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.

Etiology

The causes of acute intrinsic renal failure (AIRF) can be divided into the following five groups:

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

Glomerular and vascular disease

1. Acute Glomerulonephritis
2. Vasculitis
3. DIC
4. Thrombosis, or embolization of renal blood vessels
5. Hypothyroidism
6. Hyperlipidemia

Nephrotoxins

1. Aminoglycosides
2. Sulphonamides
3. Tetracyclines
4. Cisplatin, doxorubicin, cyclophosphamide
5. Heavy metal toxicity – As/Hg/Th/Cd
6. Radiographic contrast agents – intravenous
7. Hypercalcemia
8. Ethylene glycol
9. Mushroom poisoning, mycotoxins
10. Snake bite – elapid
11. Inhalation anesthetics
12. Endotoxin
13. Lilly toxicity, grapes, raisins

Renal ischaemic insults

1. Intravascular volume depletion
   (a) Dehydration
   (b) Shock
   (c) Blood loss
   (d) Hypovolemia
   (e) Hypoalbuminemia
   (f) Hypoadrenocorticism
   (g) Burns, peritonitis, pancreatitis
2. Decreased cardiac output
   (a) Congestive heart failure
   (b) Cardiac tamponade
   (c) Pericardial disease
   (d) Cardiac arrhythmias
   (e) Positive pressure ventilation
3. Myoglobinuria
4. Hemoglobinuria
5. General anesthesia
6. Heat stroke
7. NSAID's
8. Sepsis

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 etiopathological 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 hypoproteinemic 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 AIRF 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 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 (die 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 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 a 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 initially. 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, diarrhoea, malena, 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 – 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 Acute Intrinsic Renal Failure

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 12-24 hrs, PCV/TP, electrolytes q 4-8 hrs.

Treatment of Acute Intrinsic Renal Failure

Identify and Treat Life-threatening Complications – Fluid and Electrolyte Disorders

1. Fluid Therapy

(a) Initial fluid therapy – most patients with AIRF are volume depleted prior to initiation of therapy, however, some patients are hypervolemic (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 hypovolemia and hypotension may contribute to the genesis of acute tubular necrosis, or predispose to further renal damage, volume depletion should be corrected rapidly.
  - 0.9% NaCl or Lactated Ringers' solutions are appropriate initial fluid choices.
  - Modify replacement fluid based on electrolyte, acid-base, etc.
  - 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.
  - Patients that remain oliguric following restoration of vascular volume and blood pressure are at risk for developing over-hydration.
  - Rate of fluid administration – Correct hypovolemia within 1 hour of patient presentation. Typically, this involves administering fluids at up to 60-90 ml/kg/hr (dog) and 30-50 ml/kg/hr (cat).
  - Monitoring tools used in assessment of normovolemia 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.

(b) Correct hydration deficits – calculate hydration deficits, and replace over 2-6 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 (dyspnea, elevated jugular veins, diastolic gallop rhythms, pulmonary edema). The aim of rehydration fluid therapy is to produce mild extracellular volume expansion i.e. to produce a 3-5% bodyweight gain over normal bodyweight.

(c) Fluid therapy during maintenance and recovery phases of AIRF – fluid therapy during maintenance and recovery phases of AIRF is directed at preventing hypovolemia, and maintenance of fluid and electrolyte balance. Sub-clinical volume depletion may promote additional azotemia and renal damage. Therefore, as mentioned above, we 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.

2. Therapy for Oliguria

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, however, they are still of benefit in most patients with oliguria unresponsive to fluid volume replacement. Initiation of diuresis in these patients 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 700Da) 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.
- 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 natiuretic peptide.
- **DOSE** – 0.25-0.5 g/kg given intravenously over 10 minutes, repeat if diuresis ensues, every 4-6 hours, or give as CRI over the following 24 hours. Maximum dose 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, if no diuresis within 1 hour, give 4-5 mg/kg IV, and combine with dopamine at 2.5 ug/kg/min CRI; if no diuresis within a further hour, give 6-8 mg/kg IV. If diuresis is successful, furosemide may be used at a dose of 2-5 mg/kg q 4-8 hours as required to maintain urine output of 2-5 ml/kg/hr.
- 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 hypervolemia 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 he 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 Hyperkalemia

(a) Etiology – hyperkalemia 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 – Hyperkalemia 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. Hyponatremia, hypocalcemia, and acidemia may exacerbate the clinical signs of hyperkalemia. Hyperkalemia 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. Hyperkalemia of this magnitude often responds to intravenous fluid therapy, and elimination of extra-renal causes of hyperkalemia. If the potassium level is above 6-8 mEq/l, or if cardiotoxicity is present, emergency therapy for hyperkalemia should begin immediately. Clinical signs that result from hyperkalemia include muscle weakness, lethargy, depression, vomiting, tachycardia and bradycardia. It should be noted that although electrocardiographic abnormalities do occur in patients with hyperkalemia, ECG's are not a reliable substitute for evaluation of serum potassium concentration.

(c) Factors that promote hyperkalemia

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

(d) Clinical signs of hyperkalemia 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 hyperkalemia associated with cardiac toxicity require immediate therapy

- Permanent oscilloscope monitoring is advised, if available.
- Glucose – 0.5-1.0 g/kg. IV administration of this dose as a 10% solution over 10-15 minutes will cause an intracellular shift of potassium from the ECF. This effect occurs with or without the administration of exogenous insulin. Administration of exogenous insulin offers little additional benefit over the effects of glucose alone. The effects of glucose therapy are rapid in onset (within minutes) and last for several hours. The patient should be maintained on IV fluid therapy, with glucose added to make a 2.5-5% solution.
- 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 1 ml/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.
- Sodium bicarbonate – see section on metabolic acidosis. Bicarbonate promotes the intracellular movement of potassium, enhancing restoration of normal transcellular gradients. The effect of bicarbonate begins within minutes, and lasts several hours. 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 hypocalcemia, as bicarbonate decreases serum ionized calcium levels, and may precipitate clinical signs of hypocalcemia.
- Maintenance phase – hyperkalemia present in the maintenance phase of AIRF may be managed by restricting oral intake of potassium, eliminating extra-renal factors that promote hyperkalemia, promoting urine output, and administering diuretics (furosemide).

- Peritoneal dialysis – may be required if conventional methods of serum potassium reduction are unsuccessful, or fail to provide lasting resolution of hyperkalemia. Peritoneal dialysis is described in Appendix A.

4. Therapy for Hypokalemia

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

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. Alkalinization therapy should be considered for patients with blood pH less than 7.2; 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.

- 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
- Bicarbonate dose (mEq) = base deficit x 0.3 x body weight (kg)
- Complications include iatrogenic metabolic alkalosis, hypokalemia, hypernatremia, 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.

6. Therapy for Uremia

(a) Dietary management – Acute renal failure is often associated with anorexia, gastrointestinal disease or symptoms, and hyper-catabolism. Protein and calorie malnutrition exacerbates many of the clinical signs of uremia, contributes to the production of uremic toxins, increases susceptibility to infections, and produces glucose intolerance, electrolyte and acid-base disturbances. Nutrition plays an important role in the management of the patient with acute renal failure. Support o the gastrointestinal tract to reduce nausea, vomiting and gastroparesis often required prior to initiating enteral nutritional support. Once the patient is able to tolerate enteral feeding, an appropriate diet should be fed. Diets should be restricted in dietary phosphorus, provide limited quantities of a high quality protein, and provide adequate quantities of non-protein calories to minimize catabolism of body protein to produce energy. Dietary protein restriction also minimizes production of nitrogenous waste products that may be responsible for many clinical signs of uremia

(b) Control of uremic vomiting – uremic gastritis is a major cause of vomiting in patients with renal failure. Gastrin clearance by the kidneys is decreased in renal failure. Hyper-gastrinemia results in prolonged stimulation of histamine H_2-receptors in parietal cells, promoting gastric acid secretion, gastric hyperacidity, mucosal irritation, and gastro-duodenal ulceration (which further contributes to azotemia). Cimetidine 5-10 mg/kg iv q 4-6 hours, or ranitidine 0.5-1.0 mg/kg IV q 8 hrs are effective choices for decreasing gastric acid secretion mediated by this mechanism. Because these drugs are eliminated by renal excretion, their dose frequency should be reduced over standard intervals until renal function has improved. Uremic vomiting may also be caused by CRTZ stimulation by poorly identified uremic toxins, therefore metoclopramide given at 0.2-0.5 mg/kg SC q 4 hrs, or by constant rate infusion may decrease nausea and vomiting associated with this mechanism. Note that metoclopramide is a dopamine antagonist – withhold use if dopamine is being used to assist renal blood flow and diuresis.

7. Hyperphosphatemia

Hyperphosphatemia results from renal retention of phosphorus. During the maintenance phase, hyperphosphatemia may induce hypocalcemia and soft tissue mineralization. Administration of oral phosphate binders such as aluminium hydroxide may be beneficial in some patients.

8. Uremic bleeding diathesis

Therapy involves control of azotemia, administration of blood products as necessary.

9. Uremic pneumonitis

Is a form of acute respiratory distress syndrome that is caused by a combination of arterial hypertension, cardiac arrhythmias, and vasculitis. Uremic pneumonitis generally resolves with correction of azotemia; is an indication for dialysis therapy.

10. Uremic Stomatitis

Contributes to patient discomfort, morbidity, and anorexia. Treatment options include administration of chlorhexidine washes, and lignocaine gel.

11. Analgesia

May be provided with opioids such as butorphanol, fentanyl or buprenorphine, and may be beneficial in patients with concurrent diseases such as pancreatitis, or renal pain or urinary tract obstruction.

12. Tapering Intravenous Fluid Therapy

- Taper fluid therapy when azotemia has resolved, magnitude of azotemia has reduced, and creatinine and BUN concentrations are stable for a period of at least 3 days with improved clinical status.
- Reduce volume of administered fluids by 25% per day for 3 days; monitor body-weight to ensure animal is drinking sufficiently to maintain hydration; monitor azotemia during fluid withdrawal; continue fluid therapy if azotemia worsens, and attempt weaning after further 2-3 days fluid therapy.

13. New Directions in Renal Support

Research into protection of kidneys known to be under stress from hypoxic or toxic injury is ongoing. Some of the more recent developments are:

(a) Meprin inhibitors – Meprin is a renal brush border enzyme that is associated with accelerated renal injury following ischemic injury. During cell damage, activated Meprin is able to accumulate in renal tubular cells, and degrades cellular components and other substrates. Inhibition of Meprin is cytoprotective in models of ischemic renal injury, and may offer additional benefit in renal protection in coming years in patients with conditions predisposing to renal ischemia.

(b) Calcium-channel blockers – Diltiazem administration to patients with renal ischemia results in greater glomerular filtration rates, improved renal clearance of creatinine, improved renal concentrating ability, and less renal damage than patients treated with intravenous fluid therapy alone. Diltiazem may be considered a valuable treatment in patients with post-ischemic renal failure, that are able to tolerate administration of the drug, i.e., patients that are not hypotensive, suffer from poor systolic function etc. Verapamil has similar effects, but may produce hypotension and a more profound reduction in myocardial contractility.

(c) Prostaglandin E_1 – has shown similar benefits to diltiazem in studies of ischemic renal failure. Prostaglandin E_1 produces mild renal vasodilatation in the renal medulla, reduces glomerulo-tubular feedback, and hence improves renal blood flow and glomerular filtration rate, and improves renal blood flow to the renal medulla, reducing hypoxic cell damage to renal tubules.

(d) Colloid fluid therapy – In patients suffering from septic process such as pancreatitis, administration of synthetic colloids such as dextran 70 improves renal blood flow, and attenuates decreases in renal blood flow commonly associated with these disease processes. Administration of aprotinin, a trypsin inhibitor, increases renal blood flow in experimental models of pancreatitis-induced renal failure, and may be of benefit in supportive management of patients with severe pancreatitis.

(e) ATP: Magnesium complex – it is no surprise that administration of ATP may provide a potential benefit to patients with renal ischemia, as it provides a direct source of energy substrate to renal tubules. To date, this therapy has only been used in preservation of kidneys prior to renal transplantation.

Therapy for Specific Causes of Acute Renal Failure

Ethylene Glycol Toxicity

Pharmacology

- Low molecular weight (approx 60 Daltons) compound.
- Rapid absorption from the gastrointestinal tract.
- Metabolized initially by the liver, then by the kidneys.
- Widely distributed to all body tissues.
- Ethylene glycol is not toxic, however, the metabolites are toxic.

Ethylene glycol is metabolized in the liver by **alcohol dehydrogenase** to glycoaldehyde, which is thought to uncouple mitochondrial oxidative phosphorylation. Subsequent steps in metabolism produce glycolic acid, glycolate, glycoxylic acid, and calcium oxalate. Glycolic acid is primarily responsible for the severe metabolic acidosis that occurs in ethylene glycol toxicity. Renal tubular injury results from glycoaldehyde, glycolic acid, and calcium oxalate crystals (from oxalic acid) deposited within renal tubular lumen. A severe high anion gap normochloremic metabolic acidosis develops within 3 hours of ethylene glycol ingestion, and persists for 12-24 hours.

Inhibition of the alcohol dehydrogenase enzyme responsible for the first oxidative step in ethylene glycol metabolism, results in excretion of unmetabolized ethylene glycol, and forms the basis for therapy.

Clinical signs – Immediately following ingestion, animals may be completely asymptomatic, may show signs of euphoria, ataxia, or depression due to the presence of glycol in the brain, that exerts narcotic or euphoric effects similar to those seen with alcohol. Many animals appear to recover from initial intoxication, but experience recurrence of symptoms, with severe depression, stupor, coma, nausea, vomiting, anorexia, polydypsia and polyuria, and dehydration, development of azotemia, and a terminal metabolic acidosis in some cases (pH 6.8-7.0).

The patient may show fluorescence of the mouth under ultra-violet light if ingestion has been recent.

Laboratory values supportive of ethylene glycol ingestion include an increased serum osmolality and anion gap, and elevated blood urea nitrogen, phosphorus and potassium. Urinalysis may reveal evidence of calcium oxalate, or hippuric crystals, renal casts, and tubular epithelial cells.

Treatment

- If patient is seen within 2 hours of ingestion, induce vomiting, perform gastric lavage, and colonic enema.
- Intravenous fluid therapy with an isotonic replacement solution is recommended, initially given at 2-4 times maintenance. Avoid potassium-containing fluids such as Hartman's until the patient is urinating well.
- Prevention of metabolism of ethylene glycol is achieved by administration of ethanol (competes for alcohol dehydrogenase). Therapeutic levels are required for 72 hours, and are indicated by a depressed or semi-comatose patient.
  - Dogs – 20% ethanol @ 5.5 ml/kg IV q 4 hrs for 5 treatments, then q 6 hrs for 4 treatments.
  - Cats – 20% ethanol @ 5 ml/kg IV q 6 hrs for 5 treatments, then q 8 hrs for 4 treatments.
  - Dogs – 4-methylpyrazole – inhibits alcohol dehydrogenase; 20 mg/kg of 5% solution IV initially, then 15 mg/kg IV at 12 and 24 hours, then 5 mg/kg at 36 hours.

Lethal dose of ethylene glycol is 1.5 ml/kg in cats, and 4.5 ml/kg in dogs. The toxic doses may be lower than these doses.
Ethanol enhances many of the metabolic effects of ethylene glycol, including CNS depression, metabolic acidosis, and increased serum osmolality – this makes assessment of the patients mentation difficult, and renders blood gas analysis difficult to interpret following starting of therapy.

Additional therapy that may be employed includes peritoneal dialysis, gastrointestinal protectants such as H_2 antagonists, metoclopramide and sucralfate, calcium gluconate for those patients showing symptoms of hypocalcemia, and nutrition with a restricted protein diet.

Prognosis is grave for patients showing symptoms of toxicity on presentation, despite intensive therapy. For patients that have been seen to ingest ethylene glycol, early and intensive therapy may prevent serious renal damage.

Hypercalcemia

Etiology

Hypercalcemia may be due to non-pathological, or transient causes, or may be due to pathological disease processes that, if not treated, may lead to serious damage to organs.

Non-pathologic, transient, or inconsequential causes of hypercalcemia include:

- Lipemia.
- Growing dogs.
- Hemoconcentration/dehydration.
- Hypoproteinemia.
- Hypoadrenocorticism.

Pathological causes of hypercalcemia include:

1. Malignancy – the most common cause of hypercalcemia in dogs and cats is hypercalcemia associated with malignancy. There are three (3) mechanisms:

   - Hypercalcemia of malignancy – caused by the production and release of PTH-related protein, which activates PTH receptors in the kidney, to increase renal tubular reabsorbtion of calcium, and stimulate production of 1,25 DHCC; and also stimulates osteoclastic resorption of bone through binding to PTH receptors on osteoblasts. In addition, tumor necrosis factor, and interleukin-I stimulate osteoclastic resorption of bone.
   - Hypercalcemia induced by metastasis of solid tumors to bone.
   - Hematological malignancies growing in bone marrow.

   Malignant, non-parathyroid neoplastic lesions are most common cause of hypercalcemia in dogs.

   - Humoral hypercalcemia of malignancy is characterized by the following:
     – Hypercalcemia, hypophosphatemia.
     – Hypercalciuria.
     – Increased osteoclastic resorption of bone.
   - **Lymphoma** – 10-40% of lymphomas have hypercalcemia associated with humoral hypercalcemia of malignancy. Hypercalcemia associated with lymphoma is usually the result of T-cell neoplasms.
   - **Perirectal apocrine gland adenocarcinomas** – arise from the wall of the anal sac, and result in humoral hypercalcemia in 80-90% of cases. There is a predilection for older female dogs. These tumors demonstrate PTH-like activity in a protein secreted by the tumor (PTH-related hormone). These tumors are characteristically found in middle-aged female dogs; metastasis to sub-lumbar lymph nodes is common. Treatment is surgical removal of the tumor and affected lymph nodes. Survival times 2-21 months (average 8.8 months).
   - **Multiple myeloma, lymphoma** – are hematological malignancies, that, when present in bone marrow, may cause local resorption of bone due to the action of TNF, IL-I, and PTH-related protein. Prostaglandin E_2 may also cause local bone resorption.

2. Chronic renal failure – usually these patients have hyper-phosphatemia, with normo-calcemia. Causes include decreased renal phosphorus secretion, resulting in functional hyperparathyroidism due to hyperphosphatemia, resulting in increased intestinal absorption of calcium and exaggerated response to vitamin D.

3. Hypervitaminosis D – increases in serum vitamin D_3, vitamin D_2, or vitamin D analogues result in increased receptor binding in target organs causing increased release of calcium from bones, increased calcium absorption from the gastrointestinal tract and increased calcium resorption from the distal renal tubules. Causes include excess vitamin D supplementation, day blooming jasmine (a calcitrol-like compound is present in leaves), and cholecalciferol rodenticides. Clinical signs include depression, anorexia, vomiting,

tremors, constipation, polyuria; hyperphosphatemia, and azotemia; usually present within 1-2 days of vitamin D ingestion.

4. Primary hyperparathyroidism – is uncommon, but occurs in older dogs. PTH binds to receptors in the bone, gut, and kidney. PTH also enhances renal conversion of vitamin D to calciferol (1,25-DHCC).

5. Pancreatic, lung, thyroid, testicular, nasal cavity tumors

6. Metastatic bone tumors

7. Blastomycosis

8. Septic osteomyelitis

9. Disuse osteoporosis

10. Hypothermia

11. Idiopathic hypercalcemia of cats

12. Hypoadrenocorticism

Pathophysiology and Clinical Signs

- Increased serum ionized calcium concentrations decrease cellular function by altering cell membrane permeability, and cell membrane calcium pump activity. Any alteration in cell membrane permeability, or alteration/inactivation of the cell membrane calcium pump causes:
  - Deranged cell function.
  - Decreased cellular energy production.
  - Cell membrane disruption.
- Organs most importantly affected are the central nervous system, heart, lungs, gastro-intestinal tract and kidneys. Clinical signs are dependent on the rapidity of development of hypercalcemia, the magnitude of hypercalcemia, and the duration of hypercalcemia.
- Clinical signs are most severe when hypercalcemia develops quickly, as in hypervitaminosis D, and iatrogenic intravenous administration.
- Mineralization of soft tissues occurs when the product of calcium and phosphorus is greater than 50 mg/dl; and occurs in particular in the heart and renal tissue.

Clinical signs observed are:

- Anorexia.
- Vomiting.
- Constipation.

- Polyuria and decreased urinary concentrating ability – early clinical signs, resulting from a decreased tubular reabsorbtion of sodium, and impaired action of ADH on the collecting duct tubular cells mediated by calcium sensing receptors on the renal epithelial cells in response to hypercalcemia.
- Decreased excitability of smooth muscle.
- Direct CNS depression – depression, lethargy, may progress to coma.
- Decreased excitability of skeletal muscle causes weakness.
- Increased PR interval, decreased QT interval.
- Ventricular fibrillation – cardiac changes develop as a result of rapid mineralization of heart muscle, and elevated ECF calcium.
- Renal tissue – mineralization of the tubular basement membranes, tubular degeneration, and interstitial fibrosis contribute to renal structural changes. These changes are reversible, but may become permanent if hypercalcemia persists.
- Azotemia is common, and results from pre-renal (dehydration – due to polyuria, vomiting, diarrhoea) and renal causes. A compensatory polydypsia may diminish as hypercalcemia causes worsening depression, with polyuria still persisting, leading to dehydration.

Treatment for Hypercalcemia

1. Removal of the underlying cause:

    - Cease vitamin D supplementation in cases of hypervitaminosis D.
    - Excision of neoplasms.

2. Supportive therapy:

    - Volume expansion – correct hypovolemia and dehydration, as dehydration and volume contraction increase the Ca x PO_4 product. 0.9% NaCl – increases GFR, and decreases reabsorbtion of calcium, and is the fluid of choice for initial resuscitation.
    - Diuretic therapy – following rehydration, administration of diuretics promotes urinary calcium loss. Administer furosemide 1-4 mg/kg IV q 8 hrs.
    - Glucocorticoids – are useful in management of hypercalcemia caused by lymphoma, hypervitaminosis D, hypoadrenocorticism, granulomatous disease, thymoma, multiple myeloma, and hypervitaminosis A. They reduce bone resorption through decreasing development of mature osteoclasts; decrease intestinal absorption of calcium, and increase renal calcium excretion.

      NB – withhold administration of glucocorticoids until a diagnosis is made of underlying disease, as lympholysis which follows steroid administration, may make histopathological diagnosis of lymphoma very difficult.
    - Therapy for hypervitaminosis D includes fluid therapy for 7 days minimum due to the long half-life of 25-DHCC; furosemide, low calcium diet and administration of oral phosphate binders such as aluminium hydroxide.

Hypoadrenocorticism (Addison's Disease)

Etiology

- Idiopathic adrenal atrophy.
- Immune-mediated adrenocortical destruction.
- Iatrogenic.
- Hemorrhage or infarction of the adrenal glands.
- Mycotic, granulomatous disease.
- Neoplastic destruction of the adrenal gland.
- Adrenalectomy.
- Anterior pituitary gland insufficiency.

Pathophysiology

- Glucocorticoid deficiency results in impaired gluconeogenesis and glycogenolysis, decreased sensitivity of blood vessels to catecholamines, impaired water retention by kidneys, depressed appetite, lethargy and depression.
- Mineralocorticoid deficiency
  - Hypo-aldosteronism – excessive sodium and chloride excretion, increased potassium and hydrogen retention. Hyponatremia results in lethargy, blood volume contraction, mental depression, decreased cardiac output, acute renal failure, and hypovolemic shock. Hyperkalemia results in muscle weakness, hyporeflexia, impaired cardiac conduction, bradycardia, atrial standstill, and peaked T waves, small P waves.

Clinical signs

- Thin body condition.
- Vomiting.
- Sudden onset of collapse.
- Weak pulses, muscle weakness, depressed mentation.
- Shallow respiration, pale mucus membranes, delayed capillary refill time, cardiac arrhythmias.
- Na: K ratio 20:1, hypochloremic metabolic acidosis, hyperphosphatemia.

Protocol following admission

- Draw blood for CBC, biochemistry panel, basal plasma cortisol assay.
- Begin intravenous infusion of 0.9% NaCl at 40-90 ml/kg/hr.
- Begin therapy for hyperkalemia if required.
- Give 2-5 mg/kg dexamethasone sodium phosphate (prednisone will interfere with cortisol assay).

- Administer 0.25 mg alpha 1,24-corticotrophin IV/IM.
- Blood test 1 hour later for cortisol assay.
- Administer fluid therapy to restore cardiac output and electrolyte balance.
- Insert urinary catheter to measure urine output.
- Provide ventilatory support if required.
- Administer fludrocortisone acetate at 0.1 mg/10 kg PO.
- Treat hypoglycemia if present with dextrose 1 gm/kg slow IV over 15 minutes, then begin a 2.5-5% solution at 1-2 ml/kg/hr.

Renal Emergencies – Renal Trauma

Etiology

- Blunt trauma/contusions.
- Lacerations/hematomas.
- Avulsion of vascular pedicle with profound hemorrhage.
- Laceration/avulsion of ureter or renal pelvis.

Pathophysiology – the kidneys are well protected by surrounding fat, a fibrous capsule, ribs, and lumbar musculature. Bruising or contusions of the kidneys seldom cause serious organ dysfunction, with a mild, self-limiting hematuria being the most common sequela to this type of injury.

Hematomas may result in local ischaemic injury to the parenchyma. Occasionally, torsion of the kidney about the renal vessels may occur following damage to the renal capsule or its attachments.

Severe crushing injuries, damage to the vascular pedicle, or lacerations, allow blood and urine to accumulate in the retroperitoneal space, causing pain and cellulitis. If blood and urine drain into the abdominal cavity, hypovolemic shock, anemia, and sterile peritonitis results, and clinical signs of uremia and abdominal discomfort become apparent.

Diagnosis

- Clinical signs and history of recent trauma.
- Macroscopic or microscopic hematuria.
- Red blood cell casts in the urine.
- Dorso-cranial abdominal or sub-lumbar pain.
- Progressively enlarging retroperitoneal mass, or free abdominal fluid.
- Abdominal fluid creatinine > serum creatinine.
- Radiography – retroperitoneal swelling, free abdominal fluid, excretory urography.

Treatment

- Intravenous fluid therapy.
- Monitor urine output, monitor presence of persistent hematuria, aim for urine output of 2-4 ml/kg/hr while the patient is on intravenous fluid support.
- Contusions – usually require no specific therapy.
- Hematoma – leave undisturbed unless enlarging from continued bleeding.
- Laceration of the renal capsule – laparotomy with suturing of the defect.
- Renal pole injury – partial nephrectomy.
- Maintain urine output as above, repeat excretory urography in 10-21 days to assess renal blood flow and integrity.

Ureteral Emergencies – Ureteral Trauma

Pathophysiology

- Acute injury to the ureter may be mild and self limiting, or serious (avulsion from the kidney or bladder). Hydro-ureter and subsequent hydronephrosis may result from hematoma formation within the ureteral wall lumen, or from temporary failure of ureteral peristalsis.
- Ureteral trauma generally results in extravasation of urine into the retroperitoneal space, with or without extension into the peritoneal cavity, and causes cellulitis, (and sterile or septic peritonitis is peritoneal cavity involvement occurs) The development of peritonitis leads to systemic illness and dehydration, resulting in pre- and post-renal azotemia.

Clinical Signs

- Symptoms are often vague and non-localizing.
- Retroperitoneal pain is associated with cellulites.
- Abdominal discomfort, distension, splinting abdominal pain, pyrexia, vomiting, sub-lumbar pain.
- Hydroureter and hydronephrosis associated with ureteral stricture may take several weeks to develop.
- Azotemia may not develop if unilateral ureteral obstruction is present.

Diagnosis

- History and clinical signs.
- Radiography – abdominal effusion evident – loss of serosal detail, soft tissue densities in region of trigone of bladder, or in region of kidneys; excretory urography is useful.
- Urinalysis – hematuria.
- CBC, biochemistry profile may be suggestive.
- Diagnostic peritoneal lavage – analyze urea/creatinine concentrations against plasma concentrations; culture and sensitivity.

Treatment

- Intravenous fluid therapy, correction of acid/base and electrolyte disorders, correction of hypovolemia or shock, and hydration deficits; maintain urine output at 2-5 ml/kg/hr.
- Analgesia – butorphanol 0.1 mg/kg iv q 4 hrs, buprenorphine 0.01-0.025 mg/kg sc q 8 hrs.
- Antibiotic therapy – broad spectrum antibiotics are indicated if sepsis suspected, or the presence of a penetrating wound. Obtain culture and sensitivity of tissue and abdominal fluid at time of surgery.
- Exploratory surgery early in the course of disease may allow definitive repair.

Monitoring

- Urine output.
- Electrolyte levels, BUN, creatinine, hemogram on daily basis.
- Excretory urography at 3-5 days, 14 days, and 1-3 months will allow assessment of ureteral patency.

Appendix A: 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.
2. 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 72 mg/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 (with stylet) 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. The Penrose drain is secured to the abdominal wall along with the catheter.

The Procedure

1. Dialysate is infused at 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, hypo-albuminemia (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.

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