The Vet Education Webinar Series 2014

“Acute Renal Failure!”

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Acute Intrinsic Renal Failure

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Definition
Acute renal failure is defined as a potentially reversible syndrome of diverse etiology characterized by an abrupt and sustained decline in renal function, including glomerular filtration, tubular reabsorption, and tubular secretion, producing an impaired excretion of metabolic wastes, impaired ability to maintain fluid, electrolyte, and acid base balance, and uremia.

Aetiology
The causes of acute intrinsic renal failure can be divided into five groups. These are as follows

1. Renal ischaemic insults
2. Nephrotoxic compounds
3. Glomerular and vascular disease
4. Trauma
5. Obstruction of the urinary tract

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<th>Glomerular and vascular disease</th>
<th>Renal ischaemic insults</th>
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<td>1. Intravascular volume depletion</td>
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<td>2. Vasculitis</td>
<td>a. Dehydration</td>
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<td>3. DIC</td>
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<td>4. Thrombosis, or embolization of renal blood vessels</td>
<td>c. Blood loss</td>
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<td>5. Hypothyroidism</td>
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<td>6. Hyperlipidemia</td>
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<td>f. Hypoadrenocorticism</td>
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<td>g. Burns, peritonitis, pancreatitis</td>
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<table>
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<th>Nephrotoxins</th>
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<td>1. Aminoglycosides</td>
<td>2. Sulphonamides</td>
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<td>3. Tetracyclines</td>
<td>4. Cisplatin, doxorubicin, cyclophosphamide</td>
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<td>5. Heavy metal toxicity - As/Hg/Th/Cd</td>
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<td>7. Hypercalcaemia</td>
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<td>9. Mushroom poisoning, mycotoxins</td>
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<td>a. Congestive heart failure</td>
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<td>b. Cardiac tamponade</td>
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<td>c. Pericardial disease</td>
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<td>d. Cardiac arrhythmias</td>
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<td>e. Positive pressure ventilation</td>
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<td>3. Myoglobinuria</td>
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<td>4. Haemoglobinuria</td>
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<td>5. General anesthesia</td>
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<td>6. Heat stroke</td>
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<td>7. NSAID’s</td>
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<td>8. Sepsis</td>
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Obstructive uropathy
Trauma

Objectives in the Management of Acute Renal Failure

From the table above, it can be seen that there may be many conditions that may lead to the development of acute renal failure that are potentially treatable. By identifying the underlying causes, specific therapy can be formulated to stop further development of renal lesions, by altering the underlying aetiological processes. Depending on the biological behavior of disease, some forms of renal failure may be reversible e.g. antibiotic therapy in bacterial nephritis, relief of obstructive uropathy etc.
The first step in management of acute renal failure is the recognition and monitoring of patients at increased risk for the development of acute renal failure. This entails being familiar with the conditions listed in the table above, and instituting therapeutic and monitoring modalities to avoid the development of acute renal injury. This may include such measures as prophylactic fluid therapy, in older patients, or in patients having sedation of anesthesia, colloid therapy in hypoproteinaemic or septic patients, and monitoring urine output and blood pressure in at-risk patients. In addition, the age and behavior of patients may aid in identification of ingestion of toxins, or possible envenomation.

**Pathophysiology of Acute Intrinsic Renal Failure**

Each kidney receives approximately 12% of cardiac output. Despite receiving such a large part of cardiac output, the kidney is extremely sensitive to changes in perfusion and oxygen delivery. In order to understand the importance of renal ischemia in the pathogenesis of acute renal failure, we must understand kidney function.

- The majority of renal blood flow is directed at the glomerulus in the renal cortex. This is necessary in order to produce solute in renal tubules for purification and removal of metabolic toxins.
- The renal medulla is the site of the greatest energy consumption in the kidney. The outer medulla is the site where most countercurrent solute transport takes place and the creation of the tissue solute gradients necessary to achieve urine concentration. The energy required to generate renal solute gradients also consumes oxygen. The net result is that oxygen saturation of arterial blood in renal circulation in the renal medulla is low under normal circumstances. This results in mild or relative tissue hypoxia under normal circumstances.
- The combination of relatively high oxygen consumption, and low oxygen delivery, makes the renal medulla extremely sensitive to any event that would reduce oxygen delivery to the kidney – for example, hypotension, low cardiac output, sepsis, hemorrhage, systemic hypoxia etc.
- Typically, renal injury occurs in the renal medulla before the renal cortex is affected. This is why renal tubular damage is the predominant injury seen in acute renal failure.
- When there is an imbalance between oxygen delivery and oxygen consumption in the ascending loop of Henle, renal tubular ATP stores are depleted and adenosine is released. Adenosine is a powerful afferent renal arteriolar vasoconstrictor, and causes a decrease in blood pressure to the glomerulus. This decreases solute delivery to the renal medulla, and reduces tubular oxygen consumption in an attempt to prevent severe tubular hypoxia. However, if renal ischemia persists, renal tubular necrosis results.

A common event in both ischemic and nephrotoxic acute renal failure is structural and functional damage to renal tubules, giving rise to the term “acute tubular necrosis”. Both forms of acute renal failure display gradients of sub-lethal to lethal renal cell injury, decreased cellular energy production, cellular swelling, and increased permeability of renal tubular cell membranes.

The pathophysiology of acute intrinsic renal failure is generally divided into three (3) phases – the induction phase, the maintenance phase, and the recovery phase. These are briefly described below.

**Induction Phase of AIRF** - is defined as the time from the occurrence of the renal insult, until the time of development of azotemia, defective urine concentrating ability, or oliguria or polyuria. Histologically, this period is characterized by sub-lethal injury to tubular epithelial cells. If the renal insult continues, cells sustain lethal injury. Clinical signs are not usually apparent, therefore, an index of suspicion based on patient exposure to ischaemic episodes, or toxins causing AIRF will be necessary, and will allow early treatment to begin in an effort to minimize damage to renal tissue.
**Maintenance Phase of AIRF** - develops after a critical amount of irreversible renal epithelial cell injury occurs. Both glomerular filtration rate (GFR) and renal blood flow (RBF) are reduced, but GFR is reduced to a much greater degree.

Glomerular filtration rate and urine output decrease in acute renal failure due to -

- Tubular obstruction, which occurs due to the formation of tubular casts, swollen and damaged tubular endothelial cells, the presence of myoglobin/hemoglobin casts, and compression of the tubular lumen due to tissue inflammation and edema secondary to the renal insult
- Back-leakage of tubular fluid into the interstitium facilitated by tubular obstruction, and increased intra-tubular pressure. This may account for up to 50% of the loss of glomerular filtrate
- Primary filtration failure, caused by decreased RBF, afferent arteriolar constriction (RAAS, catecholamine stimulated vasoconstriction), efferent arteriolar dilation (due to renal hypoxia, resulting in decreased capillary hydrostatic pressure), and cellular swelling within the glomerulus. Contraction of the mesangium following renal insult by ischaemia, toxins, endothelin, platelet-activating factor etc. during the induction phase also reduces glomerular surface area.
- Intra-renal vasoconstriction may decrease renal blood flow by as much as 50%. Initially, blood flow is decreased to the renal cortex, but medullary blood flow is also significantly reduced in the maintenance phase

Removal of the inciting, or causative factor during this phase does not result in rapid improvement of renal function, even when supra-normal RBF values are achieved. Azotemia will be progressive or constant, despite the correction of pre-renal factors or removal of the renal insult. Renal blood flow is reduced in the cortex more than the medulla in ischaemic and nephrotoxic AIRF (RAAS is thought to play a part in this).

Note that non-oliguric AIRF tends to result from less severe renal injury, whereas oliguric AIRF develops after more severe renal injury.

The maintenance phase lasts for up to two to three weeks before renal function begins to return, as pathology caused by the renal insult resolves. If resolution of renal lesions occurs by nephron loss, interstitial fibrosis and interstitial inflammation (characteristics of chronic renal disease pathology) then return of normal adequate renal function may not occur. The patient must be maintained and supported adequately during this phase to increase the chances of renal healing and recovery.

**Recovery Phase of AIRF** – Glomerular filtration rate is able to increase to the point that azotemia either resolves, or to the point where symptoms of uremia are low-grade. Glomerular filtration rate is still reduced when evaluated by renal clearance techniques. Urinary concentrating and acidifying abilities may be permanently impaired but are often not clinically significant to the patient.

The recovery phase is characterized by the onset of diuresis in oliguric acute renal failure, and the resolution of azotemia in non-oliguric acute renal failure.

During the recovery phase, single-nephron glomerular filtration rate increases as an adaptive response to a reduction in functional nephron mass.

**NB** - the presence of azotemia may indicate pre-renal, AIRF, chronic renal failure, post-renal obstruction, or post-renal uroperitoneum, the final diagnosis of which may not be apparent on initial patient presentation. Urine output, urinalysis, and repeat blood tests are often required to establish a diagnosis once treatment is underway. Post-renal and pre-renal causes of azotemia are included as potential causes of AIRF as they contribute to the mechanisms of reduced urine outflow and tubular obstruction, and reduced glomerular filtration rate.
Clinical Findings in Acute Intrinsic Renal Failure

- History of exposure to a nephrotoxic or ischemic episode
- Depression
- Lethargy
- Collapse
- Anorexia, uremic odor to breath
- Vomiting, diarrhea, melena, nausea
- Anuria/oliguria occur in early AIRF, polyuria may be evident subsequently
- Tachycardia or bradycardia
- Acute weight loss may be present due to dehydration or fluid loss
- Evidence of other organ dysfunction - icterus, petechiae, ecchymosis, tachycardia, bradycardia, hypothermia, hyperthermia, alterations in mucous membrane color, uremic pneumonitis (acute respiratory distress syndrome), pulmonary edema, presence of thromboembolism, aspiration pneumonia

Diagnosis, Syndrome Identification and Analysis

Problem-specific Data Base - Includes the following -

- History and physical examination
- Urinalysis, culture and sensitivity prior to treatment
- CBC
- Biochemistry - BUN/creatinine/electrolyte/acid-base/calcium/phosphorus/amylase
- Kidney and bladder survey radiographs
- Blood pressure evaluation
- Urine output – obtain using urethral catheterization – intermittent catheterization preferred.
- Abdominal ultrasound, renal biopsy, IVP may be required. Note that some renal contrast agents are nephrotoxic
- Blood gas analysis
- Thoracic radiography
- Coagulation profile, anti-thrombin III assay
- Renal biopsy, serology for leptospirosis and ethylene glycol

Assume azotemia results from acute renal failure until proven otherwise

The above statement is critical in early patient management. Whereas chronic renal failure is typically irreversible and progressive, acute renal failure is potentially reversible if the underlying cause is identified and corrected. Although patients with acute renal failure may not regain total renal function, if appropriately managed, they have the potential to eventually regain adequate renal function to sustain life without the need for extensive and prolonged therapy.
Approach to the treatment of AIRF

1. Identify and treat life-threatening complications
   - Hyperkalemia
   - Hypokalemia
   - Metabolic acidosis
   - Volume depletion
   - Iatrogenic over-hydration
   - Infection
   - Underlying disease process e.g. Cardiovascular disease (tamponade, congestive heart failure, arrhythmias)
   - Iatrogenic drug events

2. Catheterize the patient’s bladder to determine urine output

3. Localize azotemia to pre-, post- or renal azotemia
   - History and physical examination
   - Assess urine concentrating ability
   - Urinalysis
   - Repeated BUN and creatinine concentrations

4. Differentiate between CRF and ARF or both

5. Identify a specific cause

6. Initiate specific therapy directed at the inciting cause (if known)

7. Monitoring
   - Central venous pressures q 8 hrs
   - Serial body-weight q 4-6 hrs aids in detection of fluid loss
   - Urine output q 1-6 hrs, Compare with fluid inputs to ensure fluid therapy is adequate
   - Blood pressure q 8 hrs
   - Biochemistry q 12-24hrs, PCV/TP, electrolytes q 4-8hrs

Treatment of Acute Renal Failure

Repeating our definition, acute renal failure is a serious, life-threatening disease of diverse aetiology that results in an abrupt decline in renal function, and the subsequent development of severe fluid, electrolyte and acid-base disturbances. As a result, fluid therapy in the management of acute renal failure is crucial to treatment success, regardless of the aetiology. Fluid therapy goals are firstly to ensure intravascular volume is replete, to correct disorders in red cell number and colloid oncotic pressure, and to correct life-threatening electrolyte disorders. Thereafter, the patient requires rehydration, fluid therapy for maintenance and ongoing losses, and management of the underlying disease. A brief summary of fluid therapy requirements in acute renal failure follows...

1. Fluid Therapy –
   a. Initial fluid therapy - many patients with acute renal failure are volume depleted prior to initiation of therapy, due to fluid losses from vomiting, diarrhoea, reduced renal concentration ability, and also from reduced fluid intake due to illness and inanition. However, it is important to recognize that some patients may be hypervolaemic (most notably those with cardiac disease). Therefore, the decision to administer fluid therapy should be based on clinical assessment of the presence of intravascular volume deficits, patient hydration status, blood pressure measurement, mucous membrane characteristics, and patient signalment and clinical signs.
   - Correct blood volume depletion (regardless of urine volume). Because hypovolaemia and hypotension may contribute to the genesis of acute tubular
necrosis, or predispose to further renal damage, volume depletion should be corrected rapidly
  o 0.9% NaCl or Lactated Ringers’ solutions are appropriate initial fluid choices.
  o Modify replacement fluid based on electrolyte, acid-base, etc.
  o The end-point of initial fluid therapy is return of normal or slightly supra-normal blood pressure, normalization of heart rate, and initiation, or augmentation of urine output, to provide urine output of 2-5 ml/kg/hr.
  o Patients that remain oliguric following restoration of vascular volume and normalization of blood pressure are at risk for developing over-hydration.
  o Rate of fluid administration - Correct hypovolaemia within 1 hour of patient presentation. Typically, this involves administering isotonic crystalloid fluids at up to 60-90 ml/kg/hr. (dog) and 30-50 ml/kg/hr. (cat) using small volume resuscitation protocol boluses.
  o Monitoring tools used in assessment of normovolaemia include restoration of normal urine output, normal pulse rate and heart rate, normal peripheral blood pressure, and a central venous pressure of 2-4 cm water. Once these parameters are normal, intravenous fluid rates should be decreased to provide for maintenance, hydration replacement and ongoing losses.

b. **Correct hydration deficits** - calculate hydration deficits, and replace over 2-8 hours. A slower rate of replacement may be indicated in patients with impaired cardiac function, or who demonstrate intolerance to fluid administration, or develop symptoms of over-hydration (dyspnoea, elevated jugular veins, diastolic gallop rhythms, pulmonary oedema).

c. **Fluid therapy during maintenance and recovery phases of AIRF** - fluid therapy during maintenance and recovery phases of AIRF is directed at preventing hypovolaemia, and maintenance of fluid and electrolyte balance. Sub-clinical volume depletion may promote additional azotemia and renal damage. Therefore, aim to induce a state of mild over-hydration for 12-36 hours in non-oliguric patients with normal cardiopulmonary function. Urine volume and losses through vomiting, diarrhoea, burns, peritonitis etc. will greatly influence the volume and type of fluid required to provide adequate maintenance therapy. The volume of fluids to be administered = urine volume + contemporary fluid losses + insensible losses. It is important to weigh the patient on a twice-daily basis in order to detect changes in bodyweight that may suggest inaccurate maintenance fluid calculation, leading to sub-clinical dehydration, or over-hydration. A suitable fluid rate following intravascular volume replacement and replacement of hydration deficits is 2-4 times maintenance fluid requirements. Allow for weight loss of 0.1-0.3 kg per 1000 calories required per day, in those patients that are anorexic, or are receiving insufficient caloric intake. The fluid type used is usually determined by electrolyte concentrations, but LRS for 24 hours, followed by 0.45% NaCl + 2.5% dextrose with potassium supplementation is usually required

Fluid administration must be monitored carefully. Patients that remain oliguric following restoration of vascular pressure and volume are at high risk for developing iatrogenic over-hydration, as mentioned above and should have their fluid rates reduced to sub-maintenance levels, or stopped completely, until dialysis can be achieved. In fact, in oliguric or anuric patients non-responsive to fluid therapy and diuretic administration, excessive fluid administration is associated with worse renal outcome – underlying the importance of monitoring and adjusting fluid therapy as indicated.
2. Therapy for Oliguria

An appropriate renal response to blood volume loading, rehydration and 3-5% fluid loading is a return of normal urine output. In a patient that is normovolaemic, well hydrated and on intravenous fluid therapy, urine production of below 2 ml/kg/hr. is considered oliguric. Anuria is classified as no urine production at all. If oliguria or anuria persists despite correction of hypovolaemia and dehydration, most clinicians attempt to convert oliguria to non-oliguria using diuretics. There is, however, no evidence that diuretics improve outcome in acute renal failure. However, in a non-referral setting, where peritoneal or haemodialysis may not be readily available, an attempt to convert oliguria to non-oliguria can make patient management less intensive, and can enable intravenous fluid therapy and other supportive therapies to be administered to the patient with somewhat out concern of over-hydration and volume overload. Indications for therapy include oliguric patients unresponsive to fluid volume replacement.

a. Diuretics - diuretics have been found to be of most benefit to patients in experimental models when they are administered either before, or shortly after renal injury, but, as mentioned above, are not associated with improved outcome. Initiation of diuresis in patients following diuretic administration does not correlate with a change in glomerular filtration rate, renal morphology, or the clinical course of renal failure. It should be noted that administration of diuretics should not be attempted prior to adequate fluid therapy. Mannitol and dopamine have no beneficial effect in patients that have inadequate renal blood flow prior to administration.

b. Mannitol - is a small molecular weight (MW approx. 182Da) molecule that is eliminated by glomerular filtration and has almost no tubular resorption. It has the following effects:
   - May enhance renal function by minimizing renal tubular cell swelling by exerting an osmotic effect within the renal tubules, which may relieve tubular obstruction
   - Mannitol exerts its diuretic effects along the entire nephron (c.f. furosemide - thick ascending loop of Henle)
   - Mannitol expands extracellular volume, and decreases renal vascular resistance
   - Aids in protection against oxidative free radical damage
   - Improves renal microcirculation by reducing swelling of vascular endothelial cells through exerting an osmotic effect across the cell membranes
   - Inhibits renin release, and increases release of atrial natriuretic peptide
   - **DOSE** – administer an intravenous bolus of 0.25-0.5 g/kg over 10 minutes. If diuresis ensues, the dose of mannitol can be repeated every 4-6 hours, or administered as a constant rate infusion at a rate of 1-2 mg/kg/min. Doses in excess of 2-4 g/kg/day may cause acute renal failure. The maximum suggested dose is 1.5 g/kg in any 24 hour period due to the potential for plasma hyper-osmolality
   - **Contraindications** - do not give in the over-hydrated or volume-overloaded oliguric patient; hydrate patients adequately before administration

c. Furosemide - is a diuretic with the following effects:
   - Decreases electrolyte (chloride and sodium) absorption in the thick ascending loop of Henle, enhancing tubular flow rate; Decreases resorption of sodium and chloride in the distal renal tubules; Directly affects electrolyte transport in proximal tubule. These three actions result in increased excretion of water, sodium, potassium, chloride, calcium, magnesium, hydrogen, bicarbonate, and ammonium from the kidneys.
   - Following intravenous administration, the peak activity effect occurs within 30
minutes, with a serum half-life of 2 hours

- **DOSE** - initially 2 - 6 mg/kg IV. Diuresis should be apparent 30-60 minutes after an intravenous dose of furosemide. A second dose may be administered if no diuresis is observed, however, doses of furosemide of more than 10 mg/kg in 1-2 hrs, may cause adverse effects in animals, such as anorexia, apathy, hypotension and tremors. If there is no response to high doses of furosemide, the drug should be discontinued. If a response does occur, a constant rate infusion of 0.25-1.5 mg/kg/hr. Because electrolyte and fluid balance disorders can develop rapidly with profound diuresis, frequent monitoring is necessary.

- Furosemide exacerbates gentamicin toxicity, and should not be used in this setting.

d. **Hypertonic Glucose** – may be used in volume-overloaded patients in place of mannitol, as there is less risk of hyper-osmolality and life-threatening hypervolaemia with glucose administration. 10-30 ml/kg of 20% glucose is administered intravenously over a 1-2 hour period. Hypertonic glucose may not be as effective as mannitol in establishing urine flow, and has no anti-oxidant free-radical scavenging properties. However, risk with use is minimal in the oliguric patient.

e. **Dopamine** – is a catecholamine, and a biologic precursor to noradrenaline. Dopamine has no evidence to support a benefit in the management of acute renal failure and is no longer recommended. It is reported to have the following effects

- Potentially may increase renal blood flow, glomerular filtration, and renal sodium excretion
- 0.5 - 1.0 ug/kg/min - activates dopamine-specific DA$_1$ and DA$_2$ receptors on vascular smooth muscle cells, and post-ganglionic sympathetic nerves to induce vasodilatation
- 2-3 ug/kg/min - activates beta 1 adrenergic receptors to increase cardiac output
- Higher doses are associated with alpha-adrenergic stimulation and vasoconstriction

3. **Therapy for Hyperkalaemia**

a. **Aetiology** – hyperkalaemia is a common finding in oliguric acute renal failure, and occurs due to the following

- Decreased potassium secretion resulting from decreased glomerular filtration rate
- Decreased delivery of sodium to the cortical collecting ducts
- Injury to potassium secretory sites along the nephron
- Cell lysis due to tissue injury, toxins, or tissue hypoxia.
- Extracellular shifts of potassium as a result of metabolic acidosis
- Potassium-containing fluid administration in oliguric patients
- The use of potassium-sparing drugs such as ACE-inhibitors

b. **Pathophysiology** - Hyperkalaemia reduces the neuromuscular resting membrane potential, causing it to become less negative, thereby lessening the rate of elevation of the action potential, and causing action potentials to have smaller amplitude. This results in increasing membrane irritability, and slowing of electrical conduction. Hyponatraemia, hypocalcaemia, and acidaemia may exacerbate the clinical signs of hyperkalaemia. Hyperkalaemia is less often a problem in non-oliguric patients because increased tubular excretion of potassium may partially compensate for the decrease in GFR present. Potassium concentrations that do not exceed 6 mEq/l typically do not induce life-threatening cardiotoxicity. Hyperkalaemia of this magnitude often responds to intravenous fluid therapy, and elimination of extra-renal causes of hyperkalaemia. If the potassium level
is above 6-8 mEq/l, or if cardiotoxicity is present, emergency therapy for hyperkalaemia should begin immediately. Clinical signs that result from hyperkalaemia include muscle weakness, lethargy, depression, vomiting, tachycardia and bradycardia. It should be noted that although electrocardiographic abnormalities do occur in patients with hyperkalaemia, ECG’s are not a reliable substitute for evaluation of serum potassium concentration.

c. Factors that promote hyperkalaemia

- Enteral feeding solutions
- Drugs - digitalis, heparin, ACE inhibitors, NSAID’s, B-blocking drugs, alpha-adrenergic agonists
- Acidaemia
- Hyper tonicity - hypernatremia, hyperglycemia
- Hypoadrenocorticism
- Insulin deficiency
- Catabolic states - infection, pyrexia, burns, myositis
- Tumor lysis syndrome
- Transfusion

d. Clinical signs of hyperkalaemia relate to its effect on the neuromuscular resting membrane potential, and include the following

- Muscle weakness
- Muscle fasciculation
- Muscle pain
- Reduced cardiac contractility
- Bradycardia
- Tall peaked T waves, flattened P waves, prolonged QRS and PR intervals, atrial standstill, prolonged
- Q-T interval, heart block, cardiac arrest

e. Treatment - animals with hyperkalaemia associated with cardiac toxicity require immediate therapy

i. Glucose - 0.5-1.0 g/kg. Prepare a 10% solution by taking 1 ml/kg of 50% glucose solution, and diluting it 1:5 with 0.9% sodium chloride solution. Administration the 10% solution over 10-15 minutes will cause an intracellular shift of potassium from the ECF. Insulin, at a dose of 0.1 unit regular insulin (Actrapid) IV may cause a more rapid intracellular movement of potassium. The effects of glucose therapy are rapid in onset (within minutes) and last for several hours. Following glucose +/- insulin therapy, the patient should be maintained on IV fluid therapy, with glucose added to make a 2.5-5% solution

ii. Calcium gluconate - calcium gluconate causes the threshold potential in neuromuscular membranes to become less negative, thereby increasing the difference between the resting and threshold membrane potentials. Administer 10% solution IV to effect, with the total dose not to exceed 1ml/kg of the 10% solution. Effects are immediate and last approx. 15 minutes. Calcium gluconate does not correct hyperkalemia, and is intended as a short-term measure to sustain the patient while other therapy is being initiated. Infusion of calcium gluconate should be discontinued when the heart rate increases, or when arrhythmias detected by ECG are controlled. Calcium gluconate should not be administered concurrently with sodium bicarbonate solutions to avoid precipitation of calcium carbonate.
iii. Sodium bicarbonate – is rarely required – even in severe cases, and should not be used as routine practice, as it can cause respiratory depression, and severe acidosis in the brain. In addition, bicarbonate should always be used with extreme caution, especially in patients that are oliguric, or in cardiac failure, because it may induce volume overload. Bicarbonate should also be used with caution in patients with hypocalcaemia, as bicarbonate decreases serum ionized calcium levels, and may precipitate clinical signs of hypocalcaemia.

iv. Maintenance phase - hyperkalaemia present in the maintenance phase of AIRF may be managed by restricting oral intake of potassium, promoting urine output, and administering diuretics (furosemide).

v. Peritoneal dialysis – may be required if conventional methods of serum potassium reduction are unsuccessful, if urine output is unable to be established, or if hyperkalemia persists despite treatment.

4. Therapy for Hypokaemia

a. Hypokaemia may result from renal losses during the diuretic phase of acute renal failure, gastrointestinal losses, and administration of potassium-free fluids. Symptoms of hypokaemia typically involve neuromuscular system (weakness, lethargy), cardiac muscle (arrhythmias), metabolic and gastrointestinal systems (vomiting, gastroparesis, anorexia) and renal (defective urinary concentrating ability) Hypokaemia may exacerbate decreases in renal blood flow by altering systemic haemodynamics and vascular tone, and may contribute to further impairment of renal function. Attention to the treatment of hypokaemia is essential to the success of fluid therapy in the management of acute renal failure. Potassium supplementation to intravenous fluids is made according to the following table.

<table>
<thead>
<tr>
<th>Serum Potassium (mEq/L)</th>
<th>mEq KCL to add to 1 litre of IV Fluid</th>
<th>Maximum infusion rate (ml/kg/hr.)</th>
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<tr>
<td>&lt;2.0</td>
<td>80</td>
<td>6</td>
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<tr>
<td>2.1-2.5</td>
<td>60</td>
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<tr>
<td>2.6-3.0</td>
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<td>3.1-3.5</td>
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<td>16</td>
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<tr>
<td>&lt;3.6</td>
<td>20</td>
<td>25</td>
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5. Therapy for Metabolic Acidosis - Metabolic acidosis develops due to decreased excretion of hydrogen ions by the damaged kidneys, resulting from tubular cell damage, and reduced buffering capacity within the renal tubules due to hypoxia, cell swelling, obstruction of tubules with debris, and conditions predisposing to metabolic acidosis (sepsis, ethylene glycol toxicity, diabetic ketoacidosis etc.). Metabolic acidosis typically has little immediate effect on the patient unless the pH is below 7.1. Therefore, not all patients with metabolic acidosis require immediate treatment of their acid-base disorder. In addition, bicarbonate therapy has not been shown to improve survival in human studies of severe metabolic acidosis, indicating treatment may not be required in many patients. Alkalization therapy may be considered for patients with blood pH less than 7.1; or with bicarbonate levels of less than 10-12 mEq/l. Therapy should be aimed at ameliorating the adverse cardiovascular effects associated with metabolic acidosis (decreased myocardial contractility, peripheral arteriolar vasodilatation, central venular-constriction etc.) rather than normalizing the blood gas disorder.

- Blood bicarbonate levels post treatment of 14 mEq/l or greater usually indicate adequate
correction of metabolic acidosis in patients with normal respiratory compensation.

- **DOSE** - 0.5 mEq/l - give half the dose over 30-60 minutes, then repeat blood gas analysis and reassess the need for further therapy
- Complications include iatrogenic metabolic alkalosis, hypokalaemia, hypernatraemia, and paradoxical CSF acidosis. Clinical signs associated with bicarbonate toxicity and paradoxical CSF acidosis include the following
  - Tachypnoea, increased tidal volume (Kussmauls respiration);
  - Decreased cardiac contractility, arrhythmias
  - Peripheral arteriolar dilatation, central vasoconstriction that can aggravate pulmonary edema
  - Depression, lethargy, stupor
  - Increased skeletal muscle breakdown, causing increased urea production, loss of body mass

**Peritoneal Dialysis**

**Definition**

Dialysis is the movement of water and solute across a semi-permeable membrane between two compartments. This process is governed by diffusion, ultra-filtration, and solute drag. The peritoneum is a semi-permeable membrane between fluid in the peritoneal cavity and the fluid of extracellular water. Water and solute can move either from the blood to the peritoneal cavity, or from the peritoneal cavity to the blood. Normally, there is very little fluid within the peritoneal cavity. However, fluid can easily be administered there – and this forms the basis for peritoneal dialysis. The type of fluid administered into the peritoneal cavity is called dialysate. Dialysate will vary in composition, volume administered, dwelling time and drainage, depending on the clinical situation. The following is a general guide to performing peritoneal dialysis in veterinary patients.

**Indications**

1. To assist the drainage of uremic solutes from the blood to the dialysate as a partial substitute for failed renal excretory function.
2. To assist delivery of free water, solutes, bicarbonate, potassium and calcium to patients with deficits caused by inadequate renal function
3. Assistance in the management of over-hydration secondary to impaired renal excretion of water, or over-zealous fluid therapy to patients with impaired renal function.
4. Pre-surgical treatment of uremia
5. Metabolic or acid-base disorders e.g. hepatic encephalopathy
6. Toxicities such as ethylene glycol, acetaminophen or salicylate toxicity

**Dialysate**

1. The Dialysate – dialysate is generally chosen to approximate normal plasma composition, but should be tailored to the individual patient in concentrations of sodium, potassium, chloride, and bicarbonate concentrations. Hypernatremia commonly occurs during peritoneal dialysis, and for this reason, dialysate solutions with a sodium concentration lower than that of plasma is commonly advised. Commercial dialysate solutions available for humans work well in dogs and cats, and are available with glucose concentrations of 1.5%, 2.5%, and 4.5%. In general, 2.5% glucose dialysate solutions are the most effective.
Homemade Dialysate – may be used as an alternative to commercial solutions, although the risk of contamination of the solution increases with each additive. A simple solution may be prepared as follows:

a. Lactated Ringer’s solution (LRS) or 0.9% NaCl + 50 ml/L of 50% dextrose – results in a 2.5% dextrose solution in 0.9% NaCl/LRS
b. Magnesium chloride is added at 72mg/L of dialysate
c. Sodium bicarbonate – is not required to be added to LRS, as LRS provides lactate equivalent to 28 mEq/L. In dialysate prepared with 0.9% NaCl, or 0.45% NaCl, sodium bicarbonate should be added at 30 mEq/L
d. Heparin is added at a rate of 1000 units/L to decrease clot formation and outflow obstruction
e. Potassium should be added at a concentration of 4-20 mEq/L to prevent hypokalemia during prolonged dialysis
f. Pre-warming of dialysate is recommended to produce mild vasodilatation within the peritoneal space

The Catheter

- A 14 Fr multi-fenestrated catheter e.g. Jackson-Pratt drain, is inserted into the abdominal cavity via a small incision 2 cm caudal to the umbilicus, just lateral of the midline, and is directed caudally and dorsally until the catheter and fenestrations are within the abdominal cavity. The catheter is then advanced until it is well within the abdominal cavity. A purse-string suture is placed at the site of the skin incision, and the catheter secured to the abdominal wall. If long-term use is desired, the catheter should be placed via a small flank incision, as this position minimizes fluid leakage through the insertion site. There are a few specifically designed catheters for long-term use in the dog, however their availability is frequently limited, and they have not achieved long-term use.
- Problems with catheters include leakage at the insertion site, poor drainage, and infection. Poor drainage is generally due to the omentum migrating to the catheter, and blocking fenestrations. Blockage of fenestrations can be reduced by inserting the catheter into a sheath of sterile inert material such as a Penrose drain – although this is rarely required when using Jackson-Pratt drains.

The Procedure

1. Dialysate is infused at 20-40 ml/kg, at 100-300 ml/minute. The abdomen should be palpably distended following dialysate infusion to ensure maximal contact of the fluid with peritoneal surfaces. Dialysate should be collected in the same bag it is administered in, and the bag then discarded.
2. Dwell-time for dialysate is between one hour and 4 hours; with more frequent dialysate changes required in patients early in the treatment course.
3. Drainage of dialysate is by gravity over a period of 15 minutes. Effluent volume during the first one or two exchanges may be less than the volume infused due to sequestration within the abdomen, or absorption of some fluid. However, subsequent effluent volumes should closely match infused volumes. Failure to retrieve 90% of infused volumes usually indicates and mechanical problem with drainage. Altering the animal’s position, and flushing of the catheter with heparinized saline may be required to re-establish drainage
4. Dialysis is continued until renal function returns to normal, or until enough renal excretory function is returned so the patient can survive without dialysis.
Complications

Complications resulting from peritoneal dialysis include peritonitis, catheter blockage, hypoalbuminaemia (due to exudation of protein-rich fluid into the abdomen as a result of mechanical irritation by the catheter), and electrolyte disturbances. These complications should be addressed as they arise, using appropriate fluid therapy, antibiotic therapy and catheter replacement.

References:

Placement of a Peritoneal Dialysis Catheter in the Dog and Cat

Peritoneal dialysis catheter placement is indicated in patients with oliguric or anuric acute renal failure in order to provide a third space for infusion and retrieval of dialysate in the short to medium management of the maintenance phase of acute renal failure.

The following is a guide to the placement of a peritoneal dialysis catheter in the dog and cat. The drains most commonly recommended are Jackson-Pratt drains, as they react minimally with omentum, and therefore provide for low-maintenance and effective drainage of peritoneal dialysate.

Some reference state that this procedure may be performed under sedation and local anaesthesia. However, many patients will find this procedure uncomfortable, and general anaesthesia is recommended for most patients.

Step 1: anaesthetise and surgically prepare the ventral abdominal skin from the xiphoid to the pubis

Step 2: place a urinary catheter for the purposes of monitoring urine output (if not already completed) and ensure the bladder is empty prior to surgery
Step 3: after surgically draping the patient, incise the skin, subcutaneous tissues and abdominal wall lateral to the midline (usually on the right side of the abdomen to avoid the spleen) and caudal to the umbilicus (indicated by the cross).

Step 4: Place the peritoneal dialysis catheter into the abdominal cavity. Close the abdominal wall and skin using a snug purse-string suture(s) to minimise leakage of dialysate into the subcutaneous tissues.

A Jackson-Pratt drain is a multi-fenestrated drain ideal for use in peritoneal dialysis. The drain is typically placed within the abdominal cavity using Carmalt forceps through a small abdominal muscle incision.
Step 5: The catheter is secured to the patient using a finger-trap suture pattern with a minimum of 6 ties. Silver-based or chlorhexidine-based ointment is placed around the tube exit site and the abdomen bandaged lightly to keep the drain in place.