REPTILE AND AMPHIBIAN URINARY TRACT MEDICINE: DIAGNOSIS AND THERAPY

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ABSTRACT

The urinary tract includes kidneys, ureters, cloaca, and bladder in reptiles and amphibians. Problem-oriented medicine includes identifying clinical problems, defining diagnoses for each problem, implementing a plan to address each diagnosis, and reformulating the plan as indicated in follow-up evaluations. This paper is intended to serve as an instructional aide for those who are preparing for certification in reptile and amphibian practice.

Introduction

This paper describes problem-oriented reptile and amphibian urinary tract medicine for practitioners who are working towards specialty certification in reptile and amphibian practice. It is limited to problems of the kidneys, ureters, cloaca, and bladder even though the urogenital tract does include the gonads and related tubular structures. Diseases of reproduction will be covered at a future date because the clinical approach differs substantially and adequate coverage is outside the limitations of publication space and presentation time. Surgical procedures are mentioned when relevant to the diagnostic or therapeutic plan.

A specialty-level practitioner solves clinical problems by overtly documenting the process of gathering information; defining problems; implementing a diagnostic, therapeutic, and client education plan for each problem; and following up as necessary over time. Basic information for each case includes the signalment, history, physical examination, and minimum objective database. Problems are identified in subjective and objective data, in evidence-supported pathophysiologic reasoning, and in etiology-specific diagnostic tests. Each problem is associated with one or more body systems and a list of differential diagnoses is proposed for each problem. An accurate diagnosis is required to choose appropriate therapy and predict prognosis. The reliability of a diagnosis is based on the validity of the information available to support it. A specific etiologic diagnosis usually requires a combination of validated diagnostic tests that can include hematology, clinical chemistry, cytologic examination, imaging, serology, isolation of pathogens, pathogen-specific nucleic acid testing, and histopathology. Substantial background information is required to understand species-specific anatomy, physiology, disease prevalence,

and captive care requirements. Specialist practitioners regularly scrutinize the best available evidence to interpret diagnostic test results, choose therapies, and predict prognoses.

The aim of this paper is to review pertinent literature as it applies to the solving of clinical problems in reptile and amphibian urinary tract medicine. It is intended to assist applicants in writing case reports during the credentialing process and should be useful as a study guide for the examination. The review is not comprehensive, and special emphasis is given to sources that are likely to become a part of the required reading list for certification in reptile and amphibian practice. This paper avoids the topics of reptile and amphibian urogenital anatomy, physiology, pathology, and gout, which are thoroughly covered in accompanying articles within these proceedings.

Signalment

Species identification is essential for numerous reasons including the likelihood that disease prevalence is species-specific and that knowledge of appropriate environmental conditions and nutritional requirements is required to make a diagnosis and prescribe therapy. Methods used to identify reptile and amphibian species are numerous.[4,9,24,41,51,56,57,71,72] Age is difficult to accurately estimate without specific knowledge of the hatch date. It can, however, be roughly approximated using historic data of nutrition and environmental conditions combined with knowledge of the individual species growth rate, maximum size, age-related morphologic changes, and longevity.[41,50,60] Sex should be determined as accurately as possible using the most accurate, least invasive method available.[17] Species-specific dimorphic, dichromatic, or behavioral sex differences can be used for many species.[17,23,36,50,59,60,62,64] Nucleic acid tests are available to determine the sex of juvenile green iguanas, (*Iguana iguana*);[29,74] hemipenile bones, or hemibaculae, are evident on radiographs of the tail base in males of many species of monitors (*Varanus* spp.);[12,17,23] coelioscopy (or coeliotomy) can be used to obtain visual images of the reproductive organs in those species that do not have other distinguishing characteristics.[17,23,36,50,68,72]

Urinary Tract Problems Identified in the Presenting Complaint and History

Signs of amphibian urinary tract disease that might be identified in the presenting complaint include lethargy, anorexia, weight loss, poor weight gain, change in skin color, change in skin texture, distended coelom, coelomic mass, prolapsed tissue from the vent, and change in urine output.[15,19,38,69,72] Problems that might lead to amphibian urinary tract disease and can be identified in the history include inadequate or inappropriate water provision, inadequate environmental humidity, inadequate or excessive dissolved solutes in water, feeding high oxalate diets (including insects fed high oxalate vegetation), feeding inadequate vitamins and/or minerals, excess vitamin D_3 supplementation, feeding improper protein, and exposure to

neprotoxins (e.g., heavy metals, improperly cured PVC glue, history of nephrotoxic drug [aminoglycoside] administration).[15,66,72,73] Urinary tract disease can cause death with no premonitory clinical signs in amphibians.[15]

Signs of lizard urinary tract disease that could be identified in the presenting complaint include changes in activity, anorexia or inappetence, generalized weakness, muscle fasciculations (tremors), constipation or obstipation, dyschezia, bloat, prolapsed tissue from the vent, and chronic weight loss.[3,10,31,39,46] Clients infrequently report polydipsia or polyuria.[5, 11, 31] Problems that might contribute to lizard urinary tract disease and can be identified in the history include prior history of nutritional secondary hyperparathyroidism (NSHP), recent septicemia, feeding of improper type of protein (e.g., organ meats fed to herbivores), excessive dietary protein, dietary vitamin and mineral excesses or deficiencies, feeding improper quantities of electrolytes, inadequate dietary moisture, acidogenic diets, inadequate environmental humidity, inappropriate or inadequate water provision, inadequate ultraviolet B (UVB) radiation, improper environmental temperature range, exposure to nephrotoxins (e.g., aminoglycosides, non-steroidal anti-inflammatory drugs [NSAIDs], heavy metals, excess vitamin D_3), and exposure to recently captured or wild reptiles.[2,3,5,20,31,39,46,52]

Signs of snake urinary tract disease that could be identified in the presenting complaint include changes in activity, anorexia or inappetence, generalized weakness, constipation, obstipation, dyschezia, dysecdysis, prolapsed tissue from the vent, localized swelling in the caudal half of the body, and chronic weight loss.[31] Problems that might contribute to snake urinary tract disease and can be identified in the history include inadequate or improper water provision, inadequate environmental humidity, recent septicemia, and exposure to nephrotoxins (e.g., aminoglycosides, NSAIDs).[20]

Signs of chelonian urinary tract disease that could be identified in the presenting complaint include anorexia, changes in activity, excessive weight gain or loss, constipation, dystocia (egg binding), dysuria, strangury, decreased urination, prolapsed tissue from the vent, poor growth, hind limb paralysis/paresis, hematuria.[44,48,49] Potential problems that might contribute to chelonian urinary tract disease and can be identified in the history include inadequate or inappropriate water provision, high oxalate vegetation, recent hibernation, recent septicemia, past episode of NSHP, feeding of improper type of protein (e.g., organ meats fed to herbivores), excessive dietary protein, dietary vitamin and mineral excesses or deficiencies, feeding improper quantities of electrolytes, inadequate dietary moisture, acidogenic diets, inadequate environmental humidity, inadequate UVB radiation, improper environmental temperature range, exposure to nephrotoxins (e.g., aminoglycosides, NSAIDs, heavy metals, excess vitamin D_3), and exposure to recently captured or wild reptiles.[8,20,31,39,49,52]

Signs of crocodilian urinary tract disease that could be identified in the presenting complaint include anorexia, changes in activity, weight loss, prolapsed tissue from the vent, and poor growth.[31] Problems that might contribute to crocodilian urinary tract disease and can be identified in the history include inadequate or improper water provision, recent septicemia, past episode of NSHP, dietary vitamin and mineral excesses or deficiencies, improper environmental temperature range, inadequate UVB radiation, and exposure to nephrotoxins (e.g., aminoglycosides, NSAIDs, heavy metals, and excess vitamin D_3).[20, 31]

Urinary Tract Problems Identified in the Physical Examination

Problems that could be associated with the urinary tract and can be identified in the physical examination of amphibians include dermal signs of septicemia, dermal nodules, listlessness, anorexia, coelomic masses, emaciation, coelomic distension, and ascites.[15]

Clinical signs of renal failure in reptiles are usually not specific to the urinary tract and include weakness, flaccid paresis, decreased response to stimuli (depressed activity), coelomic distension, muscle fasciculation, palpably enlarged kidneys (per cloaca or per cutaneous), coelomic pain, reduced skin elasticity, ropey saliva, pharyngeal edema, poor body condition, and prolapsed cloaca.[10,19,31] Reptiles with acute renal disease are usually in good body condition as opposed to those with chronic renal insufficiency that are substantially underweight.[31]

Urinary Tract Problems Identified in the Minimum Objective Database

A minimum database of objective data is necessary to sufficiently characterize the above problems and indicate that diagnostic efforts should focus on diseases of the urinary tract.

Hematologic parameters for the minimum objective database include hematocrit; erythrocyte count; thrombocyte count; hemoglobin concentration; total leukocyte count; and cytologic examination of a differentially stained blood smear for erythrocyte and leukocyte morphologic descriptions, counts, and staining characteristics.[11,70,72] Erythrocyte parameters including mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, and mean corpuscular volume are calculated using hematocrit, erythrocyte count, and hemoglobin concentration. Clinical biochemical parameters for the minimum objective database include total protein (biuret method), albumin (by electrophoresis), globulins (by electrophoresis), alkaline phosphatase (ALP), aspartate aminotransferase (AST), alanine aminotransferase (ALT), creatinine phosphokinase (CPK), lactate dehydrogenase (LDH), glucose, blood urea nitrogen (BUN), creatinine, uric acid, ammonia, cholesterol, triglycerides, ionized calcium, total calcium, phosphorus, magnesium, sodium, potassium, and chloride.[11,70,72] Urinalysis data includes gross visual characteristics including color and clarity; specific gravity by refractometer; stained and unstained microscopic examinations of wet and dry smears of sediment; microbiologic culture;

and dipstick colorimetric tests including pH, protein, and glucose.[26,31,34,35,40,65] Minimum fecal examination includes microscopic examination of direct wet-mount and floatation.

Interpretation of amphibian hematology, clinical chemistry, and urinalysis is particularly challenging when samples from unaffected conspecifics living in the same environment at the same time are not available for comparison because few studies of reference ranges are available and wide variation occurs among species, by season, and with environmental conditions.[14,15,54, 65,70] Problems identified in the amphibian hemogram that can be associated with urinary tract disease include signs of inflammation including leukocytosis with heterophilia or monocytosis; morphologic evidence of infectious agents; changes in erythrocyte volume; changes in erythrocyte count; and changes in hematocrit.[15,70] Keep in mind that hematocrit, or packed cell volume, is affected by both erythrocyte volume and erythrocyte count. Erythrocyte abnormalities can occur with dehydration and/or anemia.[70] Amphibian serum or plasma biochemistry problems associated with urinary tract diseases include hyperphosphatemia, especially when phosphorus concentration is greater than calcium concentration; hypocalcemia; and hypoglycemia.[15] Urinalysis abnormalities can include presence of infectious organisms, inflammatory cells, RBCs, neoplastic cells, crystals, casts, and possibly high protein.[34,65]

Reference ranges for clinical pathologic parameters are available for many reptile species, and vary with season, sex, reproductive activity, sample collection site, and environmental conditions.[11,16,18,21,30,37,42,43,47,53,58,67] Problems identified in reptile hematology that can occur with urinary tract diseases include decreased RBCs, increased or decreased PCV, lack of regenerative response to anemia, leukocytosis (heterophilia and/or azurophilia), leukopenia, or monocytosis.[31] Reptile biochemical problems can include increased or decreased total calcium, increased inorganic phosphorus, total calcium:inorganic phosphorus ratio less than 1:1, hyperuricemia, increased BUN, increased ammonia, elevated AST, increased CPK, increased GGT, increased LDH, hyperkalemia, and hypoalbuminemia.[10,31,46,49,61] Problems identified in the reptile urinalysis can include dark amber color, crystals, RBCs, leukocytes, renal casts (containing microorganisms), parasites, bacteria, epithelial cells, neoplastic cells, pathogenic bacterial growth on culture, glucosuria, abnormal pH for the species, and proteinuria.[31,39,49]

Differential Diagnosis and Pathophysiologic Rationale

Subjective and objective problems identified in the signalment, presenting complaint, history, and minimum objective database provide a basis for "working" clinical diagnoses that are hypothesized through assimilation of knowledge about anatomy, captive care requirements, pathophysiology, and disease prevalence. Acute renal failure, chronic renal failure, renomegaly, renal secondary hyperparathyroidism, urolithiasis with or without obstruction, urinary tract infection, and abnormal urination are examples of working clinical diagnoses; they are not

etiologic diagnoses. These disease syndromes are essentially hypotheses that must be supported or refuted using the results of problem-specific diagnostic tests for etiology.

Water deprivation, inadequate environmental humidity, and inadequate moisture in the diet can all contribute to pre-renal azotemia and dehydration.[49] It is possible for dehydration to precipitate renal disease or exacerbate existing renal problems because uric acid, though formed in the liver, is actively secreted by the proximal renal tubules and, when glomerular filtration rate is decreased, can distend renal tubules and ducts.[49]

Diets high in purines or animal protein fed to herbivorous reptiles have been suggested, but not verified, to precipitate renal failure in reptiles.[49] Purine-rich diets are associated with hyperuricemia and should be avoided.[49] Diets that cause accelerated growth, inadequate skeletal mineralization, and NSHP are likely to increase the probability of future renal failure, possibly due to renal tubular mineralization.[49] Diets high in oxalates might cause oxalate crystaluria and associated renal disease.[15]

Non-regenerative anemia is a feature of chronic renal disease and is characterized by decreased RBCs, decreased hematocrit, normochromia, few immature erythrocytes, and uniform cell size (normocytic with low red cell distribution weight percentage).[11,19,39,67] Differential diagnoses for normochromic, normocytic anemia include dilution with lymph, chronic inflammatory diseases, hepatic disease, and neoplasia.[11,67] Environmental factors and inflammation of other sites must be considered as differential diagnoses when leukocyte changes consistent with inflammation are found in reptiles and amphibians with urinary tract disease.[11,31] Inadequate environmental temperatures can prevent reptiles from mounting an appropriate leukocyte response to inflammation.[31] Keep in mind that hemoconcentration can obfuscate mild anemia.[31]

Total calcium:inorganic phosphorus ratio less than 1:1 can occur with renal insufficiency in many reptiles and amphibians.[15,46,61] It is not useful in some chelonians.[49] The ratio can also be less than 1:1 in cases of hypocalcemic NSHP and diseases that cause intestinal malbsorption.[7,46] Total calcium includes ionized calcium, protein-bound calcium, and chemically complexed calcium (e.g., to citrate or phosphate).[43] Ionized calcium is the metabolically active form and comprises a variable proportion of total calcium that cannot be accurately estimated with formulas developed for mammals.[43,67] Ionized calcium should be measured directly, as a part of the minimum objective database, to help differentiate changes in active (ionized) calcium vs. bound or chemically complexed calcium.[11] Total calcium and inorganic phosphorus both increase during normal vitellogenesis.[1,11,28] Elevations in total calcium can be due to excessive calcium supplementation, hypervitaminosis D, primary hyperparathyroidism, pseudohyperparathyroidism, osteolytic bone disease, lipemia, hyperalbuminemia, as well as an increase in vitellogenins, which is noted clinically as hyperglobulinemia.[11,49] The Indigo Snake normally has very high total calcium and inorganic phosphorus levels relative to other species of

reptiles.[11] Differential diagnoses for hyperphosphatemia include excessive dietary phosphorus, hypervitaminosis D, severe tissue trauma, and osteolytic bone disease.[11] Hemolysis and delayed separation of plasma or serum from RBCs can also cause falsely elevated phosphorus.[11,43]

Several authors have hypothesized that a substantial increase in the blood concentration of total calcium, inorganic phosphorus, or both can cause mineralization of soft tissues.[19,49,61] "Solubility index" is calculated by multiplying total calcium concentration by inorganic phosphorus concentration and is hypothesized to be useful in predicting the probability of soft tissue mineralization. Multiply calcium values in mg/dL by 0.2495 to convert to mmol/L.[13] Multiply phosphorus values in mg/dL by 0.3229 to convert to mmol/L.[13] The value above which diseased tissue is hypothesized to mineralize (dystrophic mineralization) has been suggested to range from at least 4 to 9 mmol/L.[19,49] The value above which healthy tissue is hypothesized to mineralize (metastatic mineralization) is 12 mmol/L.[19] It is possible that these mineralization threshold values are poorly defined because multiple cellular events must occur in combination, because crystal nidus inhibitory factors must be inactivated, or because, in herpetofauna, total calcium concentration is not correlated to the concentration of ionized calcium, which is the form most likely to be involved in crystal formation.[25] Solubility index should be considered a rough guideline for the probability of soft tissue mineralization until further study more clearly defines factors that contribute to it in reptiles.

Elevation of uric acid (hyperuricemia) is not a reliable or sensitive indicator of renal disease because it also occurs when dehydration or decreased renal perfusion reduces the glomerular filtration rate.[49] It does, however, usually increase in end-stage renal failure.[31,61] Excessive dietary protein can also lead to hyperuricemia.[49] Uric acid is formed in the liver, so decreased liver function can lead to decreased blood uric acid.[49] It is important to distinguish among pre-renal, renal, or post-renal hyperuricemia with problem-specific diagnostic tests.[49] Serial measurement of uric acid can be useful to differentiate among dehydration, renal insufficiency, and as a measure of response to therapy.[61]

Elevated BUN can occur with dehydration, renal disease, or muscle catabolism;.[49] it should not be considered a sensitive indicator of renal insufficiency.[11,31,39] Many amphibians excrete urea primarily through the skin, with the kidneys playing only a minor role.[34] Creatinine is not useful for diagnosis of renal disease in reptiles or amphibians.[11,31,39,49] Creatine might be more useful than creatinine, but this hypothesis has not been well studied and the assay is not widely available.[31] Some authors have hypothesized that BUN might be a useful indicator of prognosis in chelonians, namely that extremely high values could be associated with a poor prognosis.[49]

Elevations in AST, ALT, LDH and CPK activities, though not organ-specific, can occur in renal disease; enzymes may be lost in the urine rather than into the blood in cases of renal tubular cell damage.[10,11,31,63] Elevation of AST or LDH activity without increased CPK activity provides

stronger evidence of hepatic or renal damage.[67] Differential diagnoses for elevated CPK activity also include skeletal muscle injury, cardiomyopathy, injection site necrosis, and traumatic venipuncture.[67] Differential diagnoses for increased AST activity also include cardiomyopathy, skeletal muscle injury, stomatitis, intussusception, and septic arthritis.[67]

Albumin is probably lost to reptile and amphibian urine when there is damage to the glomerular basement membrane. This loss could lead to hypoalbuminemia and contribute to proteinuria. Increased blood albumin occurs with dehydration.[67] Albumin levels vary widely among species, between sexes, with season, with nutrition, and according to environmental conditions. Differential diagnoses for hypoalbuminemia also include malnutrition, malabsorption, maldigestion, intestinal parasitism, severe blood loss, and hepatic insufficiency.[58]

Hyperkalemia could occur with decreased renal secretion of potassium, muscle catabolism, severe acidosis, excessive dietary potassium, or failure of fluid to enter the bladder, which results in decreased excretion.[11,31,49] Electrolyte imbalances, such as decreased sodium and increased potassium, are likely to occur with renal tubular diseases in reptiles and amphibians, but this requires further research because blood electrolyte concentrations are also influenced by the extrarenal salt glands, cloaca, colon, skin, and/or bladder.[31] Hemolysis causes hyperkalemia together with hyperphosphatemia.[11]

Urinalysis abnormalities must be interpreted in light of post-ureteral (i.e., bladder, colon, or cloaca) urine alterations. Urine specific gravity by refractometer is normally hyposthenuric in many amphibians and reptiles that produce liquid urine because reptile and amphibian nephrons lack the loop of Henle.[61] Specific gravity could approach or exceed isosthenuria with severe dehydration or when refractile molecules from the urinary, digestive, or reproductive tract are present (e.g., mucus).[26,39,67] Reptiles with elevated urine specific gravity by refractometer might be at increased risk of hyperuricemia, especially if associated with decreased glomerular filtration rate.[49] In tortoises, urine pH varies by season, with diet, and with hibernation (brumation) status.[35,40] Acidic urine however, especially in herbivorous chelonians, is seen with chronic starvation and is probably a result of muscle or fat catabolism.[35,49] Catabolism of fat probably leads to ketonemia and ketonuria, but urine dipstick ketone assays might not measure the major ketones formed by reptiles.[31] Marked glucosuria (>50 mg/dL) without hyperglycemia could be associated with renal disease in chelonians, and would most likely be due to decreased tubular reabsorption.[26,40] Most urine dipsticks test primarily for albuminuria, which occurs during glomerular disease, although false-positive test results could occur with hematuria, pyuria, or proteins from the reproductive or digestive tract in reptiles and amphibians.[31] Hematuria determined by dipstick and confirmed by cytologic examination, could indicate hemorrhage in the reproductive, digestive or urinary tract. Hemoglobin, myoglobin, and intact erythrocytes will all cause positive dipstick test results.[31] Reptile urine, whether collected via cystocentesis or "free catch," is not normally sterile because it must pass through the cloaca both

before entering the bladder or colon for storage, and again when voided through the vent.[31, 40] No report of normal urine microbiologic flora for any reptile or amphibian species exists to the author's knowledge. Casts identified on cytologic examination of reptile urine could be evidence of renal tubule cell sloughing that might occur in tubulonephrosis or pyelonephritis.[49] Increased numbers of leukocytes, transitional epithelial cells, and squamous epithelial could suggest inflammation or damage to the renal tubules, ducts, pelvis, ureters, or bladder.[31,40] Urinary tract parasites such as *Hexamita parva, Entamoeba invadens, and E. ranarum* must be differentiated from intestinal protozoa that are found commonly in urine and fecal examinations, and are not associated with urinary tract disease.[15, 49]

Prolapsed tissue from the vent must be diagnosed as digestive tract, reproductive tract, or urinary tract. Prolapse of the urinary bladder can occur with cystic calculi, parasites, or diseases that cause straining such as dystocia and constipation.[6] The urinary bladder participates in water balance, but most patients with cystectomy can be medically managed.

Problem-Specific Diagnostic Tests

Differential diagnoses are ruled in or out using problem-specific diagnostic tests. Many of these tests will provide an etiologic diagnosis, which is the highest level of diagnostic refinement. The etiologic diagnosis provides the information necessary to prescribe specific therapy and accurately predict prognosis. Few scientific studies have been performed to validate available therapeutic regimes and document prognostic probabilities in reptile and amphibian medicine. Specialty practitioners must begin by routinely obtaining etiologic diagnoses. Only then can randomized, blinded, controlled clinical trials be constructed to gain the evidence needed to choose therapies that have a predictable probability of success.

Ultrasound-guided coeliocentesis should be performed in reptiles or amphibians with evidence of coelomic fluid accumulation.[15,34] Specific gravity by refractometer, Gram-stained dry smear, differentially stained dry smear, and packed cell volume should be evaluated.[15] Clinical biochemistries can include electrolytes, ammonia, urea, total protein, and albumin.[15] The sample can also be submitted for aerobic, anaerobic, fungal, and mycobacterial cultures and aerobic sensitivity.[15]

Species-specific diagnostic assays for parathyroid hormone are not available, though some authors do suggest testing.[31] Blood levels of 1,25-hydroxycholecalciferol can be useful to assess for vitamin D deficiency or toxicity. Tear gland secretion of green sea turtles (*Chelonia mydas*) varies with hydration status.[67] Blood culture can identify systemic bacterial infections that have spread to the kidneys.[49] Urine cytologic examination and Gram stain can be useful to characterize cells and bacteria. Urine culture could be useful if a uniform population of pathogenic bacteria are cultured.[49] Consider testing for blood lead, zinc, and copper.[15]

Imaging including radiography, endoscopy, ultrasonography, CT, MRI, and nuclear scintigraphy can be useful to evaluate renal size, presence of renal cysts, presence of soft tissue mineralization, and calculi.[27,31,33,49,61] Indications for the various modalities are similar to other vertebrate classes. Urate calculi are not evident on radiographs unless complexed with calcium.[44] Constipation is frequently seen on radiographs of lizards with severe renomegaly, and obstructive dystocia can occur.[31,61] Negative contrast coelomography (gas injected into the coelomic cavity) or gastrointestinal barium can be useful to outline coelomic organs.[31, 61] Intravenous urography with aqueous iodine contrast material can be used for positive contrast study of the kidneys and ureters, especially to outline masses and radiolucent calculi; injections must be placed into veins in the cranial part of the reptile because caudal vein administration is likely to produce different results as the contrast material passes through the renal portal system before entering general circulation and then moving on to the glomeruli.[31]

Renal function tests, such as iohexol clearance, hold great promise for routine screening and early diagnosis of renal insufficiency; this assay has been validated for green iguanas and is ready to be studied in controlled clinical trials.[31,32] Abnormal urinalysis values, including increased specific gravity and proteinuria, are suggested by the author as indicators for renal function testing.

Renal biopsy, especially when performed early in the disease process, can be useful to diagnose most renal diseases including tubulonephrosis, glomerulonephrosis, nephrosclerosis, interstitial nephritis, nephrocalcinosis, glomerulonephritis, hexamitiasis, amyloidosis, and neoplasia; unfortunately there are few indications for early renal biopsy.[31,32,49] Several different approaches can be used to collect urinary tract biopsy samples, most notably via coelioscopy, cranial dorsolateral tail keyhole in lizards, and coeliotomy.[31,61] Ultrasound guided biopsy has been discussed by some authors, but lesions are likely to be missed.[31] Biopsy samples should be submitted for histopathology, aerobic culture and sensitivity, anaerobic culture, fungal culture, and mycobacterial culture.[15,61]

Treatment of Urogenital Tract Diseases

Environmental temperature management during hospitalization must be tailored for each individual case and is essential for success.[61] Ectothermic patients that are too ill for normal behavioral thermoregulation should be maintained at an environmental temperature that sustains core body temperature in a range likely to allow for optimal metabolism. Patients that are able to thermoregulate should be maintained in an enclosure that provides an appropriate and accessible thermal gradient.[39] For example, spot heat can be provided for many heliophilous basking species with a light-producing heat element such as a mercury vapor or tungsten filament lamp; lamp wattage and distance from the basking site are selected by measuring the temperature at the basking site. Species-appropriate humidity and lighting (spectrum, intensity, diurnal cycling)

must also be provided. Visual security (including absence of reflections) could reduce territorial stressors and might aid in recovery from illness. Many species will do well in a glass aquarium with newspaper substrate, water pan, and hide box. Some species, however, require specific microhabitat parameters for optimal recovery including large rocks for saxicolous lizards, leafy branches for arboreal amphibians and squamates, or brackish water for the diamondback terrapin (*Malaclemys terrapin*). Cleanliness is particularly important to reduce exposure of immunocompromised reptiles and amphibians to nosocomial or environmental opportunistic pathogens.[49] Prescribed soaking in water (temperature chosen according to species; approximately 24–26°C [75–80°F]) once or twice a day for 10 - 30 min will encourage drinking and urination.[49]

Most urinary tract diseases in reptiles and amphibians require fluid therapy. Calculate fluid deficit and replace over 48 - 72 hours, but avoid fluid rates in excess of 40 ml/kg/day.[39] Enteral fluids are preferred, but fluids can also be delivered via the subcutaneous, intravenous, or intraosseous routes.[61] Some authors recommend avoiding subcutaneous fluids in snakes.[61] The author discourages injection of fluids into the coelomic cavity because absorption rate is difficult to monitor and the location of coelomic structures is predictable neither among species, between individuals, nor in the same individual over time. Fluids are chosen using data from the minimum objective database including blood albumin, electrolytes, glucose, and if available, lactate. Crystalloids include Plasmalyte (Baxter, North Chicago, IL), Normosol-R (Abbott, New Providence, NJ), lactated Ringer's solution, and 0.9% sodium chloride.[45] Some authors recommend diluting crystalloids with dextrose in water to more closely approximate normal reptile blood osmolality.[39,61] Natural colloids include whole blood, plasma, concentrated albumin, and polymerized bovine hemoglobin (Oxyglobin, Biopure, Cambridge, MA); synthetic colloids include hydroxyethyl starches, and dextrans.[45] Autologous or homologous whole blood transfusion seems reasonable in cases of severe anemia; it has been anecdotally reported.[45] Monitor urine output, but consider behavioral influences on urination patterns. Adequately hydrated chelonians should be expected to void urine approximately every other day and the volume is reported to be approximately 0.5 to 3.0% of body weight per day.[49] Urinating less than once every five days can occur with hyperuricemic or hyperkalemic renal failure in chelonians, even when bathed and treated with appropriate fluids.[49]

Fluids, energy (i.e., glucose), and supportive nursing care are more important than feeding a normal diet during initial stabilization.[49] Feeding a dehydrated, cachexic reptile can precipitate a set of life-threatening metabolic events termed "re-feeding syndrome," which is characterized by severe hypokalemia and hypophosphatemia.[20] Begin feeding after rehydration, and slowly increase the amount over time to meet calculated energy requirements.[20] Nutritional support must be tailored for the species, should generally be low in protein and phosphorus, and can be provided by oral syringe, orogastric intubation, or esophagostomy tube.[39] Parenteral vitamin B complex and vitamin C are indicated for anorexic reptiles and amphibians.

Coelomic dialysis has been suggested as a treatment for uremia by one author,[22] and another author advises the use of bladder lavage and fluid diuresis.[49]

Allopurinol inhibits xanthine oxidase, which prevents conversion of hypoxanthine and xanthine (highly soluble in water) to uric acid (poor water solubility); it does not alter renal excretion of uric acid.[55] Probenecid is recommended by some authors, but could be contraindicated in some species.[49,61] Systemic antibiotics or antifungals are chosen based on culture and sensitivity data, cost, safety, ease of administration, spectrum of activity, and pharmacokinetics to treat bacterial diseases of the urinary tract.[49] Systemic antibiotics are also justified when immunosuppression is likely because of concurrent herpesviral infection, inappropriate environmental conditions, or chronic malnutrition.[39,49] Some authors suggest anabolic steroids such as stanozolol to stimulate appetite, reduce protein catabolism, and stimulate erythropoeisis.[49,61] Antiprotozoal medications, such as metronidazole, are indicated to treat renal protozoonosis.[15,49] Trematodes should be treated with praziquantal.[15] Anticoccidial drugs should be administered to control coccidia, though efficacy can be poor. Anuria should be treated with diuretics, such as mannitol and possibly methylxanthines including aminophylline.[39,61] So-called "loop" diuretics, including furosemide, are not likely to be effective in species without a loop of Henle, though this hypothesis has not been studied.[39]

Hypocalcemia should be treated with parenteral calcium gluconate, and blood ionized calcium levels monitored closely to avoid causing hypercalcemia.[39,61] After the initial crisis, calcium should be supplemented per os as calcium glubionate or calcium carbonate.[61] Vitamin D_3 should not be administered parenterally, though UVB radiation should be provided to stimulate dermal production of pre-vitamin D_3. Hyperphosphatemia should be treated initially with fluid diuresis.[61] Oral phosphorus binders, such as calcium carbonate or calcium glubionate, should be administered for long-term management.[7,61]

Cloacal calculi can usually be crushed with forceps and removed through the vent.[39] Cystotomy via coeliotomy is indicated for removal of large cystic calculi that are not likely to pass through the neck of the bladder.[39,61] Nephrotomy or nephrectomy may be indicated to remove large renal calculi.[61] Lithotripsy and laser stone ablation have not been reported in reptiles or amphibians to the author's knowledge.

A prolapsed urinary bladder can be reduced (replaced) if the tissue is healthy and the predisposing cause is manageable.[6] Devitalized or non-viable urinary bladder tissue must be surgically resected either per cloaca or via coeliotomy, depending upon the circumstances.[6] Cloacal prolapse should be replaced promptly to prevent tissue edema and devitalization; the underlying cause must also be diagnosed and treated.

Prognoses of Urinary Tract Diseases

Prognoses for urinary tract diseases in reptiles and amphibians have not been studied systematically to the author's knowledge. Prognosis can be expected to vary according to species, specific etiology, severity, stage in disease progression, and response to therapy. Assessment of response to treatment can be based on repeated evaluation of clinical abnormalities.[49] Prognosis for chronic renal failure is anecdotally reported to be poor to grave in chelonians if therapy does not lead to improvement in clinical signs, when profound edema or ascites occurs, or when blood uric acid remains >2000 micromoles/L (33.6 mg/dl) and potassium remains >8.5 millimoles/L (8.5 mEq/L).[49] The author recommends predicting short-term and long-term prognoses for each case based on the highest level of available evidence. Examples of sources for prognostic evidence include unsystematically recorded personal experiences, systematic retrospective studies, and prospective cohort studies.

Client Education

Any surgical site should be pointed out and the plan for post-operative management described in detail. Clients should be instructed on drug dosage, route, and possible side effects. All details of daily soaking should be described in detail, including water temperature and depth. Reptiles and amphibians will attempt to move out of water that is too hot or too cold. Weak animals will drown in water that is too deep. Nutritional support must be defined including nutrition source(s), quantity, frequency, and level of assistance. Husbandry instructions should emphasize proper water provision and long-term nutrition for the species.[31] All basic husbandry should be discussed to ensure species-appropriate thermal gradients and cycling, humidity, light quality, light intensity, light cycling, substrate, cleanliness, enclosure parameters, and habitat setup. Make specific product recommendations and describe their use in detail. Clients should be informed of prognosis and plans for diagnostic and therapeutic follow-up. Written instructions help convey this large amount of information in a short period of time and provide a reference that can be reassuring to the client.

Follow-up and Changes in Plan

Physical examination should be performed at least daily in the initial period and at increasing time intervals with improvement. Glomerular filtration rate should also be monitored at reasonable intervals. Monitor trends in blood biochemistry by rechecking any abnormal hematologic or blood biochemical values, and continuing to monitor hematocrit, uric acid, BUN, sodium, and potassium. Trends in body weight and condition score should be monitored. Any test with abnormal results should be repeated at reasonable intervals to monitor for response to treatment. Antimicrobials should be continually re-evaluated based on repeated cultures and evidence of inflammation. Observations of appetite, activity, eating, and drinking should be

recorded and trends plotted. Plans should be reformulated to accommodate new and changing information. Euthanasia should be considered in cases with a grave prognosis.[61]

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