Doxorubicin and methotrexate are commonly associated with renal failure in feline patients. Renal failure can also be induced by a variety of malignant conditions (e.g., transitional cell carcinoma, renal lymphoma).

Doxorubicin induces acute and chronic renal failure in cats. One study suggested that renal damage in cats is dose dependent, but this observation has not been repeated. Renal failure in cats has been induced with variable cumulative doses of doxorubicin. Another unrelated drug, methotrexate, is eliminated primarily by the kidneys and has been associated with the development of nephrotoxicity.

Renal failure in cancer patients may also be due to causes unrelated to chemotherapy. Cats with transitional cell carcinoma of the bladder, urethra, or prostate may develop partial urethral obstruction that may lead to hydrourereter, hydronephrosis, and renal dysfunction. The concurrent septic cystitis seen in most cats with bladder tumors may induce secondary pyelonephritis, which can result in acute and chronic renal failure. Renal lymphoma may cause transient renal insufficiency, which improves or resolves upon successful treatment.

**Diagnostic Criteria**

**Historical Information**

**Predisposing Factors**

The most common predisposing factors associated with the development of acute renal failure in feline medicine are cancer and administration of nephrotoxic drugs, including chemotherapeutic agents. Therefore, when chemotherapeutic agents are used in feline patients, other nephrotoxic drugs, such as aminoglycosides and piroxicam, should be avoided. The vast majority of feline oncology patients are geriatric and thus may have preexisting renal disease. This must always be taken into consideration when designing a therapeutic protocol and selecting and administering medications. Other risk factors associated with the development of acute and chronic renal failure in cats are decreased cardiac output, urinary tract infection, sepsis, dehydration, fever, liver disease, hypokalemia, and hypercalcemia.

**Laboratory Findings**

Acute and chronic renal failure are a result of decreased glomerular filtration rate, with or without tubular damage. The parameters used to diagnose these syndromes are related to damage of the glomeruli and tubules. Because at least two-thirds of kidney function must be abnormal before renal insufficiency becomes evident, significant renal disease may be present for variable periods before clinical, hematologic, and biochemical abnormalities are identified.

Acute renal failure may be associated with oliguria or anuria. Regardless of the amount of urine, it is usually isoosmolar or minimally concentrated with a high sodium content (>40 mEq/L). Glucose, protein, and renal epithelial cells may be detected in urine. Serum urea nitrogen, creatinine, and phosphorus concentrations rise acutely. In oliguric or anuric renal failure, body weight, heart rate, and central venous pressure may increase if fluids are administered before urine flow is reestablished.

TREATMENT RECOMMENDATIONS

The best treatment for acute or chronic renal failure is prevention. Substantial data exist to show that chemotherapy-induced nephrotoxicity can be reduced and almost eliminated with adequate hydration. The incidence of doxorubicin- and methotrexate-induced renal failure can be reduced by avoiding these agents in cats with preexisting renal disease and by increasing the duration of administration.

The initial goals for treating drug- and tumor-related acute renal failure in cats are to discontinue all potentially nephrotoxic drugs, document pre- or postrenal abnormalities, and initiate fluid therapy. The primary objectives of fluid therapy are to correct deficits (e.g., dehydration) and excesses (e.g., volume overload) seen in oliguric renal failure, supply maintenance needs, and supplement ongoing losses due to vomiting and diarrhea. Each cat must be assessed carefully, and a treatment plan must be tailored based on the patient’s hydration status, cardiovascular performance, and biochemical data.

Initial Treatment

- **Cease administration of nephrotoxins:** Discontinue methotrexate, doxorubicin, and aminoglycosides; avoid anesthesia
- **Assess patient status:** CBC, urinalysis, and biochemical profile to determine:
  - Percentage of dehydration
  - Amount of ongoing losses (e.g., vomiting, diarrhea, blood loss)
  - Maintenance fluid requirements
  - Electrolyte and biochemical abnormalities
  - Cardiovascular performance
  - Urine output
- **Select and administer specific fluids:** Tailor therapy to the individual needs of each patient:
  - Administer isotonic polyionic fluid initially, preferably potassium-free (e.g., NaCl)
  - Correct dehydration over 6 to 8 hours to prevent further renal ischemia while watching carefully for pathologic oliguria and subsequent volume overload
  - Meet maintenance requirements (approximately 66 ml/kg/day)
  - Meet ongoing losses (e.g., due to vomiting and diarrhea)
  - Induce a mild to moderate diuresis. Potassium supplementation may be needed after adequate urine output is established.
- **Monitor urine to ensure adequate output:** Collect urine via a metabolism cage or indwelling catheter. For patients with inadequate urine output (<2.0 ml/kg/hr), administer:
  - Mannitol or 50% dextrose (0.5–1.0 g/kg via slow IV bolus)
  - Furosemide (2–4 mg/kg IV q1–3h as needed)
  - Dopamine (1–3 µg/kg/min IV [50 mg dopamine in 500 ml of 5% dextrose = 100 µg/ml solution])
- **Correct acid–base and electrolyte abnormalities:** Initiate specific treatment to correct malignancy-induced hypercalcemia, if identified.
- **Provide mild to moderate diuresis:** If urine output is 2 to 5 ml/kg/hr, monitor body weight, heart and respiratory rates, and central venous pressure for signs of overhydration.
- **Consider peritoneal dialysis if no response:** Temporary or chronic ambulatory peritoneal dialysis with specific dialysate solution may be helpful.
- **Initiate long-term plans:** Continue diuresis until blood urea nitrogen (BUN) and creatinine normalize or until these values stop improving despite aggressive therapy; in the clinically stable patient, gradually taper fluids.
- **Control hyperphosphatemia,** if indicated. Consider cimetidine (2.5 mg/kg PO or IV bid) to correct hyperacidity.

Supportive Treatment

Maintenance fluid requirements vary, but a simple formula is to use 66 ml/kg/day plus sufficient fluids to replace external losses, such as through vomiting and diarrhea. This amount is needed for daily maintenance. In cats with renal failure, 1.5 to three times this amount of fluid is administered daily to achieve diuresis, the success of which can be monitored by documenting adequate urine output (> 2 ml/kg/hr). In addition to meeting daily needs and replacing ongoing losses, fluid therapy also needs to correct dehydration. The percentage of dehydration should be determined, and approximately 75% of the fluid needed to correct dehydration should be administered during the first 24 hours. Fluid therapy should be altered to correct electrolyte and acid–base abnormalities. Because systemic hyperkalemia often develops in cats with acute renal failure, potassium-containing fluids are generally not advised initially in these patients. Until more is known about the systemic effects of sepsis, lactate-containing fluids should be avoided—sepsis and cancer are associated with hyperlactatemia, which worsens with the administration of lactate-containing fluids.

Oliguric Renal Failure

If oliguric renal failure is present, a diligent and aggressive effort to increase urine output should be made. This can be done by first increasing glomerular filtration rate and renal blood flow. Additionally, osmotic diuresis can increase urine flow. If urine output is <0.5 to 2.0 ml/kg/hr despite aggressive fluid therapy, furosemide should be administered every 1 to 3 hours. Furosemide increases the glomerular filtration rate and enhances diuresis in many cats. If furosemide is ineffective,
mannitol or 50% dextrose can be used as an osmotic diuretic to enhance urine production. The advantage of dextrose over mannitol is that dextrose can be detected on a urine glucose test strip. If furosemide and osmotic diuretics are not effective, dopamine in 5% dextrose can be administered via constant-rate infusion. Dopamine enhances renal blood flow and increases urine output secondarily.

If the cat does not respond to the preceding therapies, peritoneal dialysis may be necessary. Temporary or chronic ambulatory peritoneal dialysis with specific dialysate solutions may be helpful in this situation.

**Patient Monitoring**

Cats that are being diuresed should be monitored for signs of volume overload (increased body weight, heart and respiratory rates, and central venous pressure). BUN and creatinine should be monitored and diuresis continued until these values normalize or at least stabilize. Therapy should then be tapered over several days, and a home treatment plan that includes avoiding nephrotoxic drugs; feeding a high-quality, low-protein diet; maintaining a low-stress environment; and providing fresh, clean water ad libitum should be developed. Treatment for hyperphosphatemia (such as phosphate binders) may be necessary, and cimetidine may be helpful in controlling gastric ulceration.

**RECOMMENDED READING**

