Acute Renal Failure

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ABSTRACT

Acute renal failure (ARF) may occur within hours to days following injury to the kidneys. Early recognition of the disease, knowledge of risk factors, and anticipation of renal damage are key to the successful management of patients with ARF. This article focuses on intrinsic renal failure, defined by persistent azotemia and lack of urine-concentrating abilities. Initial clinical signs of ARF (e.g., lethargy, anorexia, nausea, depression, vomiting, diarrhea, dehydration) are vague and nonspecific. An accurate history, thorough physical examination, and hematologic and biologic profiles should be obtained; other diagnostics may be indicated as well. The first step of treatment is to identify and address any life-threatening emergencies, including hyperkalemia, metabolic acidosis, and hypovolemia; fluid therapy is essential and should be instituted at once. The next steps include promoting urine production, correcting potassium imbalances, controlling metabolic acidosis, vomiting, and uremic gastritis, preventing hypertension, and providing nutritional support. For patients that survive the initial stages of uremic crisis, functional renal recovery may occur in 2 to 4 weeks, albeit with compromised glomerular filtration rate.

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The kidney is a complex, multifunctional organ that regulates essential homeostatic functions such as the balance of body water, acid-base status, and electrolytes; the production, modification, and degradation of hormones; and the excretion of metabolic and nitrogenous waste products (Box 1).[1] To meet these demands, the kidneys receive approximately 20% of the normal cardiac output, thus rendering them vulnerable to injury and intoxication.[2] When an inciting insult occurs, acute renal failure (ARF) may ensue within hours to days and the resulting clinical syndrome of spiraling systemic chaos leads to significant morbidity and mortality in our small animal patients. The key to successful management of patients with ARF lies in the early recognition of disease, knowledge of risk factors (such as exposure to toxins or ischemic insults), and anticipation of renal damage. In this way, preventative strategies may be implemented to avoid fulminant or progressive organ failure and aggressive therapeutic intervention employed.

BOX 1
Functions of the kidney

Maintenance of the extracellular fluid environment
- Excretion of metabolic waste products
  - Urea
  - Creatinine
  - Uric acid
- Water balance
- Electrolyte balance
- Acid-base balance

Hormone secretion
- Regulation of systemic and renal hemodynamics
  - Renin
  - Angiotensin II
  - Prostaglandins
  - Bradykinin
- Red blood cell production
  - Erythropoietin
- Calcium/phosphorus regulation
  - 1, 25-dihydroxycholecalciferol; calcitriol

Other
- Gluconeogenesis in starvation
- Catabolism of peptide hormones

BOX 2
Risk factors for the development of acute renal failure

- Advanced age
- Dehydration
- Pre-existing renal insufficiency
- Shock; decreased cardiac output
- Trauma
- Electrolyte abnormalities
  - Hyponatremia
  - Hypocalcemia
  - Hypokalemia
- Metabolic acidosis
- Concurrent nephrotoxic drugs
  - Furosemide
  - Chemotherapeutics
  - NSAIDs
- Concurrent disease
  - Neoplasia
    - Hypercalcemia
  - Hemolytic anemia
    - Hemoglobinuria
  - Liver failure
  - Pancreatitis
  - Heart failure
  - Fever
  - Sepsis

BOX 3
Selected etiologic agents of acute renal failure

Nephrosis

Renal ischemia
- Dehydration
- Hypovolemic shock
- Hemorrhage, trauma
- Sepsis, burns, heat-stroke: DIC
- Decreased cardiac output: failure, tamponade, dysrhythmias
- Thromboembolism, vasculitis, hypertension
- Hyperviscosity: multiple myeloma, polycythemia
- Pigments: hemoglobinuria, myoglobinuria
- NSAIDs

Nephrotoxicosis
- Ethylene glycol
- Antibiotics: aminoglycosides, sulfonamides, IV tetracyclines, cyclosporin
- Chemotherapeutics: amphotericin B, *cis*-platinum, doxorubicin
- Anesthetics: methoxyflurane
- Heavy metals: lead, thallium, zinc, arsenic, mercury
- Hypercalcemia: malignancies, hyperparathyroid, vitamin D toxicity
- Other causes: carbon tetrachloride, chloroform, iodinated radiocontrast media

Nephritis

Infections
- Leptospirosis
- Leishmaniasis
- Bacterial pyelonephritis

Inflammatory
- Glomerulonephritis
- Allergic: drug-induced

BOX 4
Systemic manifestations of acute renal failure

Fluid, electrolyte, and serum biochemical disturbances
- Anuria, oliguria, polyuria/polydipsia
- Dehydration
- Azotemia: increased urea and creatinine
- Metabolic acidosis
- Hyperphosphatemia
- Hyperkalemia
- Hypercalcemia/hypocalcemia (ethylene glycol toxicity)
- Peripheral insulin resistance and glucose intolerance

Gastrointestinal disturbances
- Anorexia
- Vomiting and diarrhea
- Halitosis
- Oral ulceration/stomatitis
- Gastropathy, gastritis, gastric, and duodenal ulceration and bleeding

Hematological disturbances
- Platelet function defect/bleeding tendencies
- Blood loss anemia
- Lymphopenia
- Neutrophilia

Cardiovascular and pulmonary disturbances
- Systemic arterial hypertension
- Uremic pneumonitis

Neuromuscular disturbances
- Weakness
- Lethargy
- Depression
- Uremic encephalopathy
- Coma/death

PATHOPHYSIOLOGY OF DISEASE

The term acute renal failure is commonly ascribed to all forms of azotemia; for this article, however, we are concerned with acute intrinsic renal failure that is a result of damaged renal tubular cells. Intrinsic renal failure is defined by persistent azotemia (increased blood urea nitrogen and creatinine) and lack of urine-concentrating abilities when pre- and postrenal concerns have been addressed and ruled out.[2] Individual patient susceptibility to developing ARF when exposed to various ischemic conditions or toxins is to a large extent dependent on the state of the animal and the presence of any underlying risk factors including age, general health, and concurrent systemic illnesses (Box 2). Many causes of ARF have been reported in small animals, but few occur with any regularity. The potential etiological agents have been divided into two categories: nephrosis and nephritis.[2–4]

Nephrosis is the death and degeneration of renal tubular cells due to ischemic damage or toxins (Box 3). Prolonged prerenal azotemia of various origins results in decreased effective renal blood flow, ischemia, and intrinsic renal damage. In human medicine, almost 50% of ischemic ARF follows surgery.[5] Toxins may exert their effects of tubular necrosis by inducing renal

BOX 5
Clues to the differentiation of acute versus chronic renal failure

	Acute renal failure	*Chronic renal failure*
History	Previously healthy	PU/PD, inappetence, weight loss
Body score	Normal	May be thin to cachectic
Kidney size	Normal to enlarged	Variable; normal, small and irregular, or enlarged
Anemia	Possible from blood loss or hemolysis	Common, due to lack of erythropoietin
Potassium	± Hyperkalemic	± Hypokalemic
Phosphorus	Hyperphosphatemic	Hyperphosphatemic (same)
Urine sediment	Active: casts, debris	Inactive usually
Urine production	Anuric, oliguric, or polyuric	Polyuric
Prognosis	Potentially reversible	Irreversible but manageable

vasoconstriction (nonsteroidal antiinflammatory drugs or NSAIDs), interfering with cellular respiration (ethylene glycol and aminoglycosides), or inflicting direct tubular injury (hemoglobinuria). The most frequently encountered causes of nephrosis include ethylene glycol toxicity, ischemia, and acute decompensation of chronic renal failure.

Nephritis is the destruction of renal tubular cells due to infection or inflammation (Box 3). Pyelonephritis and leptospirosis are two of the most common initiating infections, both of which may also induce a chronic, slowly progressive rather than acute course of disease.

RECOGNITION OF THE PATIENT IN ARF

The early clinical signs of ARF are vague and nonspecific, such as lethargy, anorexia, nausea, depression, vomiting, diarrhea, and dehydration. In later stages, fulminant systemic changes become apparent and may be expressed as coagulopathies, disseminated intravascular coagulation, weakness, recumbency, respiratory distress, and coma (Box 4). The more time that passes before recognition of disease and institution of therapy, the poorer the prognosis of salvaging any remaining kidney function. The diagnosis of ARF is confirmed by obtaining an accurate history and physical examination in conjunction with the results of a urinalysis, laboratory investigations, and imaging studies.[6–8] Every effort should be made to determine the presence of, and to address, the underlying cause, but in general the basic approach to the diagnosis and therapy of renal failure is the same whatever the cause.

History

It is essential that the clinician has a full and accurate history including the presence of risk factors (Box 2) and the potential of exposure to nephrotoxins (Box 3).[9] If the animal has experienced gastrointestinal upset, it is important to inquire as to whether hematemesis or melena is present. Hypergastrinemia, resultant hyperacidity, hypovolemia, and ischemia of the bowel contribute to anorexia, vomiting, and the development of gastric and duodenal ulcerations, which may be further exacerbated by uremic coagulopathies.

Animals may present with an apparent acute onset of clinical signs and yet have chronic disease as evidenced by poor body condition, historical weight loss, and polyuria/polydipsia. This distinction between acute and chronic disease is an important one to make prognostically (Box 5) because ARF patients have the potential to recover completely and retain adequate renal function, whereas the chronic renal failure patient with acute decompensation is typically in much worse condition and any successful recovery is often short-lived.[10]

Physical examination

Examination of the ARF patient does not necessarily yield information specific to the presence of renal disease but it is crucial in alerting the clinician to systemic effects of disease that require immediate attention. Full physical examinations with particular attention to hydration status, mental state, cardiopulmonary function, and abdominal palpation should be performed.

Dehydration is a contributing factor to ischemic renal failure

BOX 6
The use of urinalyses in the differentiation of azotemia

Source	*Urine analyses*
Prerenal azotemia	• Increased urine specific gravity > 1.045 in cats and > 1.030 in dogs (except in Addison's disease) • Urine osmolality > 500 mOsm/L (concentrated) • Fractional excretion of sodium < 1% • Inactive urine sediment
Renal azotemia	• Urine specific gravity 1.008–1.012; isosthenuria • Urine osmolality < 350 mOsm/L (dilute) • Fractional excretion of sodium > 2% • Dipstick evaluation: blood, glucose, bilirubin, protein • Active urine sediment: casts, cells, debris, crystals • Urine culture: always rule out pyelonephritis
Postrenal azotemia	• Cannot differentiate by urine analyses: physical examination and imaging studies are the most helpful techniques

and requires immediate correction. An increased respiratory rate may result from metabolic acidosis, uremic pneumonitis, hypovolemia, anemia, or thromboembolic disease. Depression, weakness, and mild ataxia are commonly associated with uremic encephalopathy, but disorientation, seizures, and neurological deficits are more likely to be due to a toxicity such as ethylene glycol. The mucous membranes may be dry and tacky from dehydration or wet from nausea and should be closely inspected for petechiation, pallor, or oral ulcerations. The heart rate and rhythm may reflect hypovolemia, as in sinus tachycardia, or arrhythmias may be present due to uremic myocarditis. A fundic examination may also reveal petechiation or, more seriously, retinal detachments, which can be an unfortunate sequela of hypertension. On palpation of the abdomen, the kidneys may be normal to enlarged and are often smooth and regular unless previous renal insults have occurred. Other pertinent findings to note include the presence of ascites, the size of the bladder, and other organomegaly.[6–8]

Laboratory investigations

Hematological and biochemical profiles should be obtained on every acutely ill patient.

Biochemical profile

The presence of azotemia alerts the clinician to suspect renal failure. It is important to note that increased blood urea nitrogen (BUN) may be influenced by other factors such as gastrointestinal hemorrhage, dietary protein intake, and dehydration. In the absence of rapid access to laboratory results, a minimum database of packed cell volume (PCV), total protein, chemstrip (BUN), and blood glucose should be obtained. The physical parameters of hydration may be difficult to interpret in the obese or ill patient, but a high PCV and total protein concentration support dehydration.

Other essential biochemical parameters to assess immediately include potassium, phosphorus, and calcium, all of which accumulate with decreased renal excretion. High serum potassium concentrations interfere with electrical conduction in the heart and, if left uncorrected, may result in fatal bradydysrhythmias. Calcium and phosphorus retention leads to soft tissue cal-

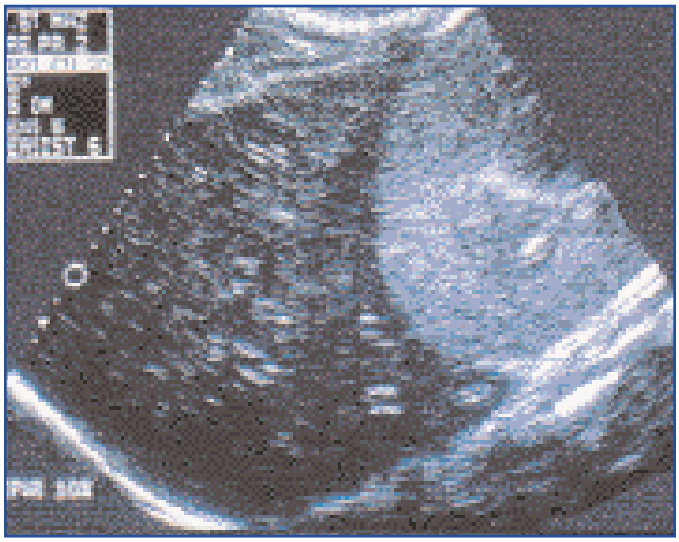

Figure 1
Hyperechogenicity of the renal cortex in comparison with the echogenicity of the medulla is a common finding in patients with ethylene glycol toxicity. Photo courtesy C. Lamb

cification; although not immediately dangerous, levels should be monitored and, with appropriate therapy, should decrease. Hypercalcemia is often mild as a result of renal failure but may induce ARF if excessive (e.g., >3.4 mmol/L) and warrants investigation for an underlying malignancy, toxicity, or endocrinopathy. Hypocalcemia can occur with ethylene glycol intoxication from the chelation of calcium and leads to neurological signs such as weakness and seizures.

Hematological profile

A complete blood count may reveal a regenerative, blood loss anemia, thrombocytopenia, a stress or inflammatory leukogram, or perhaps evidence of an inciting leukemia or neoplasia. Basophilic stippling of the red blood cells (RBCs) with nucleated RBCs is suspicious of lead toxicity.

Urinalysis

Upon finding azotemia on a biochemical profile, a complete urinalysis is the next most important information to be obtained *before* fluid therapy (Box 6). The urine may appear dilute or concentrated, and a urine specific gravity will help to distinguish prerenal azotemia (SG >1.030) from intrinsic renal failure. Measurement of urine sodium is commonly used in human medicine to determine if the kidney is working appropriately to conserve sodium in the face of dehydration or if it is being wasted in the urine. Turbidity or discoloration of the urine may indicate the presence of crystals, infection, or blood. A sediment examination will often reveal active disease in the form of protein, cells, debris, and crystals. The amount and type of these components may differentiate the above possibilities and help to lend support to the diagnoses of pyelonephritis or ethylene glycol intoxication (calcium oxalate crystals).

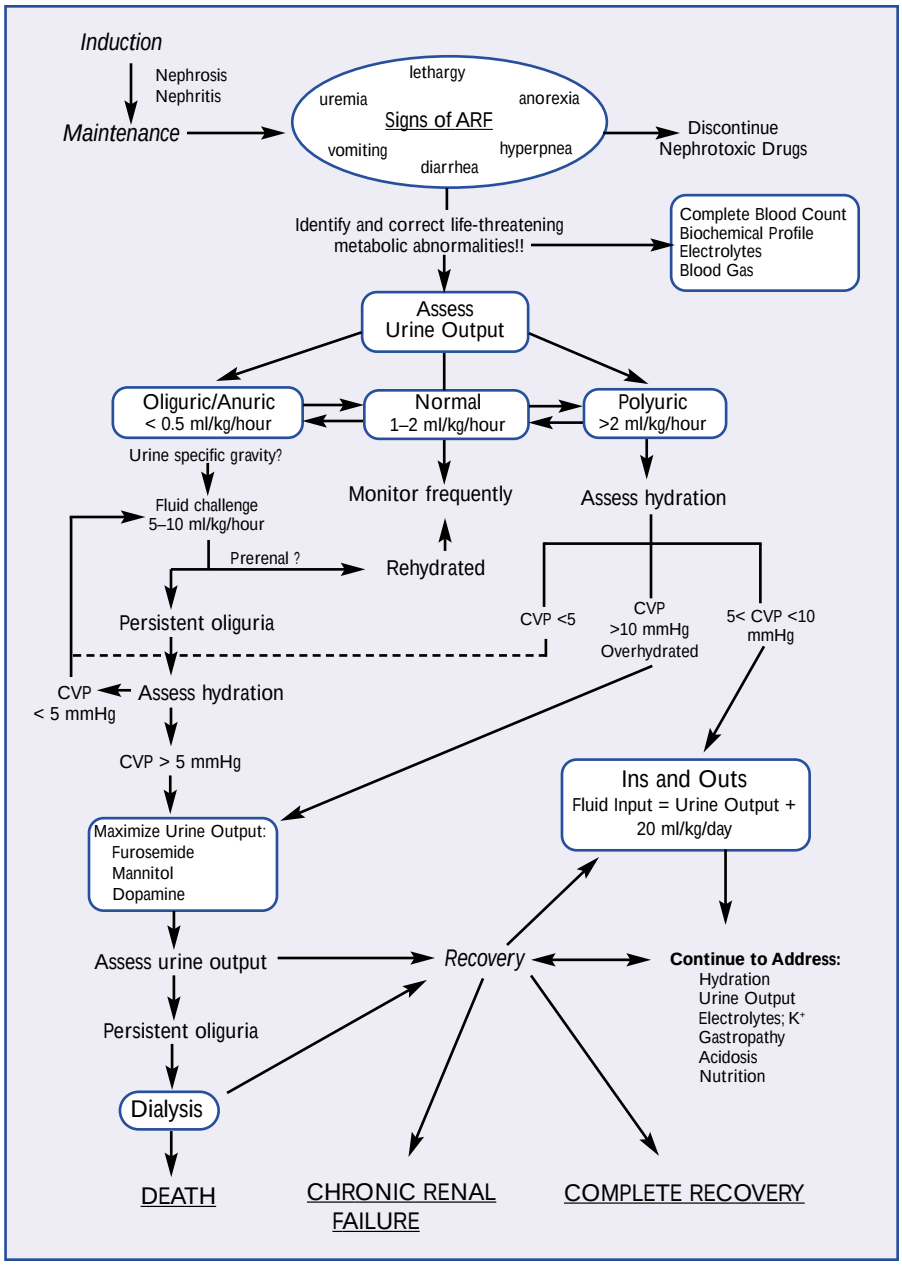

Figure 2
Algorithm for the treatment of acute renal failure.

Imaging studies

Plain radiographic studies are often performed to investigate kidney size and to detect the presence of obstructive uroliths or other abdominal pathology. Radiographic contrast studies are contraindicated in the ARF patient due to the hypertonicity of the media and potential for further renal damage. Ultrasonographic evaluation perhaps provides the most specific detail including kidney shape and size, relative internal echogenicities, and potential pelvic dilation. Hyperechoic renal cortices are classically found in ethylene glycol toxicity (Figure 1), and renal pelvis dilatation may occur with excessive fluid diuresis, obstruction, or pyelonephritis.

Other diagnostics

Other helpful, but not always readily available, tests include blood gas analysis, measurement of serum and urine osmolality, and urine fractional excretion of various electrolytes. Where a cause of ARF is not immediately apparent upon performing all the preceding investigations, further specialized studies may be indicated to rule out potential etiological agents (Box 7). These might include dark field microscopy of the urine for lep-

BOX 7

Special studies for the diagnosis of acute renal failure

Imaging studies

- Radiology—size, shape, and position of kidneys
- Ultrasound—greater detail than plain radiographs, comparative echogenicity

Renal biopsy

Indicated when:

- Cause of disease is unknown
- Prognosis or assessment of progression is required
- Excessive proteinuria is present in the absence of infection

Contraindicated in the face of:

- Bleeding tendencies
- Infection
- Solitary kidney

Other special studies

- Blood gases: assess for metabolic acidosis
- Fractional clearance of electrolytes; assess renal wasting of potassium, sodium
- *Leptospira* titers, dark field microscopy
- *Leishmania* titers
- Ethylene glycol metabolites; serum or urine
- Serum and urine osmolality
- Serum lead concentrations; suspect if basophilic stippling of red blood cells and neurological signs are present

tospires, serum titers, assays for ethylene glycol metabolites, and serum lead concentrations.

TREATMENT

Phases of renal failure

Renal failure is often described as progressing through three phases: induction, maintenance, and recovery. The induction phase is that period of initial injury to the onset of azotemia and is often characterized by a few vague clinical signs. If renal injury is suspected from known exposure to toxins or ischemia, intervention at this point may allow reversal of damage, prevention of progression, and complete recovery. Unfortunately, most cases progress into the maintenance phase, where aggressive therapy up to and including dialysis is required to support remaining renal function. If an animal survives the maintenance phase, it enters the recovery phase, which is characterized by a decreased glomerular filtration rate (GFR) and persistent azotemia that, with appropriate therapy, may gradually improve over weeks to months (Figure 2).

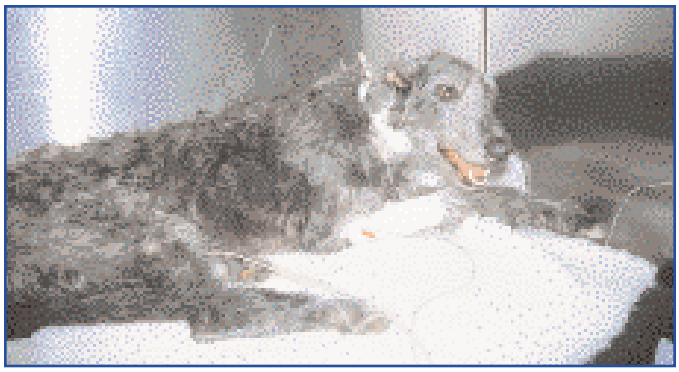

Figure 3
Irish wolfhound with acute renal failure. A jugular catheter delivers fluids and medications and is also used for measurement of central venous pressure. Limb leads are attached to an ECG to detect electrical disturbances associated with hyperkalemia.

Identify life-threatening abnormalities

The diagnostic samples of blood and urine are obtained before initiation of any therapy; however, it is not usually possible to wait for all the results before administering treatment. It is essential to recognize and address life-threatening metabolic abnormalities as soon as possible; these include hyperkalemia, metabolic acidosis, and hypovolemia (Box 8). Clues to the presence of these aberrations—such as bradycardia, hyperventilation, and decreased skin turgor, respectively—may be gleaned on physical examination.[10,11]

Fluid therapy

Fluid therapy is essential to the correction of hyperkalemia, metabolic acidosis, and hypovolemia and should be instituted immediately, preferably through a centrally placed catheter that can also be used to measure central venous pressure (CVP) (Figure 3). The amount of fluid required may be calculated by estimating the patient's percent dehydration (5% to 8% is likely to be a safe starting point) and multiplying this by its body weight (kg). The resultant figure is the fluid deficit in liters required to restore hydration and should be administered over the first 4 to 6 hours.

The fluids of choice for replacement of deficits are isotonic solutions such as lactated Ringer's (Hartmann's) or 0.9% NaCl. Once hydrated, however, it is best to change to a fluid with a lower sodium content (e.g., 0.45% NaCl with 2.5% dextrose) to avoid hypernatremia, particularly in patients with heart disease. Intensive diuresis is now employed to encourage excretion of uremic waste and to optimize renal blood flow and GFR. Close monitoring of urine output, weight, and, ideally, CVP is essential to avoid overhydration and pulmonary edema in the oliguric patient.[12]

Figure 4
The measurement of central venous pressure requires a water manometer, a three-way stopcock, extension tubing, and a ~10 ml syringe with sterile saline. Photo courtesy B. Hanson

Measurement of CVP

CVP measurement allows a less subjective way of monitoring patient hydration status and is relatively easy to do in practice with water manometry (Figures 4 and 5). The CVP represents the hydrostatic pressure within the intrathoracic portion of the cranial vena cava, and, in a dog with otherwise normal cardiac status, repeated measurements will give information relative to the vascular volume and compliance. Rapid infusion of 10 ml/kg of replacement fluids should increase the CVP by 2 to 4 cm H_2O above the baseline that then returns to normal within 15 minutes. If no increase is seen, this implies reduced vascular volume and more fluids are required. If the CVP returns to normal very slowly, this implies blood volume is close to normal. If necessary, repeated fluid boluses may be given until the CVP reaches 10 to 15 cm H_2O. Beyond this value, the patient is at risk of developing pulmonary edema. Monitoring the CVP allows the clinician to avoid overhydration and ensure adequate fluid volume to optimize renal blood flow.[13]

Ins and outs

Once adequate hydration is established, the rate of fluid administration must match fluid loss to maintain this delicate balance. This is referred to as the "ins and outs" of fluid therapy and requires measurement of urine output and calculation of insensible losses (20 mg/kg/day divided into 24 hours), including an estimate of fluids lost from vomiting and diarrhea. The rate of fluid replacement is then adjusted accordingly every 2 hours. Urine output may be estimated by weighing incontinence pads and/or catching urine samples. A more accurate method is facilitated by the sterile placement of a urinary catheter attached to a closed urine collection system (Figure 6).

Conversion of oliguria to nonoliguria

If an animal remains oliguric after rehydration, the conversion to nonoliguria represents a prognostic turning point and aggressive intervention is required. The first line of action is to use diuretics such as furosemide, mannitol, and dopamine. Furosemide is administered intravenously and repeated every hour for 3 hours to effect. Dopamine is considered to be synergistic with furosemide and acts to increase renal blood flow at the appropriate dosage (Box 8). At higher doses, dopamine may induce a tachycardia. Mannitol is used as an osmotic diuretic agent and in the experimental animal may also act as a renoprotective, free-radical scavenger if given in the induction phase or prior to insult. These drugs are discontinued once nonoliguria is achieved.[10–12]

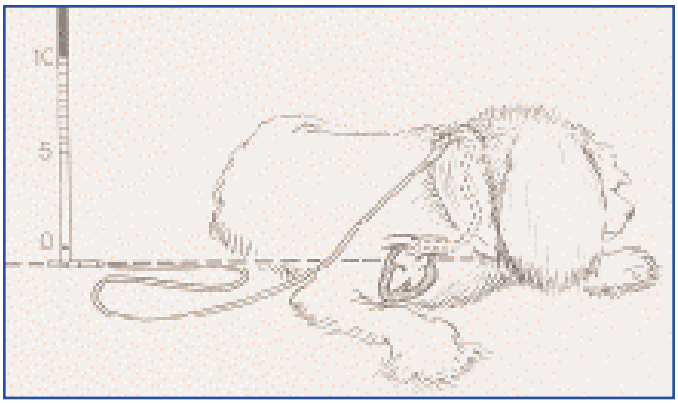

Figure 5
The water manometer is placed at the level of the patient's heart and filled with sterile saline beyond 20 cm H_2O. The water column drops to the level consistent with the central venous pressure and may be read from a centimeter calibration on the manometer or from a nearby placed meter stick (cm H_2O). Illustration courtesy B. Hanson

Figure 6
A closed urine collection system consisting of a Foley urinary catheter attached to a fluid administration set and an empty, sterile fluid bag. Photo courtesy B. Hanson

Correction of metabolic abnormalities

Hyperkalemia and acidosis

If mild to moderate hyperkalemia or acidosis existed before fluid therapy, these are often found to have normalized or improved substantially upon remeasurement. Severe hyperkalemia (>8.0 mmol/L) with concurrent physical or electrocardiographic signs (Figure 7) or acidosis (pH <7.1), however, requires immediate therapy (Box 8). Increased serum potassium concentration occurs in response to decreased secretion by the kidneys and also as a result of the movement of potassium into the extracellular fluid in exchange for hydrogen ions in states of acidosis. Insulin (IV) rapidly drives potassium back into the cell and lowers the serum potassium levels that interfere

BOX 8

Goals of therapy for acute renal failure

1 Rehydrate and maintain fluid and electrolyte balance

Fluids!

Replacement: lactated Ringer's solution 0.9% NaCl
Maintenance: 0.45% NaCl and 2.5% dextrose

Fluid deficits should be replaced over the initial 4–6 hours, and the subsequent fluid rate should reflect urinary output and promote diuresis without inducing overhydration

2 Promote urine production

***Treatment of the anuric/oliguric patient*—**the animal must be rehydrated first!

Diuretics

- Furosemide: loop diuretic, 2 mg/kg IV bolus, repeat at 5–8 mg/kg q30min, three times
- Mannitol (20%): osmotic diuretic and free radical scavenger, 0.25 g/kg slow IV bolus
- Dopamine: renal arterial vasodilator; 2–5 µg/kg/min continuous IV infusion

3 Correct potassium imbalance

***Hyperkalemia*—**failure of the kidneys to excrete potassium normally

- Mild (<6.5 mmol/L) may resolve with fluid therapy alone
- Moderate to severe (>6.5 mmol/L or electrocardiograph reveals bradycardia peaked T-waves to idioventricular rhythm)
  - Insulin: 0.25 units/kg IV, with glucose supplementation
  - Sodium bicarbonate: 0.5–2 mmol/kg IV over 15 minutes
  - Calcium gluconate (10%): 0.5 ml/kg given slowly over 15 minutes

***Hypokalemia*—**with aggressive diuresis, once the animal is in the polyuric stage, potassium can be lost from the kidneys resulting in hypokalemia

Serum potassium	*KCl/liter Fluid (mEq)**
<2.0	80
2.0–2.5	60
2.6–3.0	40
3.0–3.5	30
3.5–4.0	20

*Do not exceed an administration rate of 0.5 mEq/kg/hr.

4 Control metabolic acidosis

- Not indicated unless the pH falls to <7.1
- Mild acidosis usually corrects with appropriate fluid therapy alone
- Sodium bicarbonate: body weight (kg) x 0.6 x (25 – measured HCO_3) = mEq $NaHCO_3$ needed in replacement fluids or 0.5–2 mEq/kg slow IV

5 Control vomiting and uremic gastritis

- Antihistamines: cimetidine 5–10 mg/kg IV or PO TID; ranitidine 2 mg/kg PO BID
- Gastroprotectants: sucralfate 1 g/medium-sized dog PO TID
- Anti-emetics: metoclopramide 0.2–0.4 mg/kg SC QID

6 Prevent hypertension

- Low-salt diet: <0.3% on a dry matter basis
- Diuretics*: furosemide 2–4 mg/kg/day
- Calcium channel blockers: amlodipine 0.625 mg SID in cats, 0.5–1.0 mg/kg SID in dogs
- ACE-inhibitors*: enalapril, 0.5–1 mg/kg PO SID–BID; benazepril, 0.25–0.5 mg/kg PO SID

* Caution! These may cause hypotension and worsen renal function.

7 Provide nutritional support

- Adjust protein requirements to meet demands yet avoid exacerbating uremia. If BUN >75 mg/dl or 20 nmol/L: 2–2.2 g/kg/day of protein in dogs; 3.3–3.5 g/kg/day in cats

with cardiac rhythm; glucose, however, must be provided simultaneously to avoid hypoglycemia. Glucose infusions alone may increase endogenous insulin to help lower serum potassium. Alternatively, sodium bicarbonate may be given slowly IV to reverse the acidosis that drives potassium back into the cell. Provided that rapid administration is avoided, this can be repeated as needed or, ideally, added to the fluids as a constant rate infusion. Calcium gluconate may be given to counteract the immediate effect of potassium on the myocardium but does not lower the serum potassium concentration and must, therefore, be given in conjunction with insulin or sodium bicarbonate.

Hypokalemia

Once the patient is stabilized, the serum potassium concentrations may readily fall due to dilution with potassium-free fluids and to loss in the urine from furosemide administration and

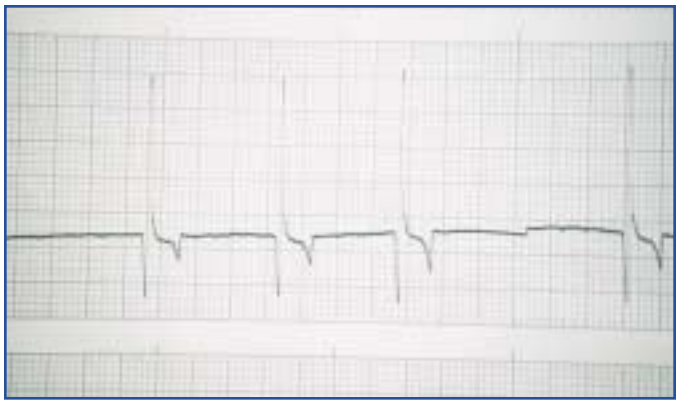

Figure 7
Electrocardiogram depicting bradycardia and absence of p-waves consistent with hyperkalemia. Tracing courtesy A. Boswood

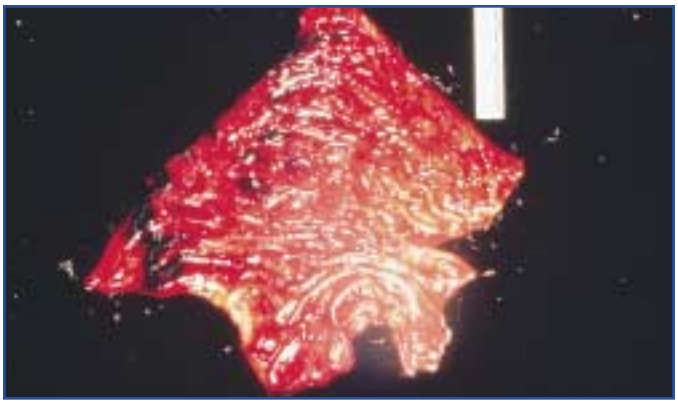

Figure 8
Uremic gastritis. Photo courtesy H. C. Rutgers

polyuria. Hypokalemia results in weakness and worsening renal failure, and potassium supplementation of the fluids during the polyuric maintenance phase is often required to maintain normal serum concentrations.[14]

Uremic gastritis, coagulopathies, and hypertension

Other manifestations of uremia can make the patient uncomfortable and place it in danger of sepsis and death. These symptoms include bleeding tendencies due to uremic platelet dysfunction and gastritis (Figure 8) leading to vomiting, anorexia, hematemesis, melena, hypertension, weakness, and calcium/phosphorus derangements. Specific therapies directed at controlling these complications are indicated as they occur. In patients with anemia due to blood loss or hemolysis (leptospirosis), blood transfusions may be warranted. Gastric protectants are commonly employed to decrease gastric acidity and irritation and to improve the appetite. Anti-emetics are useful in the vomiting patient. Rarely, systemic hypertension results in ocular changes such as retinal edema and detachment. Therapies directed at lowering blood pressure (Box 8) are indicated but should be monitored to avoid development of hypotension and exacerbation of renal disease.[14]

Calcium and phosphorus derangements

Hyperphosphatemia occurs due to decreased renal excretion, and specific therapies other than feeding diets with a decreased phosphate content and with phosphate binders added (discussed in the next two articles on the diagnosis and management of chronic renal failure in cats and dogs) are not usually employed in the acute patient. Hypercalcemia may be a cause or effect of renal failure, the former being most important to recognize and differentiate. Early detection and correction of the underlying cause of hypercalcemia can reverse failure, but, if left unchecked, particularly in association with hyperphosphatemia, the hypercalcemia may result in soft tissue mineralization and worsening renal function.

Other

Animals in ARF may be predisposed to developing urinary tract and other infections, and, once specimens are obtained for urine culture and leptospirosis identification, prophylactic, broad-spectrum antibiotics such as ampicillin may be administered. Other therapies specific for the underlying cause of disease may need to be employed—for example, ethanol or 4-methyl pyrazole in the case of ethylene glycol intoxication (Box 9). Ethanol or 4-methyl pyrazole inhibits the enzyme alcohol dehydrogenase that converts a relatively inert substance into the toxic byproducts of glycolate and oxalate.[15] The latter treatment has the benefit of not superimposing an alcohol intoxication but may be more expensive and difficult to obtain and is not helpful in the cat.

Dialysis

With aggressive therapy, the patient presenting in ARF should demonstrate a response within 24 to 36 hours as evidenced by an increase in urine output, lessening azotemia, and a subjec-

BOX 9
Treatment of ethylene glycol nephrotoxicity

Therapy must be administered within 12 hours of ingestion to inhibit the action of alcohol dehydrogenase

Ethanol (20%)

Dogs: 5.5 ml/kg IV every 4 hours for 5 treatments, then every 6 hours for 24 hours
Cats: 5 ml/kg IV every 6 hours for 30 hours, then every 8 hours for 30 hours

or

4-methyl pyrazole

Dogs only: 20 mg/kg 5% solution IV, then 15 mg/kg SID/BID, then 5 mg/kg every 36 hours

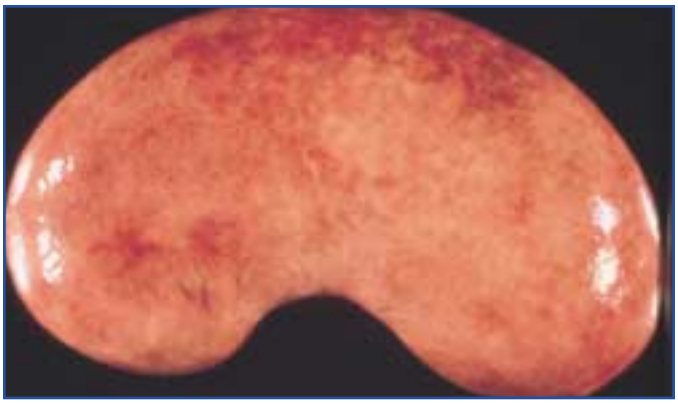

Figure 9
Gross specimen taken from a patient with acute renal failure. Photo courtesy H. C. Rutgers

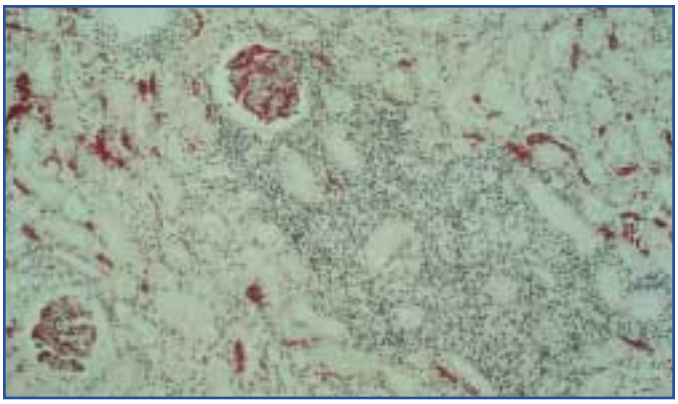

Figure 10
Renal histopathology demonstrating acute interstitial nephritis. Photo courtesy B. Smyth

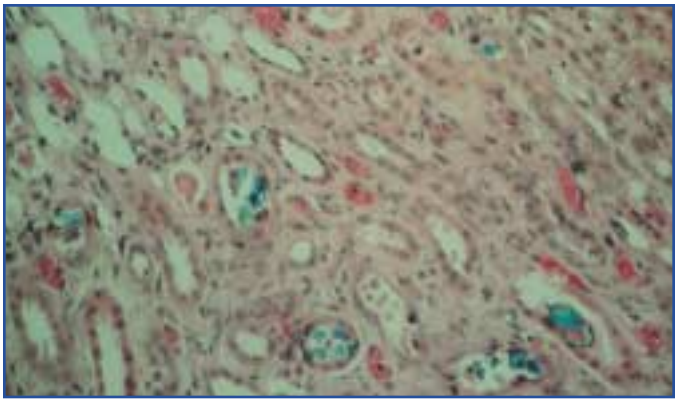

Figure 11
Renal histopathology of acute nephrotoxicosis with ethylene glycol demonstrating calcium oxalate crystals within the renal tubules. Photo courtesy H. C. Rutgers

tive reduction in the clinical manifestations of uremia. If no response is elicited, the final consideration must be dialysis. In human intensive care units, hemodialysis and peritoneal dialysis are commonly used (7% to 10% of admissions).[16] Dialysis is the science of using external means of filtering uremic toxins from the bloodstream, either by use of an artificial kidney via which blood is directed, filtered, and then recirculated (hemodialysis) or by use of a highly osmotic fluid that performs the kidneys' excretory functions by attracting uremic toxins into the peritoneal space and removing them with each fluid exchange (peritoneal dialysis).

Hemodialysis is not an option for most of our small animal patients due to limited clinical experience, availability of equipment, and the expense of intermittent dialysis.[17] Peritoneal dialysis, however, does remain a feasible option for the enthusiastic clinician. The process is very time intensive and can be cost prohibitive and therefore should ideally be reserved for animals with the potential for basement membrane regeneration on histopathology of a kidney biopsy (Figures 9 to 11). However, renal biopsies are often obtained at the same time as the peritoneal catheter is placed. Peritoneal dialysis requires the surgical insertion of a dialysis catheter into the abdominal cavity, with removal of the omentum to prevent catheter blockage, and multiple daily exchanges of a hyperosmotic solution that acts as an artificial kidney. As the kidneys heal and regain function, the frequency of exchanges decreases and are finally discontinued when the animal may be supported with fluid therapy alone.[18,19]

Nutritional support

Once the animal is beyond the initial uremic crisis, some form of nutritional support is indicated. Often the patient is not keen to eat due to residual uremic gastritis and general malaise, and feeding tubes must be employed to supply adequate nutrients. In general, diets should be highly digestible and contain good quality, yet reduced sources of, protein and adequate energy sources. Many well balanced proprietary diets are available for this purpose.

Prognosis and monitoring

In theory, the prognosis for animals in ARF is quite good but, in reality, are poor to grave. The reasons for this disparity is that ARF patients are demanding of both time and finances, particularly in the first 24 to 48 hours, and optimal care requires access to rapid return of laboratory parameters to monitor the life-threatening complications, including PCV, TP, BUN, creatinine, K^+, Ca^+, pH, and HCO_3^-. Availability of intensive 24-hour nursing care is ideal, but even in fully equipped intensive care units the success rates (i.e., recovery leading to discharge from hospital) are less than 50%.[20] The most common identifiable causes of death in patients with ARF include overhydration from overzealous fluid administration, hyperkalemia and dysrhythmias, metabolic acidosis, infections, and sepsis. It is imperative, therefore, that vital parameters are monitored as frequently as

BOX 10

Guidelines for monitoring parameters in the patient with acute renal failure

Parameter	*Frequency**
Body weight	BID/TID
Urea/creatinine	Daily/EOD
Potassium	Hourly to daily as needed
Phosphorus/calcium	Daily/EOD
Central venous pressure	Hourly to daily as needed
Hematocrit (HCT)	BID/daily/EOD
Urine output	Hourly
Urinalysis	Daily
Blood pressures	BID/daily

*The frequency of monitoring will decrease as the patient stabilizes.

possible to avoid such complications, particularly while the patient is in the dynamic state of change or when treatments are being added or adjusted (Box 10). As these parameters stabilize into relatively predictable ranges, the frequency of measurement may decline accordingly.

Once a patient is in the recovery phase and the serum creatinine and urea have stabilized at the same level for several days, fluid therapy can be tapered by 25% to 50% over 2 to 3 days while monitoring that the animal is drinking and maintaining its weight and hydration. Azotemia may continue to decline over several weeks or even months, although a mild increase is often seen when supplemental fluids are discontinued.

In general, patients with nonoliguric renal failure fare better than those presenting with severely compromised urine output.[21] The final outcome of ARF cases depends on the etiology, severity, and response to therapy. If the patient survives the initial stages of the uremic crisis, functional renal recovery may occur in 2 to 4 weeks. The majority of patients, however, are left with a compromised GFR, which may be asymptomatic, manifest as a mild renal insufficiency, or persist as chronic renal failure that can be managed for many months to years.

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