Providing the best quality care and service for the patient, the client, and the referring veterinarian.
Outline

1. Defining Acute Renal Failure
2. Pathophysiology (minimal)
3. Diagnosis of Acute Renal Failure
4. Principles of Conservative Management
Acute Renal Failure (ARF) Definition

- Sudden deterioration in renal function with ensuing accumulation of uremic waste products
- Frequently accompanied by inability to maintain acid-base, electrolyte, and fluid balance

**BY DEFINITION ... REVERSIBLE**
ARF Categories

1. PRE-RENNAL Azotemia
2. RENAL (intrinsic) Azotemia
3. POST-RENNAL Azotemia

In a patient with acute elevation in BUN and/or Creatinine …
PRE-RENAL ARF

- Intravascular volume depletion
  - GI fluid loss
  - Renal fluid loss
    - Diuretics, osmotic diuresis
  - Vasoconstriction
  - Hemorrhage
  - Capillary leak syndromes, “third space” losses
- Decreased effective arterial blood volume
  - Congestive heart failure, anesthesia, sepsis
- Altered intra-renal hemodynamics
  - NSAIDs, ACE inhibitors
- = Azotemia and “increased” specif. gravity
POST-RENAL ARF

Post-renal Azotemia

- Acute obstruction to urinary flow
- Obstruction at any level of urinary tract from renal pelvis to urethra
- Stones, blood clots, strictures, prostatomegaly, neoplasms
- The extent to which renal function recovers after relief of obstruction depends on both severity and duration of the obstruction
“Intrinsic Renal” ARF

- **Ischemic Injury**
  - Continuum of pre-renal azotemia

- **Toxic Injury to Tubules**
  - Therapeutic and non-therapeutic agents

→ *Most cases of acute intrinsic renal disease in veterinary medicine are multifactorial*
Risk Factors for ARF

- Pre-existing renal disease
- Advanced Age
- Hypotension
- Dehydration
- Decreased cardiac output
- Administration of nephrotoxic substances
Pathogenesis of ARF

- Intra-renal vasoconstriction
- Tubular injury
- Glomerular injury
ARF Causes

- **Infectious**
  - Leptospirosis, FIP, Pyelonephritis

- **Neoplasia**
  - Renal Lymphoma – most common

- **Ischemic**
  - Shock, dehydration, anesthesia

- **Miscellaneous**
  - Hypercalcemia, Toxins
ARF Causes

- **Therapeutic Agents**
  - Aminoglycosides
  - Amphotericin B
  - Cisplatin
  - NSAIDs, ACE inhibitors

- **Nontherapeutic Agents**
  - Ethylene Glycol
  - Lead, Heavy metals
  - Lilies, raisins/grapes
Rx Associated ARF

- **ACE INHIBITORS**
  - Widely used agents
  - Efferent arteriolar dilation
  - May cause pre-renal azotemia
  - Check renal panel prior to and 1 week after initiating therapy with these agents

- **NSAIDs**
  - Nonselective agents inhibit synthesis of vasodilatory prostaglandins in the kidney
  - COX 2 selective agents thought to be renal sparing – However, COX 2 is constitutively present in the kidney
Acute Renal Failure: Initiation and Maintenance

Healthy Tubular Epithelium: Normal Urine Output

Initial Sublethal Renal Cellular Damage: Normal, Poly- or Oliguria

Progressive Swelling and Death of Epithelial Cells: Oligoanuria

Epithelial Cell Lysis and Sloughing + Debris Occluding Tubule: Anuria

Hours to Days
Acute Renal Failure: Recovery

Naked, fibroed basement membrane following necrosis and lysis of tubular epithelium

Epithelial regeneration begins and some renal function returns

Restoration of tubular epithelium results in varying degrees of renal function return

Weeks to months
Clinical Features of ARF
(compared to CRF)

- Usually normal body weight
- Usually oligoanuria, but polyuric forms of ARF are seen
- Dehydration, depression
- Vomiting, diarrhea
- Halitosis, oral ulceration, lingual necrosis sometimes seen
Clinical Features of ARF (compared to CRF)

- Hypertension
  - Retinal detachment
- Mild Bruising
  - Platelet dysfunction
- Signs of fluid retention
Clinical Features of ARF (compared to CRF)

- Normal to large kidneys, may be painful
  - 2.5-3.5 x length of L2 vertebra in dogs
  - 1.5-2.5 x length of L2 vertebra in cats

- Tachypnea
  - Acidosis ± uremic pneumonitis

- Hypothermia not uncommon
  - Mechanisms unclear

- “Elevated” temperature with infection
  - Pyelonephritis
Diagnostic evaluation

- Minimum database:
  - CBC/Chem/UA//Body wt.
- Blood pressure
- Urine culture
- +/- UP:C
- +/- Lepto serology
- +/- Tick titers
Clinicopathologic Features

- Normal PCV initially (+/-)
- Moderate to severe azotemia
- Moderate to severe hyperphosphatemia
- Hypo- or hypercalcemia
- Hyperkalemia common
- Moderate to severe acidosis (TCO2/Bicarb)
- USG < 1.030 (dogs) < 1.035 (cats)
  - isosthenuria (1.008-1-012) common
  - ALWAYS try to obtain urine before initiating fluid therapy!
Clinicopathologic Features

- Active Urine Sediment
  - Casts, proteinuria, ± glucosuria ± crystalluria

- Inflammatory cells or bacteria (pyelonephritis)
Diagnostic Evaluation

- Imaging
**KEY POINT** → Look out for cats with ureteral obstruction!

BKLK – Calcium oxalate (or blood clots) incriminated in all cases
Ultrasound

Leptospirosis

Ethylene Glycol

Pyelonephritis
Renal Biopsy ...

- Indications?
- Safety?
- Technique?
Renal Biopsy …

- ARF without an obvious etiology
- ARF non-responsive to aggressive therapy
  - furnish prognosis, confirm regeneration/repair
- Patients with acute nephrotic range proteinuria and relatively normal renal architecture
  - EM and IF in addition to LM evaluation
- Chronic disease → Bx of NO BENEFIT
  - anemia, insidious history, small mis-shapen kidneys etc
  - ALL will have FINAL COMMON END-STAGE LESION
Management of ARF

ELIMINATE CAUSES OF RENAL INJURY
- Ethylene Glycol
- Infectious Causes
- Drugs
  - discontinue or modify therapy
- Hypotension/Hypovolemia

IN MANY CASES, INCITING INSULT IS NOT DETECTABLE OR HAS PASSED
Management of ARF

- Fluid Therapy
  - Foundation of medical management
  - Resolve hemodynamic compromise
  - Intravascular fluid expansion
  - Promote urine formation
  - Many animals are hypovolemic at initial presentation
  - Others exhibit signs of fluid overload
Management of ARF

- Correct extracellular volume deficits within 4-6 hours of initiating therapy
- Balanced polyionic solutions
  - LRS, Normosol-R, Plasmalyte
- Initial replacement volume
  \[ mls = [BW(kg)] \times [% \text{ deficit}] \times 1000 \]
- Caveat: heart disease, oliguria
Management of ARF
Fluid Therapy

- Evaluation for Fluid Overload
  - HR, PQ, MM, RR, RE, auscultation
  - Pulmonary or Peripheral Edema
  - Evaluate electrolytes frequently
  - Monitor urine output
    - < 1.0 ml/kg/hour is INADEQUATE
    - < 0.5 ml/kg/hour is OLIGURIA (convention)
  - Match “ins” and “outs”
  - Weigh patient at least TID!
    - Simplest means to evaluate!
  - Monitor Central Venous Pressure (CVP)
Hypervolemia

CLINICAL SIGNS:
- Increase in weight
- Edema, ascites
- Tachypnea, chemosis
- Nasal discharge
- Increased CVP
Common complication of overzealous fluid administration or failure to monitor fluid balance!

Further fluid administration is CONTRAINDICATED.

Diuretics or dialysis may be needed to resolve the fluid burden.
Management of Inadequate Urine Production

- What if oliguria persists after correction of prerenal factors ??
- Convert oliguric to nonoliguric ARF
  - Dopamine
  - Furosemide
  - Mannitol
Dopamine in ARF

- No proven benefit
  - PREVENTION OR REVERSAL OF DISEASE
  - Experimental studies in dogs
  - Large human clinical trials
- Increased urine output ≠ increased survival
- Depresses respiratory drive
- Triggers tachyarrhythmias
- Myocardial ischemia
- Suppresses anterior pituitary hormones
- Decreases T cell function
- No longer recommended for ARF patients
Furosemide (Lasix™)

- Induces a diuresis, potentially washing out obstructing cellular debris and casts
  - Increases tubular flow
  - Decreases active transport in TALH
  - Renal vasodilation
- Reduced mortality
  not demonstrated!
- Do not treat AG - induced renal failure with furosemide
Mannitol

- Osmotic Diuretic
- Increases Urine Production
- Maintains Renal Blood Flow
- Adequate Renal Blood Flow Required for Mannitol To Be Effective
Mannitol

-Putative Nephroprotective Effects:
- prevents toxins from concentrating in renal tubules
- renal arteriolar dilation $\rightarrow$ increases RBF and GFR
- free radical scavenging properties (post ischemia)
- reduces hypoxic cell swelling

- Be careful with repeated doses, particularly in patients not responding to initial dose! Mannitol rapidly expands the extracellular space! Careful with cardiac insufficiency.
OTHER CONCERNS WITH ARF
Hyperkalemia

Kidney normally eliminates 90% of ingested K⁺

- **Mild to Moderate Hyperkalemia**
  - 6.0 – 8.0 mEq/L
  - Generally corrected by establishment of diuresis (kaliuresis)
  - Non K⁺ containing IV fluids ± furosemide
  - Na bicarbonate
    - Careful!
  - Regular insulin and glucose infusion
Severe Hyperkalemia

- Life threatening > 8.0 mEq/L
- ECG Abnormalities
- 10% Ca gluconate
  - 0.5-1.0 ml/kg IV slow IV bolus
  - Corrects cardiotoxic effects only
- Insulin/dextrose
- Dialysis
Metabolic Acidosis

- Due to impaired filtration of acid load and decreased reabsorption of bicarbonate
- Mild acidosis generally resolves with fluid repletion
- Severe acidosis generally warrants treatment
  - $t\text{CO}_2 < 12 \text{ mEq/L}$ or pH < 7.2
Nausea and Vomiting

- Central effects on vomiting center and CRTZ
- Peripheral hypergastrinemia and gastritis
- Control of nausea is necessary for effective fluid and electrolyte management and for nutritional support of the patient!
GI TRACT LESIONS IN RENAL FAILURE

- Esophageal Erosions
- Gastric Ulceration

PATHOGENESIS IS NOT WELL UNDERSTOOD
HYPERTENSION

● MANAGEMENT OF SEVERE HYPERTENSION IN ICU SETTING
  – Hydralazine (Apresoline™)
  – Nitroprusside (Nitropres™)

● P.O. MANAGEMENT
  – Amlodipine (Norvasc™)
  – ACE Inhibitors
    ● enalapril, benazapril
  – β Blockers
    ● Not well evaluated
Nausea and Vomiting

- Decrease gastric acid production
- **H$_2$ antagonists**
  - Ranitidine (Zantac)
  - Famotidine (Pepcid)
- No *significant* anti-emetic effects
- Consider *sucralfate* if not vomiting
Protracted Vomiting

- Metoclopramide  CRI
- Phenothiazines
  - prochlorperazine, chlorpromazine
  - Caveat: CNS depression and vasodilation
- Ondansetron, dolasetron
- Cerenia (maropitant)
- Avoid oral meds
Management of ARF

- Hyperphosphatemia
  - Intravenous fluid therapy
  - Phosphate Binders
    - Aluminum Based
      - Alternagel™/Amphogel™
    - Calcium Based
      - Phos Lo™/Epakitin
    - Miscellaneous
      - Renagel™ (sevalemer)
      - Lanthanum

Phosphate binders of questionable value in the absence of food intake
Nutritional Management

- “Renal Failure” Diets – formulated for CRF
- Feeding Tubes

- TPN?
Antibiotics?

- Not always indicated depending upon etiology
- Commonly used empirically if pyelo or lepto is suspected
  - Usually used while culture and/or leptotiters are pending
  - Treat for 4-6 weeks for pyelo
Goals of therapy

- Diurese until renal values plateau
- Wean off of fluids
- Discharge with various therapies
  - Depends upon situation
    - Subcutaneous fluids
    - Antacid/Anti-emetics
    - +/- antibiotics
    - +/- dietary therapy
- Recheck in 5-7 days depending upon severity of azotemia when discharged