinary bladder, and uncommonly some cases are described in the ureters and cloaca.[47] 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.

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.[62,67] 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.[55,64,67] Uroliths of reptiles and amphibians all appear to be composed of a type of urate salt. This urate salt may be complexed with calcium and phosphates.[64,72] Rarely cystic calculi primarily composed of apatite (calcium phosphate) are reported.[72]

Cystic calculi have been reported leopard frogs (*Rana pipiens*) and in uricotelic species such as, waxy tree frogs (*Phyllomedusa bicolor*), painted-belly monkey frogs (*Phyllomedusa sauvagii*), and leaf frogs (*Phyllomedusa cf. tarsius*).[86,98,115]

Trematodes may be found in the urinary bladder of amphibians. They can cause damage to the transitional epithelium at attachment points.[115]

Reproductive System

Scent Gland and Hemipenile 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 one hemipenis or both hemipenes and occasionally involves the adjacent scent gland or glands.[55] This will be composed of keratin and other secretory material commonly supporting secondary bacterial and fungal infections.

Hemipenile 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.

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 (*Alligator mississippiensis*) and Florida largemouth bass (*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.[95]

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 saurians,[40] as well as a chelonian.[79] 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 (*Elaphe guttata guttata*). 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.[87]

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