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Small Animal Emergency Medicine Case Challenges for Advanced Practitioners Mini Series

Session 1: Treatment principles of Intoxications

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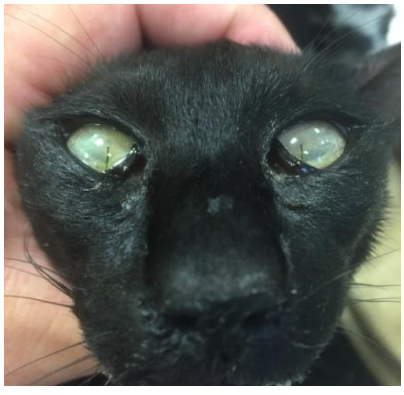

a) Preventing further absorption:

Gastrointestinal Decontamination

Emesis can be used to prevent further absorption of an overdosed drug given orally. Contraindications to inducing emesis include the following:

- Unable to protect airway
  - Neurologically inappropriate (CNS depression)
  - Absent gag
  - Laryngeal disease
- Dyspnoea
- Risk of raised intracranial pressure, seizures or altered mentation

The following substances may be used to induce emesis in the patient.

- Apomorphine (do not use in cats; alternatively to the subcutaneous injection in dogs, the same dose can be given onto the conjunctival surface of the eye, so that any remaining drug can be flushed out after the dog has vomited)
- Xylazine/medetomidine
- Hydrogen peroxide (2%)

Gastric lavage

In the case of an overdose and if contraindications to inducing emesis exist, gastric lavage can aid in removing drugs from the stomach. The dog or cat should be anaesthetized and intubated (with a cuffed endotracheal tube) to reduce the risk of aspiration. The stomach should be lavaged with warm saline so as not to induce a hyponatraemia and/or hypothermia. Activated charcoal may be placed within the stomach via the stomach tube and may further reduce absorption of the drug. Repeated dosages every 4-6 hours have been recommended for drugs that undergo entero-hepatic recirculation.

b) Enhancing elimination:

Cathartics : Cathartics such as sorbitol (2 mL/kg) can decrease the absorption of drugs by accelerating their transit time through the GI tract. Sorbitol is commonly given with the activated charcoal, but if used too frequent can lead to dehydration. Single use is preferred.

Intralipids: Intravenous administered lipid solution have originally been used in human medicine as a treatment for local anaesthetic intoxications. Several veterinary case reports have now described their use in intoxications/overdosages of ivermectin, moxidectin, permethrins, baclofen and tremorgenic mycotoxins. Two working theories of mechanisms of action exist. One is that intralipids work as a “lipid sink” for lipophilic substances and therefore enhance the elimination by binding to these substances, another one points out their ability to work as fatty acid energy substrate for the myocardium. Dosages

are derived empirically from human studies and most clinicians give 20% Intralipid solution as a bolus of 1.5 ml/kg over 5-15 min, and then possibly subsequent dosages of 0.25ml/kg/min over 1-2 hours.

Diuresis: If the drug is renally excreted, diuresis might be utilised to enhance elimination. Forced diuresis uses large volumes of intravenous fluids. Care should be taken to avoid fluid overload and electrolyte imbalances.

Extra-corporeal methods of removing certain toxins (e.g. barbiturates) through haemodialysis have been used. Unfortunately, these options are not widely available.

c) Antidotes : Antidotes are only available for a small number of specific toxins. Even if they are suitable, they might not be available in a timely fashion or their use might be cost-prohibitive. Diligent and thorough supportive care are often much more important.

Substance	Antidote
Ethylene glycol	Ethanol/Fomepizole
Paracetamol	Acetylcysteine
Organophosphates	Atropine
Cholecalciferol	Calcitonin
Zinc, lead	Ca-EDTA
Iron	Deferoxamine
Metaldehyde	Methocarbamol
Rodenticides	Vitamin K1

d) Supportive care: Principles of supportive care will be discussed throughout the lecture, but are based on principles of respiratory and cardiovascular stabilisation, maintaining renal perfusion and general medical/nursing care.

Assessment of renal function in dogs and cats

Diminished renal function will lead to disturbances of fluid balance and composition, ultimately leading to major organ disease, so it is important to be able to make a judgment on renal function, especially early in the disease process. A variety of tests have been developed and used historically to assess renal function more in detail and range from urinalysis and measurement of blood parameters to specific excretion tests and renal biopsy.

Glomerular filtration rate (GFR): Clinically, Creatinine is a useful parameter to estimate GFR somewhat. It is released by muscle tissue in a predictable, non-fluctuating way (within normal physiological function) and is not reabsorbed, filtered out or actively secreted. It just flows “downstream” and a predictable value (reference range) should be measurable if GFR is not impaired. There are small individual differences and age dependent changes, but most of them are clinically irrelevant. It is so helpful, that current IRIS

guidelines use the creatinine levels in their guidelines (see later). Mainly, Creatinine levels increase if GFR decreases, but it is not a good indicator to detect the initial stages renal dysfunction, because initially a significant drop in GFR will not affect the creatinine levels, whereas further small decreases in GFR in end stage renal dysfunction will increase the serum creatinine levels markedly.

Urea (or blood urea nitrogen;BUN) is made in the liver from ammonia and widely distributed throughout the body due to its ability to pass through cell membranes easily (non effective osmole). It is also reabsorbed by the renal tubules and antidiuretic hormone influences tubular permeability for BUN. Furthermore, BUN is not released in a “steady-state” like Creatinine. A protein meal (or e.g. a gastrointestinal haemorrhage) can increase values significantly. In dehydrated animals, urine flow decreases and BUN absorption increases, raising serum levels. Due to all these influences, BUN cannot be used as an independent assessment of GFR, but can be useful in clinical practice as an indicator of a potential problem, that needs to be further assessed. The test strips used by some clinicians as part of an initial “minimum database” can be a useful, rapid screening test.

The Urine protein to creatinine ratio (UPC) quantifies proteinuria in a patient. Quite a few renal diseases can lead to protein loss via the urine and quantification of the severity might indicate a suspicion of a certain disease process, e.g. in chronic renal disease protein loss might be mild to moderated, whereas in glomerulonephritis protein loss might be severe (In absence of an “active sediment” that occurs with urinary tract infection). Angiotensin-converting enzymes inhibitors (ACEi) are more and more used by clinicians as “kidney-protective therapy”. The concept behind this is the ability of ACEi to counteract the severe filtration that occurs in chronic renal failure patients and therefore limit the amount of protein excreted. Clinically it decreased GFR somewhat and small increases in creatinine in these patients are sometimes noticeable.

Cystatin C has been used in human medicine as an indicator of GFR, because it seemed to be a better indicator of early renal disease, but in veterinary medicine it has not shown similar advantages to date and is not widely used yet. If a more in depth GFR assessments beyond creatinine (cystatin C) is needed, clinicians could use substance clearance in which, instead of endogenous creatinine, a substance is administered, e.g. Inulin, and its clearance rate is measured and GFR is extrapolated from that.

1. Imaging of the urinary tract

Both, radiographs and ultrasonography are useful modalities to image the urinary tract further. A combination out of both will give most likely additional information that one method alone cannot provide. Cachectic patients can pose a challenge as fat is helpful in contrasting structures, e.g. retroperitoneal fat will emphasize the appearance of the renal shape. In cats, kidneys might be easier to identify than in some dogs. To assess renal size, ventrodorsal (VD) views are most helpful and as a general rule, canine kidneys are approximately 2.5-3.5x the length of the second lumbar vertebrae (L2) and feline kidneys 2-3 x the length of L2.

An excretory urogram can help with the further investigation of renal size and shape, but mainly enhances the ability to visualize the renal pelvis, ureters and bladder. It allows for detection of leakage (uroabdomen), masses, ectopic ureters, etc. 600-700mg iodine/kg are administered intravenously and as the radiopaque substance is excreted through the urinary system, radiographs can visualize structures as contrast study. Due to the fact that nephrotoxicity has been described, non-ionic agents (e.g. iohexol) are preferred in patients with known renal disease and all others have to be well hydrated with good urine output and without previously noted allergic reactions to iodine substances. To prepare the patient, enemas are sometimes used, but even if not, pre-contrast studies need to be obtained to compare contrast study pictures against. After the bolus injection is given an initial radiograph is taken straight

away and then in 1, 5, 20 and 40 minutes afterwards. VD views initially should be complimented by lateral and oblique views to visualize the ureters after 5-10 minutes.

Ultrasonography enables the clinician to assess the parenchyma of the kidneys more in detail without giving necessarily information regarding renal function. Doppler might be used to visualize blood flow (e.g. for the detection of infarction), also contrast sonography has been used to assess perfusion. The renal cortex is homogenous in appearance and is hypo-or isoechoic when compared with the liver (double window on ultrasound machine will help illustrating this). Renal cortex should also be hypoechoic in comparison to the splenic parenchyma. Cortex and medulla are clearly distinguishable, medulla appears to be more hypoechoic than the cortex.

Computed tomography (CT) can visualize the entire urinary tract and contrast studies can even enhance the accuracy further. 3D reconstruction of areas of interest might facilitate surgical planning and especially in the detection and further visualization of ectopic ureters, CT studies are used more and more. Although magnetic resonance imaging (MRI) is possible, it is not commonly used to assess the urinary tract only. Renal scintigraphy can be used to assess GFR further, because injected technetium is excreted by the kidneys according to GFR. It is used in human medicine e.g. for the evaluation of remaining renal function before planning for a nephrectomy.

Clinical reminders:

- left kidney further caudal (right kidney might be difficult to visualize by ultrasound =>try intercostal)
- renal pelvis of cats can be more radiolucent than parenchyma (due to fat)
- excretory urogram might not visualize the urinary bladder sufficiently due to dilution of the contrast medium “downstream”
- in obese cats, liver can be hypoechoic to renal cortex on ultrasound

2. a) Causes of intrinsic renal failure:
   The main result that leads to renal function impairment is cell damage and/or death after diminished renal blood flow. Diminished blood flow, as in shock, prevents sufficient delivery of nutrition and oxygen to the cells and consequently, metabolic disturbances can lead to cell death if no remedied. Those molecular changes activate destructive enzymes and the sodium-potassium-pump is influenced, changing intracellular electrolyte concentration and dynamics. This triggers an inflammatory cascade. Neutrophils are releasing cytokines that alter vascular permeability. Resulting cell oedema can contribute to tubular obstruction. Radical oxygen substances can form direct toxic substances that continue to “melt” the original renal architecture, diminishing GFR and leakage of fluid through tight junctions, which ultimately leads to loss of urine concentration ability and further cell lysis and death.

   Some causative conditions leading to renal injury:

   - Ischaemia (e.g. hypoperfusion, infarct)
   - Sepsis
   - Many toxins
     - E.g. Ethylene glycol, lily intoxication (cats), grapes/raisin intoxication (dogs)…
     - Heavy metals
     - Haemoglobinuria

- Drugs
    - NSAIDS
    - Contrast agents
    - Aminoglycosides
- Infectious
    - Pyelonephritis
    - Leptospirosis
- Hypercalcaemia
- Hypervisicosity

b) Treatment principles of acute renal failure:

As we have seen before, there are numerous conditions that can ultimately lead to dramatic renal impairment and severe kidney injury. As with most sequelae of severe disease, the most effective treatment addresses the underlying disease process and aims to diminish further damage by supportive care and treatment. Depending on those factors, renal function may ultimately be restored. In some patients, renal function might, after initial successful treatment, remain impaired permanently.

Acute kidney injury can be divided pathophysiologically into four stages:

1. Initiation phase: the initial insult results in some renal tissue damage.
2. Extension phase: Damage from the initial insult extends by spreading inflammatory response (see above under 4a). Clinically, there might be no indication of renal impairment yet, no azotaemia, no casts within the urinary sediment, etc.
3. Maintenance phase: The initial insult and resulting inflammatory response are well established and maintain damage to the cellular structures of the kidney. Now we see azotaemia and later oliguria/anuria (can last days to weeks!)
4. Recovery phase: Repair processes are active, some renal tubules might return to function which improves azotaemia and we might see a marked increase in urine output due to osmotic diuresis of accumulated solutes.

Again, as in many intoxications, the earlier we can intervene within this cascade after the initial insult, the better.

PRINCIPLE ONE: Address/Treat the initiating problem, e.g. if patient is receiving non-steroidals, discontinue them! In pyelonephritis, perform a urinary culture and start antibiotic treatment. In ethylene glycol intoxication (if early enough) consider ethanol/fomepizole treatment. Treat hypercalcaemia, treat hyperviscosity, etc. The initial “spark” needs to be dealt with and exstinguished, otherwise the concurrent supportive care will be inefficient.

PRINCIPLE TWO: Supportive care

Fluid therapy: Most patients will have a “water/hydration” deficit and this should be replaced as soon as possible. As always, take the deficit, maintenance needs, and ongoing losses into the calculation. Hartman’s is a good solution to start with, but after re-hydration fluid choice needs to be reassessed based on electrolyte and acid-base status. It would be intuitive to think that “the more the better-approach” is reasonable, but not all the infused fluid might be filtered through the glomerula and will then lead to overhydration. There is sufficient evidence in human studies, that overhydration is detrimental to survival. So, we would aim to optimise fluid therapy to achieve

sufficient renal blood flow, but no overhydration. A typical scenario would see decreased urine production leading to us thinking of increasing the fluid rate to “push more fluids through the kidneys”, but again, this might lead to overhydration, so cautions monitoring of hydration and fluid volume parameters are essential. Check the mucous membranes for moisture (watch for nausea induced hypersalivation), capillary refill time, heart rate, blood pressure, haematocrit/total solids, urine output (catheter, closed collection system), renal biochemistry parameters (Crea, Bun, Phos) and other electrolytes and acid base status.

What happens if my patient does not produce enough urine (during the above described approach to therapy, urine output should be in excess of 2mls/kg/hr)? Check if the patient is properly hydrated! If hydration is not restored, lower urine output rates might be physiological. Check the “ins-and-outs” by calculation and make sure the urinary catheter is not obstructed! Match the urine produced by an appropriate intravenous fluid rate to avoid overhydration. Despite appropriate fluid therapy, severe metabolic acidosis can feature in these patients. Due to the possible significant “side-effects” of bicarbonate therapy (csf acidosis, etc.), it is usually only considered in severe acidosis after re-hydration. What to do if urine output drops? There are different therapies available to increase urine output:

Furosemide will help us in diminishing fluid overload by acting diuretically on the tubules, but it will not increase renal blood flow or GFR directly. Theoretically, as described above, if urine output ceases we should stop fluid therapy to avoid fluid overload. The administration of furosemide makes a continuation of the supportive care possible when urine output diminishes. Instead of bolus administration, furosemide can also be administered as CRI (one study showed increased diuresis by CRI in comparison to intermittent injections, but this was investigated only in normal dogs). Recommended dose is 0.5-1mg/kg/hr.

Mannitol can be considered but care should be taken. As an osmotic diuretic it could contribute to overhydration, if the patient is oligo-/anuric. In high dosages (>2g/kg) it can contribute to kidney injury. Usual dosages (0.5-1g/kg/over 20-30 minutes) can not only increase urine output, but also acts as a free radical scavenger, and has other positive effects that might contribute to diminish renal injury.

Dopamine? Theoretically could increase renal blood flow and GFR, leading to an increase in urine output, but several studies (others than in normal dogs) showed contradictive results. In human medicine, dopamine is not longer recommended in the treatment of acute kidney injury. *Fenoldopam?* Shown to be renoprotective in human studies, controversial in veterinary medicine due to lack of clinical studies. Maybe a role in the future…

Diltiazem has been considered due to its possible effect to reverse renal vasoconstriction and by causing natriuresis. It has been used in human medicine and one veterinary study showed an increase in urine output in dogs suffering from leptospirosis, but results were not statistically significant. Future use?

Peritoneal dialysis.

Potential complications of peritoneal dialysis:

Peritonitis, Respiratory compromise, Catheter blockage, Leaking of catheter site, Abdominal distention, Hypovolemia, Hyperglycemia, Hypothermia

Difference between peritoneal (PD) and intermittent hemodialysis (IHD) regarding dialysate preparation and composition:

IHD – Prepared by the dialysis machine from ultrapurified water with added electrolytes and bicarbonate to a prescribed quantity of sodium to mimic plasma concentrations

PD – Prepared commercially, available in bags of peritoneal dialysate, with electrolyte concentrations similar to plasma, and 1 to 4% dextrose

Differences regarding anticoagulation

IHD – Heparin dosing throughout treatment.

PD – none needed (no extracorporeal circuit), some recommend adding heparin to dialysate.

Differences regarding ultrafiltration

IHD – Vacuum applied to dialysate circuit post-dialyzer – fluid follows area of lower hydrostatic pressure (vacuum applied)

PD – Peritoneal surface exposed to solution of higher dextrose concentration creating an osmotic gradient.

Differences regarding blood pump mechanism

IHD – machine blood pump

PD – heart

Differences regarding the exchange surface

IHD - Dialyzer of hollow tube semipermeable membranes, various compositions depending upon desired goal. Protein not filtered

PD – Peritoneal surface

b) Haemodialysis

Potential complications of hemodialysis:

Hemorrhage, hypotension, dialysis disequilibrium, anaemia, hypoproteinemia, catheter sepsis, catheter thrombosis

c) Continuous renal replacement therapy (CRRT)

CRRT works to replace normal kidney function by exposing the patient's blood in an extracorporeal chamber to a semi-permeable membrane. Substances are removed from the blood by way of diffusion, convection, and/or adhesion, depending on the modality chosen. CRRT differs from traditional intermittent hemodialysis (IHD), as therapy is continuous with gradual removal of substances, and IHD uses diffusion exclusively as its modality. The purpose of CRRT is to gradually and effectively eliminate uremic and other blood-borne toxins, correct electrolyte and acid-base imbalances, and modulate fluid balance. The most common use is in the treatment of acute renal failure, however its use may extend to treatment of toxicities or drug overdoses, fluid overload such as that with congestive heart failure, and sepsis. There are four different possible modes of operation in CRRT.

1. Slow continuous ultrafiltration (SCUF) technique uses convection for solute and fluid transport and works by driving blood through the filter and creating a positive pressure gradient, allowing fluid and solute passage through the pores, creating the ultrafiltrate. This fluid is not replaced before the blood is returned to the body. This technique is used in cases of fluid overload, as fluid is removed and blood volume drops.

2. Continuous veno-venous hemofiltration (CVVH) is similar to SCUF in that convection is used as blood is passed through the semipermeable filter and a positive pressure gradient is created, so ultrafiltrate is removed. However, in this mode, the ultrafiltrate is replaced with a replacement solution, so there is no net loss of blood volume for the patient. This mode is superior to hemodialysis in removal of larger sized particles (up to 50 kiladaltons) such as bilirubin, some toxins, and certain inflammatory mediators.

3. Continuous veno-venous hemodialysis (CVVHD) uses diffusion for solute transport. As blood is passed through the semipermeable filter, a dialysate solution is concurrently flowing outside the filter. Particles selectively move from areas of higher concentration to areas of lower concentration. Therefore, uremic solutes such as creatinine and blood urea nitrogen pass out into the dialysate, which is then discarded as ultrafiltrate. There is no net gain or loss of fluid with this modality, as solute diffusion is the main process.

4. Continuous veno-venous hemodiafiltration (CVVHDF) uses a combination of diffusion and convection, as fluid is moved through the filter with a positive pressure gradient, and dialysate solution is simultaneously flowing in the opposite direction, outside the filter. Ultrafiltrate removed is again replaced by a replacement solution, preventing net gain or loss of fluid.

Advantages of CRRT over peritoneal and haemodialysis: PD creates a risk of peritonitis, insufficient solute clearance, poor fluid removal, abdominal leaks, and respiratory dysfunction. All of these are avoided with CRRT. IHD is only able to remove smaller sized substances, as opposed to the larger substances removed by CRRT. Also, there is increased risk of hemodynamic instability and dialysis disequilibrium with IHD, where these are largely avoided with CRRT due to the slow, continuous removal of solutes. CRRT is technically less intensive than IHD and PD.

Disadvantages: CRRT requires specialized equipment and training. It is labor intensive and requires constant monitoring 24-hours per day (similar to PD)

Case example:

A 4-year old female entire Labrador was referred to you for vomiting of two days duration. Her past medical history is unremarkable. Her physical examination reveals a body condition of 5/9. She is approximately 5% dehydrated and guards her abdomen on dorsal abdominal palpation. There are no other abnormalities. Weight was recorded as 42kg.

1. *List some diagnostic tests that would be reasonable to perform at this stage. (Biochemistry, haematology, electrolyte and acid-base status, urinalysis, abdominal radiographs)*

Blood biochemistry results:

Sodium: 132 mmol/L (139 – 150)

Potassium: 4.9 mmol/L (3.4 – 4.9)

Chloride: 102 mmol/L (106 – 127)

Phosphorous: 5.01 mmol/l (0.9-1.7)

Total Protein: 49 g/l (55-75)

BUN >71.4 mmol/l (3-10)

Creat: 1229 umol/l (70-130)

ALT: 18 IU/L (10 – 120)

ALP: 15 IU/L (0 – 140)

Glucose: 6mmol/l (4-6)

Basic Complete Blood Count results:

WBC: 11.1 x10_9 /l (6-17x10_9)

HCT: 54% (37 – 55)

PLT: 314 x10_9 /l (200-500x10_9)

Urinalysis:

SpGr: 1.013

Protein: 500 mg/dL

pH: 6.0

Gluc: neg

Ketones: neg

Bili: neg

Blood: 2+

Sediment: Shows granular casts.

Abdominal radiographs show no abnormalities.

2. Generate the problem list for this dog.

Vomiting	Hypoproteinemia
Abdominal pain	Isosthenuria
Hyponatremia	Possible proteinuria
Hypochloremia	Hematuria
Hyperphosphatemia	Urinary casts
Azotemia	Renal failure

3. This dog has evidence of acute kidney injury.

a.) Is this more likely acute or chronic?

Acute renal failure (Acute kidney injury)

b.) Explain your rationale for this diagnosis using at least one piece of information from the history, physical exam, and each diagnostic procedure listed above.

History: Acute history (no previous problems noted)

Physical examination: Good body condition, dorsal abdomen painful (anatomical area of kidneys)

Radiographs: Normal bone density and renal size/shape

Biochemistry: [PO4] well in excess of [creatinine]; [K+] high-normal

CBC: Normal haematocrit

Urinalysis: Proteinuria; 2+ blood; granular cast evident in sediment

4. Please list at least 5 broad categories of possible predisposing causes for this dog's renal failure. Please list at least three examples under each category.

- Infectious (Pyelonephritis, leptospirosis, lyme disease (acute nephritis)
- Obstructive (Neoplastic, calculus (radiolucent), foreign body)
- Toxic (Ethylene glycol, NSAID, grape / raisin, cholecalciferol (rodenticide)…also: many therapeutic agents, including but not limited to: aminoglycosides, cephalosporins, tetracycline – as dog was normal prior, would have to be accidental ingestion / administration
- Ineffective circulating volume (decreased cardiac output, as from occult DCM, cardiac tamponade, or CHF; prior episode of occult hypovolemia secondary to the recent vomiting), recent hyperthermia or hypothermia, renal vessel thrombosis (possible undiagnosed pro-thrombotic endocrinopathy, for example), stenosis; hypertension
- Neoplasia (Lymphoma, renal adenocarcinoma, haemangiosarcoma …others

5. What diagnostic tests could be performed to help determine the etiology of acute renal failure in the dog? Prioritize these tests into first tier (would recommend on all patients with renal failure), second tier (will recommend on many cases based on results of first tier, geographic location, or other indications), and third tier (will only recommend if indicated based on results of other tests) (these may vary depending on geographic location, particularly for infectious diseases.

First tier: Abdominal imaging (radiographs and ultrasound) – for renal size, shape, masses, pyelectasia, hydronephrosis or –ureter, obvious obstructive structures, etc.

Urine culture (aerobic) and sensitivity

Arterial blood pressure measurement

b. Second tier

For Leptospirosis: titers, PCR, darkfield microscopy of urine, culture, other

Titers to Borrelia (regional)

Ethylene glycol test and/or calculation of osmolar gap, urine fluorescence

Thoracic radiographs (and pericardial scan for fluid)

c. Third tier

Renal aspirates/biopsy

Contrast radiography

Computed tomography

TEG, d-dimers, FDPs/FSPs – to evaluate for evidence of hypercoagulable state

6. Design a specific preliminary treatment plan (fluid therapy and other treatments, e.g. control of uraemia, treatment of uremic consequences, etc.) for this patient. What are some concerns in this patient regarding fluid therapy? Design a preliminary monitoring plan while pending diagnostic test results. Explain your rationale for each.

a. Treatment:

i. Fluid therapy:

Fluid deficit: % dehydration x body weight (kg) = deficit (L). An isotonic replacement crystalloid fluid (LRS, Normosol-R, etc.) should be administered over 4-24 hours.

5% (0.05) x 42kg = 2.1L deficit over 4-24 hours.

Maintenance needs: A maintenance fluid rate should be calculated based on the patient's weight using an accepted calculation. (30 x BWkg + 70, 70(BWkg)0.75, etc.). A maintenance fluid (containing less sodium than a replacement solution) should be chosen for this part of the fluid requirement calculation (0.45%NaCl/2.5% Dextrose, Plasmalyte-56, Normosol-M, etc.). This fluid will be run concurrently with the deficit replacement.

30 x 42kg + 70 = 1330 ml/24 hours

70(42kg) 0.75 = 1154 ml/24 hours

Abnormal ongoing losses: As the patient loses more fluid due to vomiting/diarrhea, polyuria, etc. that fluid will need to be added to the maintenance calculation. That volume is measured every 4, 6, 12 or 24 hours and the fluid rate is increased accordingly. Abnormal ongoing losses are typically replaced using a replacement fluid. No values or frequencies are available for this case. It is appropriate to either estimate these losses and add them in now, or to measure them over the next 24 hours and add them to the fluid plan after more careful quantification/assessment.

Concerns for fluid therapy:

1. It cannot be determined at this point if the patient is polyuric, oliguric or anuric. Aggressive fluid administration and overhydration should be avoided.

2. If the patient is assumed to be oliguic or anuric then maintenance fluid would not be given. The resident may instead calculate and replenish insensible losses (20-25ml/kg/day) which is typically administered as 5% dextrose.

3. Although this is an initial fluid plan, it is expected to be updated as more information is gained about the patient (CVP, urine output, abnormal ongoing losses, etc.)

ii. Medications:

Broad-spectrum antibiotics:

Not sufficient information in this case to justify the use of antibiotics (inactive sediment, normal WBC with no bands or toxicity, blood work not suggestive of sepsis or leptospirosis)

Some mentors/residents may feel that broad spectrum antibiotics are indicated while pending C/S results. Resident should justify their answer.

Anti-emetics

Uremic toxins directly affect the chemoreceptor trigger zone causing nausea. Acceptable anti-emetics include:

Metoclopramide (Reglan) 0.2-0.4mg/kg IV TID-QID or as a CRI of 1-2mg/kg/day.

Dolasetron (Anzemet) 0.3-3mg/kg IV SID

Ondansetron (Zofran) 0.1-0.3mg/kg IV BID-TID

Chlorpromazine 0.2-0.5mg/kg SQ/IM TID-QID

Maropitant (Cerenia) 1.0mg/kg SQ SID

Gastroprotectant medications

GI ulceration can be due to uremic vasculitis, or decreased renal clearance of gastrin. Acceptable gastroprotectant medications include:

Famotidine (Pepcid) 0.5-1.0mg/kg IV SID

Ranitidine (Zantac) 1-2mg/kg IV BID-TID

Cimetidine (Tagamet) 4-10mg/kg IV/IM TID-QID

(H2-blockers are in part renally excreted so lower doses may be used.)

Omeprazol (Prilosec) 0.5-1mg/kg PO SID (Oral medication may be ineffective if vomiting continues.)

Pantoprazol (Protonix) 0.7-1.0mg/kg IV SID

Sucralfate (Carafate) 1gram PO TID-QID (Oral medication may be ineffective if vomiting continues. Sucralfate treats existing gastric ulcers. Its efficacy in ulcer prophylaxis is questionable.)

Phosphate binders

Phosphate binders combine with soluble dietary phosphate and digestive secretions that form insoluble complexes. The complexes cannot be absorbed from the gut. Phosphate binders must be given with food to reduce phosphate absorption and decrease serum phosphate. If the patient is eating then a phosphate binder may be given concurrently or via a feeding tube if the patient is receiving enteral tube feedings.

Aluminum hydroxide 30-90mg/kg/day

Resident should discuss alterations in drug dosages and frequency due to decreased renal elimination.

vi. Other therapies

Nutritional support

Enteral or parenteral nutritional support should be considered in patients who have not been eating for 2-3 days. Since this patient is actively vomiting, enteral feeding may worsen the nausea. TPN or PPN may be chosen for nutritional support until the nausea is better controlled. If vomiting abates, then a

nasoesophageal or nasogastric tube could be considered. An esophagostomy or PEG tube could also be considered, but both would require general anesthesia.

b. Monitoring:

Monitor Urine Output

Place urinary catheter with closed collection system or other means of monitoring urine output. It is not yet known if this patient is polyuric, oliguric or anuric. Her fluid therapy and prognosis will greatly depend on her ability to produce urine. Although other techniques of measuring urine output are possible (collection of voided urine, weighing of solid bedding) none is accurate or efficient enough to replace urinary catheterization.

Urine output should be quantified every 4-6 hours to make sure urine production is adequate for the patient and for the amount of fluid being given.

Arterial blood pressure

Hyper- or hypotension can be seen with ARF. BP should be measured every 6-8 hours initially until a trend is determined.

Central venous pressure

A central jugular catheter should be placed to measure central venous pressure. This will help to determine if the patient's intravascular volume is appropriately expanded and may help to avoid fluid overload since large jumps in the CVP or values greater than 10cmH2O are considered abnormal. CVP should be measured every 6-8 hours.

Body weight

Body weight should be measured every 12-24 hours. This is an indirect way of assessing a patient's fluid status. Increases in weight are usually associated with increases in extracellular water. This can be a physiologically appropriate response as a patient gets better hydrated, but if patients get overhydrated they will begin to develop third space accumulations of fluid resulting in interstitial edema, ascites, and pleural fluid. Weight decreases can suggest that the patient is in a catabolic state and losing muscle mass or that they are losing extracellular/interstitial water and becoming dehydrated.

Electrolytes/venous blood gas

Electrolytes/venous blood gas should be measured 1-2 times a day. In some anuric/oliguric patients, or those with severe sodium abnormalities, electrolytes/venous blood gas may be measured every 4-6 hour during the initial hospitalization period. Changes of potassium, sodium, acid/base and azotemia can happen quickly due to the patient's disease progression or due to your therapy.

Renal panel every 24-hours

7. You place a urinary catheter to measure her urine output.

a. What conditions must be met prior to making a diagnosis of pathologic oliguria or anuria in this patient?

- UOP <0.5ml/kg/hr with isosthenuric urine
- Her MAP must be > 70mmHg. (This rules out the pre-renal cause of hypoperfusion/hypotension.)
- She must be volume resuscitated and hydrated. (This rules out the pre-renal cause of dehydration.)
- Urine collection system needs to be flowing appropriately with no kinks/obstructions. (Post-renal obstruction is effectively ruled out if urine is flowing appropriately into the collection bag.)

b. What is normal urine output? 1-2m/kg/hr

c. What is the definition of oliguria? <0.5ml/kg/hr (<0.27ml/kg/hour is sometimes quoted)

d. What is the definition of anuria? No or negligible urine output (<0.08ml/kg/hr is sometimes quoted).

e. What is the definition of polyuria? >2.0ml/kg/hr

8. Below is a list of medications that can be used in acute renal failure to potentially increase urine output. List the different mechanisms of action (MOA) for each medication and the possible adverse effects (AE) that it may cause.

a. Diltiazem

MOA: Reversal of renal vasoconstriction by pre-glomerular vasodilation resulting in afferent arteriolar vasodilation. Natriuresis, inhibition of tubuloglomerular feedback induced pre-glomerular vasoconstriction and possible cytoprotective effect by preventing cytosolic and mitochondrial calcium accumulation with calcium dependent enzyme inhibition that reduces reactive oxygen species

Adverse effects:

1. Hypotension

2. Arrhythmias

3. Decreased cardiac contractility

b. Lasix (Furosemide)

MOA: Impairment of Na/Cl resorption in the thick ascending loop of Henle. Increased tubular ultrafiltrate flow may reduce tubular obstruction by debris and vasodilation via impairment of tubuloglomerular feedback.

Adverse effects:

1. Ototoxicity

2. Hypokalemia

3. Dehydration

c. Mannitol

MOA: Osmotic diuretic. Increase in ultrafiltrate volume may reduce tubular obstruction with debris and decrease tubular cellular edema. Free radical scavenging. May improve renal blood flow by causing renal arteriolar vasodilation and decreased blood viscosity.

Adverse effects:

1. Volume overload
2. Electrolyte disturbances (hypernatremia predominantly)
3. Possible worsening of intracranial hemorrhage and increase of ICP if head trauma is present
4. Hyperosmolality

d. Dopamine

MOA: Stimulation of dopaminergic receptors resulting in renal vasodilation and improving renal blood flow. Stimulation of natriuresis. (Overall not longer recommended in human medicine for AKI)

Adverse effects:

1. hypotension
2. hypertension
3. tachycardia
4. arrhythmias
5. potential increased renal oxygen demands

e. Fenoldopam

MOA: Stimulation of the DA-1 receptor which results in renal arteriolar vasodilation and improve renal blood flow. Stimulation of natriuresis

Adverse effects

1. hypotension

Some interesting papers (summary; renal/urinary tract):

Thoen & Kerl. JVECC 2011: VAKI staging system
164 dogs
Staging system based on increase in creatinine concentration from baseline:
Stage 0: <150%
Stage 1: 150-199% or >/= 0.3 mg/dL (26.5 umol/L)
Stage 2: 200-299%
Stage 3: >/= 300%
Mortality rate greater S1-3 than S0 (54% vs 16%)
Length of hospital stay, GA, number of diagnoses, mean SPI scores – not significant
Only 4/19 (21%) S1 dogs had creat > reference, therefore small increases are important even if overall creat is within ref level

Worwag & Langston, JAVMA 2008: Acute intrinsic renal failure in cats
Definition of ARF: acute signs < 7 d, creat > 2.5, BUN > 35, USG < 1.025 or anuria, or incr creat despite tx and without CKD. Excl neoplasia, renal calculi
18/32 = nephrotoxins, 4 = ischemia, 10 = other causes
18 were oliguric
Per mEq/L increase in K+ => 57% decrease survival
Negative prognostic indicators at diagnosis: decr alb, decr bicarb
BUN, creat, other variables NOT prognostic
17 (53%) cats survived: 8 had resolved azotemia, 9 had persistent azotemia

Wohl et al. JVECC 2007: Low dose dopamine in anesthetized cats
Healthy experimental cats
Dopamine at 3 mcg/kg/hr
No significant difference in UOP, sodium excretion, HR, creatinine clearance
Transient decrease in MAP

Eubig, JVIM 2005: Grape and raisin toxicosis
43 dogs, 53% survived (of which 15/23 had complete resolution)
Azotemia, hypercalcemia, hyperphosphatemia
Dogs with histopath showed acute proximal tubular necrosis

Wakeling et al. AJVR 2009: Urinary iodide in hyperthyroid cats
Euthyroid vs hyperthyroid cats
Log[urinary iodide] was lower in cats with azotemia and untreated hyperT4
Does iodine deficiency increase chances of hyperT4?

Brunker et al. AJVR 2009: Urine NAG (N-acetyl –beta-D-glucosaminidase) and
GGT (gamma-glutamyl-transpeptidase) normal ref ranges
These are urinary enzymes in brush border of PCT or renal tubular lysosomes
Urine NAG and GGT increases might be an early biomarker for renal tubular damage dogs
NAG reference range: 0.02-3.65 U/g (M) and 0.02-2.31 U/g (F)

GGT reference range: 1.93-28.57 U/g (affected by urine pH)

Zatelli et al. AJVR 2010: Evaluation of dipstick for proteinuria in dogs
To see whether dipstick + USG could be used instead of UPC
Sensitivity >90% when 0 g/L = negative
Specificity ranged 40-60% (higher with higher USG)
A negative (0) dipstick means dogs are non proteinuric (USG doesn't matter)
Sensitivity decreased but specificity increased at higher dipstick grades
Dipstick 1+ (30 mg/dL) and USG < 1.012 (need UPC
Dipstick 1+ and USG >1.012 (non proteinuric

Raila et al. AJVR 2010: Influence of kidney function on urinary excretion of albumin and retinol binding protein in kidney disease.
UPC, UAlbC, URBPC did not correlate with plasma creatinine clearance in dogs with creatinine values within the normal range (not useful for early detection)
Increased UAlb and URBP were associated with increased UP surprise surprise
Free circulating RBP in plasma is filtered at glomerulus, reabsorbed in PCT and catabolized. There shouldn't only be trace amounts in normal urine.

Jepson et al. AJVR 2010: NAG in old cats with and without azotemia
NAG can be measured with a nonautomated colorimetric technique
But there were high interassay coefficients of variance so must interpret cautiously
NAG index in cats with CKD may indicate lysosomal activity rather than active PCT damage

Jepson et al. AJVR 2010: Urinary cauxin
Cauxin is an enzyme from the proximal straight tubule in cats – full function unknown
High urinary cauxin:creatinine was predictive of development of azotemia
But unlikely that it will provide additional info to UPC as a biomarker

Sharkey et al. JAVMA 2009: Serum cardiac troponin I in dogs with renal failure
Dogs with renal failure had higher cTNI levels than healthy dogs
They also had higher median SBP (although it didn't correlate with cTNI levels)
Cause needs further investigation – maybe subclinical cardiovascular disease?

Lyon et al. JAVMA 2009: Comparison of different methods to detect urinary albumin dogs and cats
Dipstick, sulfosalicylic acid, UPC (compared with species specific ELISA)
Dipstick and SSA: moderate specificity (70-80%), poor positive predictive value (30-40%)
Specificity improved to about 99, and PPV to about 90% at stronger positive results
Cats were even worse: specificity 11-25% with 50% PPV, increasing to 80-90% specificity with 65% PPV at stronger positive results
UPC was very specific (99%) but low sensitivity 28% dogs 2% cats!
Care when interpreting a positive result

Beatrice et al. JAVMA 2010: Comparison of UPC in free catch and cysto samples
Paired urine samples were assessed
Correlation was strong between the two methods (93% of dogs were given same IRIS substage)
Free catch samples are reliable for UPCs.

Vaden et al. JVECC 2010: Albuminuria in the ICU
105 dogs, 22 cats, prospective study
Urine collected at admission and if poss at 48 hrs for albuminuric animals
Albuminuria in 63/105 (60%) dogs and 14/22 (64%) cats
26 dogs had repeat samples: 20/26 (77%) had decreased, and 5 (19%) were undetectable
6 cats had repeat samples: 67% had decreased, and 1 (19%) was undetetctable
11/12 (92%) dogs and 3/4 (75%) cats that died within 3 d had abnormal albumin
56% dogs, 61% cats who survived > 3 d had abnormal albumin
Dogs with albuminuria were at increased risk of death
Prevalence of albuminuria is higher than reported previously (25% in one non ICU study)
Albuminuria may be transient in some patients
May be a negative prognostic indicator
Microalbuminuria = 1-30 mg/dL, >30 = overt albuminuria (this study included both)
Urine was tested with a point of care test and then quantified using ELISA (sometimes couldn't do the point of care test)

Jepson et al. JVIM 2009: Predictors of development of azotemia in cats
Nonazotemic geriatric cats were evaluated q 6 months
80% reached study endpoint by 6 months, of which 30% developed azotemia
Univariable analysis: age, SBP, creatinine, USG, UPC, UAlbC, NAG index: all significantly associated with development of azotemia
Multivariable analysis: Only creatinine with UPC or UAlbC was significant (although can't infer causation).

Maddens et al. JVIM 2010: E Coli induces transient glomerular and tubular dysfunction in pyometra
They looked at urinary biomarkers in dogs with E coli pyo versus healthy dogs, and repeat check at 6 months post spay, to help localize lesion
Urinary: IgG, CRP, Alb, and thromboxane B2 = glomerular level
Urinary: RBP, NAG = tubular level
E Coli antigens are thought to cause an immune complex mediated glomerulonephritis – BUT these have not been shown experimentally, and some histopath report suggest tubulointerstitial nephritis
They were all significantly elevated (i.e. damage at both sites) and all dropped post sx and were not different from healthy dogs

Steinbach et al. JVIM 2010: Urea generation and elimination in healthy and CKD dogs
9 dogs with CKD (IRIS 2-4) and 5 healthy dogs
Measured endogenous renal urea and creatinine clearance first: urea = 2.2 healthy, 0.4 CKD dogs
Then gave IV creatinine and urea, and measured plasma clearance
Extrarenal clearance = the difference between plasma and renal clearance
Extrarenal clearance was much higher in CKD dogs with GFR < 1 ml/kg/min (0.28 vs 0.21) and accounted for 85% of clearance
Extrarenal clearance = excretion and subsequent degradation in GI tract (fecal excretion is minimal)

Cameron et al. JVIM 2010: Effect of illness on urinary catecholamines and their metabolites in dogs
Proposed as a tool for diagnosing phaeochromocytomas, but prevalence in ill dogs was unknown – and about 50% of phaeo dogs have concurrent disease.
Urinary epi, norepi, metanephrine, normetanephrine:creatinine ratio: higher in critically ill dogs than healthy matched controls

Therefore it might be difficult to interpret this if used as phaeo screening test

Smets et al. JVIM 2010: Urinary biomarkers in healthy young and old dogs and dogs with CKD
10 dogs with CKD, 10 healthy young, 10 healthy old – all with normal PE, CBC, biochem, UA
No significant difference in anything between young and old healthy dogs
uAlb:c, uRBP:c, uNAG:c higher in CKD dogs than healthies
No significant difference uCRP (no healthy dogs, only 3 CKD dogs)

Maddens et al. JVIM 2011: AKI with pyometra – proteinuria, histopath, biomarkers
47 dogs with pyo, 10 healthy dogs
Dogs with pyometra had higher UPC than healthies (median 0.48 vs 0.08)
22/47 had UPC > 0.5, 12 > 1.0, 7 > 2.0
10 dogs who had dipstick protein 2-3+ also had kidney biopsies
Global, focal or segmental glomerulosclerosis, and tubulointerstitial nephritis
Dogs with structural changes mostly had biomarker:creat > 75th percentile
Thus dogs with UPC > 1.0 or high ratios biomarkers likely have clinically relevant lesions and should be monitored after spay

Tenhundfeld et al. JAVMA 2010: Benazepril and heparin for CKD
Dogs were randomized to benazepril 0.5 mg/kg/d, vs benazepril + heparin 150 U/kg SQ for 6 d, vs placebo
Dogs in both treatment groups did better than placebo – but there was no difference between treatment groups, ie no benefit to adding heparin

White et al. JAVMA 2010: CKD and FIV status in cats
73 cats with CKD, 69 without – categorized as < or > 11 yrs, breed, sex, vet hosp of origin taken into account.
Cats < 11 yrs old with FIV were more likely to have CKD – but who knows which came first and whether FIV affects progression etc of CKD.

Cortadellas et al. JVIM 2010: Ca and P homeostasis in dogs with different severities of naturally occurring CKD
54 dogs with CKD (used IRIS staging), 22 healthy dogs
Hyperparathyroidism in 76% of dogs with CKD, worsening with stage (36% stage 1, 100% stage 4)
Hyperphosphatemia in 68% dogs (stage 1 18%, stage 4 100%)
ROC showed that serum phos 4.5-5.5 mg/dL correctly identified presence of hyperparathyroidism in most dogs
Progressive decrease in calcitriol conc (significant by stage 3)
Hyperphos and hyperparathyroidism are frequent in dogs with CKD and occur at early stages as well – should be monitored.

Keegan and Webb, JVIM 2010: Oxidative stress and neutrophil function in cats with chronic renal failure
Measured reduced to oxidized glutathione ratio (GSH: GSSG), superoxide dismutase activity (SOD), neutrophil phagocytosis and oxidative burst
Oxidative stress is higher in cats with CRF (higher GSH:GSSG, lower antioxidant capacity, higher neutrophil burst after E coli phagocytosis.
SOD was same in CRF and control cats.

Parker and Freeman, JVIM 2011: BCS and survival in dogs with CKD
100 dogs with IRIS 2,3,4
13 (18%) underweight, 49 (68%) moderate, 10 (14%) overweight
Where 2 body weights recorded: 21/77 gained weight, 47/77 lost weight, 9 no change
No difference in survival between moderate and overweight dogs
Underweight dogs had significantly shorter survival time: median 25 d vs 190 (moderate), 365 (overweight)

Quimby et al. JVIM 2011: PK of mirtazapine in CKD cats
2 cats each from Iris 2,3,4
CKD may delay the clearance/bioavailability of mirtazapine
Single low dose (1.88 mg) had a ½ life compatible with 48 hour dosing.

Lemberger et al. JVIM 2011: comparison of urinary protein profiles: healthy, cystitis, bacterial infection, urolithiasis
Urine fibronectin content with greater for cats with idiopathic cystitis compared with controls (but not for infection/stones)
Bladder biopsies from obstructed idiopathic cystitis cats showed showed destruction of lining of bladder and severe fibrosis with few immunofluorescence signals for fibronectin (contrast controls)
Increased permeability of damaged urothelium may cause detachment and leakage of fibronectin into urine.
Fibronectin is a glycoprotein found in BM and ECM and soluble plasma form all tissues of body. Important in cell adhesion, migration, growth, differentiation. Involved in wound healing, clot formation.

Wu et al. JVIM 2011: Urodynamic evaluation of female cats with idiopathic cystitis
Cystometrograms and UPPs
None had evidence of overactive bladder
Cats with idiopathic cystitis had significantly higher:
Maximal urethral pressure at all portions of urethra
Maximal Urethral Closure Pressure (160 vs 90 cmH2O)
Threshold pressure was lower with IC but not significantly (90 vs 76 cmH2O)
Total volume infused significantly lower with IC: 4.8 vs 8.1 ml/kg
Therefore alpha adrenoceptor antagonists or skeletal muscle relaxants may be useful in cats with IC

Larson et al. JVIM 2011: Calicivirus association with idiopathic cystitis
Cats with cystitis: Viruria in 4 (6%) (3/4 had no detectable oral carriage), and oral FCV in 7 (10%).
Cats with URI: 3(12%) cats had viruria
Median Ab titres higher in cystitis (obstructive 1:256, and non obstructive 1:128) and URI (1:512) than healthy controls.
Serology suggests greater exposure to FCV.
Viruria was detected but who knows what it means.

Buffington: JVIM 2011: Idiopathic cystitis beyond the lower urinary tract
Comorbid disorders are common in both humans and cats with IC
2 forms: Type I (nonulcerative), Type II (ulcerative) – cats and humans almost always type I form (type I more likely neuropathic, type II inflammatory dz specific to bladder)

Local external abnormalities under investigation: abnormal Tamm Horsfall protein (loss of protection of urothelium), 'anti-proliferative factor', local growth factor abnormalities
Infectious causes under investigation: viruses (unclear what role), bacterial UTI prevalence of 15-43% in cats with compromised urinary tract defence mechanisms
Intrinsic abnormalities:

Landerville JVECC 2004: case report of a cat treated with CRRT for ARF of presumed toxic etiology. Continuous venovenous hemodiafiltration was performed, complications included hypothermia, and hypocalcemia episode due to citrate anticoagulation. Cat was doing well at 6 months.

Diehl et al. JVECC 2008: CRRT for 33 dogs/cats with acute or acute on chronic renal failure
Median duration 16 or 11 hrs (dogs/cats)
BUN and creat improved and metabolic acidosis and hyperkalemia resolved in most animals
Complications: iatrogenic hypokalemia, metabolic alkalosis, clinical or total hypocalcemia, filter clotting, anemia, hypothermia, neurological complications.
About 40% survived to discharge.

Martin and Acierno: JVIM 2010: CRRT for AKI/electrolyte disturbances with tumor lysis syndrome – case report
Tumor lysis syndrome: P, K, nucleic acids released into circulation
Diagnosed in patients with high tumour burden and after chemo 2 or more of:
High K, P, hyperuricemia, hypocalcemia
Also common: metabolic acidosis, azotemia
Clinical: lethargy, vomiting, hemorrhagic diarrhea, shock
Patient did well and died 1 year later

Beckel et al. JVECC 2005: Peritoneal dialysis for 5 lepto dogs
Dogs treated with IVFT and ampicillin
Median age 5 yrs
Median duration of PD was 4 days
They improved but BUN/creat not normal
Complications: 60% hypokalemia, 40% hypoalbuminemia. One each of: hypomag, pelvic limb edema, CNS signs, dialysate retention, leakage from catheter site
No peritonitis
80% survived to discharge.

Cooper and Labato JVIM 2011: Peritoneal dialysis in 22 cats
22 cats with AKI (excluded if post renal causes)
Median survival for all cats was 4 days, for cats that were discharged = 774 days
Most common complications: dialysate retention, sequestration of dialysate SQ
Indications: acute on chronic, toxins, bilateral ureteral stones or ligation, unknown causes.
Significant decrease in BUN, creat, K, phos, albumin, TP
Females did better than males (but 3 were bilat ureteral ligation and had surgical correction as well)
1 cat got peritonitis – longest time (10d) and most cycles. Bacteria was Klebsiella (same as previous study)

Simmons et al. JVIM 2006: Diuretic effects of fenoldopam in healthy cats
Fenoldopam at 0.5 mcg/kg/min induces diuresis in a delayed manner
Likely due in part to dopamine receptor mediated natriuresis

May also induce changes in GFR

Adin et al. JVIM 2003: Bolus furosemide versus CRI
More diuresis, natriuresis, calciuresis but less kaliuresis as CRI versus boluses

Nolan et al AJVR 2009: GFR by plasma clearance of gadolinium diethylenetriamine pentaacetic acid (measured by ELISA)
13/14 dogs had plasma clearance within 12% of that measured by iohexol
Remaining dog had GFR 45% higher than that with iohexol
Plasma clearance techniques are quicker and easier than urine clearance (inulin) because don't need U cath, inulin hard to get hold of, plasma must be frozen etc. The only plasma clearance method so far is iohexol – but only one lab measures it.
Good agreement so this would be OK to use

Heiene et al. AJVR 2009: GFR by iohexol in cats
There was a mean 13% difference between methods but agreement analysis was OK
2 blood samples (2 and 3 hrs after iohexol, 3 and 5 after creatinine because it takes longer to clear) versus 4 samples needed – 4 sample method more accurate, but 2 sample method acceptable
There was a small but significant negative linear relationship between body weight on estimated GFR
Estimates of GFR need a correction formula – there is a human and dog one but no cat specific formula
Ref ranges were:
Iohexol: 2.26 ml/kg/min (1.02-3.50)
Creatinine: 2.55 (1.27-3.83)

Goodman et al. AJVR 2009: Effect of metacam on GFR measured by iohexol clearance
Short term meloxicam at therapeutic doses in 6 healthy cats
No significant difference between GFR measurement at baseline and on final day of treatment

Boscan et al. AJVR 2010: Fluid balance, UOP and GFR in dogs anesthetized for ortho sx
Dogs anesthetized for TPLO and on 10 ml/kg/hr ringers – 6 dogs on carprofen, 5 dogs got lithium to measure CO
Lower UOP (0.46 ml/kg/hr) and GFR (1.84 ml/kg/hr) than normal dogs
Fluid retention of 1-2 L/30 kg dog in 4 hours – incr BW, body water volume, ECF
PCV/TP, body temp decreased linearly
No difference if carprofen or lithium
Evaluation of UOP in anesthetized dogs may not be adequate indicator of fluid balance

Heiene et al. AJVR 2010: Inulin and iohexol clearance in dogs using limited sample methods
Took 9 plasma samples between 5 mins and 6 hrs in each dog
Mean clearance of inulin 2.72 ml/kg/min and iohexol 2.48 ml/kg/min i.e. close but not same
Limited sample methods gave similar results
Iohexol gave more accurate results than inulin with limited sample methods
Accuracy of limited sample methods is acceptable for many situations

Finch et al. AJVR 2011: Correction formula for GFR estimation using slope intercept technique in cats
Slope intercept technique = clearance calculated by limited sample collection during elimination phase

Need a formula that corrects for distribution potential if using this method
There are human and dog formulas – this study worked out a cat specific formula
They derived a formula that worked with limited samples to predict multisample clearance
Results with this formula agreed with the canine formula but not the human one

Chang et al. AJVR 2011: Effect of induction agents on GFR measured by dynamic CT
Thiopental, propofol, etomidate
Used dynamic CT to measure GFR
GFR was around 2 ml/kg/min in all groups – no significant difference between induction agents

Winter et al. AJVR 2011: Effect of sedation on GFR in cats measured by scintigraphy
Only 5 cats – type II error likelihood high
Medetomidine 11 mc/kg and torb 0.22 mg/kg IM
Ketamine 10 mg/kg, midazolam 0.5 mg/kg IV
Ketamine 10, midazolam 0.5 and Ace 0.05 mg/kg IM
Control without sedation
No significant differences – no sedation protocol seemed to impact GFR
Greatest mean GFR for Dom/Torb and Ket/Midaz
No significant interobserver error apparent for this study

Sullivan et al. JAVMA 2010: Open vs closed collection systems and infection
51 dogs, open (used, sterile IV bags) vs closed collection systems
Incidence of infection in open systems was 11% compared with 8% in closed
No significant difference
Median duration of catheterization same for both groups

Childress et al. JAVMA 2011: Biopsy via transurethral cystoscopy vs cystotomy to diagnose TCC in dogs
Cystoscopy gave diagnostic quality samples (if used as first method) in 65% male dogs and 96% female
Significantly better in females

Rader and Johnson JVECC 2010: Normal intra-abdominal pressure with urinary bladder catheterization in healthy cats
20 cats sedated with Torb, midaz, propofol
5 Fr red rubber – 3 readings in each position (R lat, sternal) by 2 observers. Repeat readings when awake
Instilled 0.5 ml/kg 0.9% NaCl into bladder, zeroed at symphysis pubis
IAP median 7.00 cmH2O (5.2-8.8)
No difference between observers
No difference M/F
Statistically significant increase in IAP with:
R lat (vs sternal) recumbency
Being awake
Higher BCS
Instilling higher volume saline into bladder for measurement
Struggling when awake

Vaden et al. JVIM 2005: Renal biopsy methods and complications
Complications in 13% dogs and 18% cats
87% of biopsies were of good quality
Most likely complication was hemorrhage

Lavoue et al. JVIM 2010: Progressive juvenile glomerulopathy in 16 related French mastiffs (Bordeaux)
Typical signs of progressive glomerulonephropathy
Histopath: extensive cystic glomerular atrophy, glomerular hypercellularity, capillary wall thickening with no immune complex deposition
Mean age at death 20 months
Mean survival after diagnosis 6 months
Suspect autosomal recessive

Karmi et al. JVIM 2010: Frequency of canine hyperuricosuria gene mutation in various breeds
Hyperuricosuria predisposes to urate uroliths
3,500 dogs from 127 breeds – DNA screening test
American Staffie, American Shepherd, GSD, Giant Schnauzer, Parson JRT, Lab, Munsterlander, Boerboel, Weimeraner
Previously known in Dalmations (all of them), Bulldog, Black Russian Terriers
Autosomal recessive condition
When mutant allele frequencies are measured they can be 0 to 1
These frequencies ranged from 0.001-0.15
Breeders might want to use the test, vs vets to diagnose cause of urate uroliths

Klosterman et al. JVIM 2011: Comparison of findings/prognosis etc in dogs with glomerular disease with and without nephrotic syndrome
Nephrotic syndrome defined as decr alb, incr chol, proteinuria, extravascular fluid accumulation
Median survival shorter with nephrotic syndrome (12.5 vs 104 days) although if subgrouped based on creat < > 1.5 then was only significant for non azotemic dogs (51 vs 605 d) i.e. decr survival with azotemia regardless of NS or not
Both groups equally likely to be azotemic at time of diagnosis
Dogs with NS had:
Lower Ca, alb
Higher Chol, Phosphate, creatinine
Humans with NS have hypernatremia, hypertension, association with specific histopath diagnoses – this was not the case in dogs in this study

Wells et al. JAVMA 2009: Case report dog with rhabdomyolysis and myocardial/resp failure
Rhabdomyolysis = acute muscle necrosis with swollen muscles (pain, collapse), elevated CK, myoglobinuria
Results from injury leading to uncontrolled increase in free intracellular Ca and activation of Ca dependent proteases leading to myonecrosis
This was first report with myocardial muscle involvement

Porzio et al. olden JVECC case report – exertional rhabdomyolysis in a husky.

Shearer et al. JVIM 2009: Distal RTA and IMHA in 3 dogs
Distal RTA is frequently associated with immune mediated disorders in humans
Hyperchloremic metabolic acidosis with normal anion gap and variable urine pH (depending on site of tubular dysfunction)
Proximal RTA: PT can't reabsorb bicarb, therefore get alkaline urine but over time equilibrates to steady state with appropriately acidic urine
Distal RTA: failure to secrete H+ ions into filtrate to produce new bicarb. Plasma bicarb levels typically lower than prox RTA (10 vs 15), concurrent hypokalemia (loss of K for electroneutrality in place of H)
Dogs with RTA have positive urine anion gaps
Differentiating prox and distal RTA: calculate fractional excretion of bicarb – proximal = 15-20% versus distal < 3%.
Bicarbonate test or ammonium loading challenge: if distal RTA then persistently alkaline urine
Furosemide response test to characterize type of RTA:
If cortical H+ ATPase defect then persistently alkaline urine with increase in K+ secretion
If defect in medullary collecting tubule then appropriate increase in H+ (decr urine pH) and K+ secretion
If voltage dependent distal RTA then H+ and K+ unchanged.
Clinical signs are secondary to hypokalemia, acidosis, and may also see rickets, osteomalacia, urolithiasis due to disruption of calcium homeostasis

Cook et al. JVIM 2011: Case report distal RTA secondary to zonisamide in a dog

Schmiedt et al. AJVR 2009: effects of renal autograft ischemia/reperfusion on ABP in transplant cats
In humans posttransplantation hypertension is common, and multiple etiologies
Acute hypertension post transplant is also seen and unclear etiology
This study showed that renal autotransplantation and contralateral nephrectomy did not cause hypertension in the 14 day study period
Cold ischemia of kidneys during transplantation was 30 minutes – 3 hours

Schmiedt at al. AJVR 2010: Effects of renal autograft ischemic storage and ischemia/reperfusion on intraop hemodynamics and plasma renin conc
Same set up as last paper – some kidneys cold ischemia, some warm
Supraphysiologic renin (accumulating in JG cells while there is no blood flow) is one possible explanation for postop hypertension – hypothesis was this would happen more in cold stored kidneys
No significant difference between groups (warm, cold, length of cold) in hemodynamic variables or postperfusion plasma renin concs
No difference between warm/cold ischemia kidneys in expression of vascular related genes (renin, endothelin, ACE)

Aronson et al. AJVR 2011: Effects of cyclosporine, dexamethasone, cyclo & dex, and human CTLA4-Ig (immunosuppressive drug) on feline lymphocytes in vitro in normal cats and in immunosuppressed post transplant cats
Cyclosporine and pred are used in cats but 43/169 cats developed infection in one study, 10% developed cancer, and 13-26% have episodes of acute rejection

Rejection characteristics: Mainly T helper cells producing various cytokines. Cytokines assoc with rejection are: IFN gamma, IL2, IL4, IL10, GM-CSF
Currently trying to develop strategies that reduce graft rejection without global immunosuppression – one line of research focuses on co-stimulatory signals
T cells need 2 stages of activation: Ag exposure via MHC complex, AND co-stimulatory signal.
CTLA4-Ig is a novel immunosuppressant that blocks one of the costimulatory signals, and experimentally inhibits acute rejection, prolongs survival
All tx reduced IL2, IFN gamma and GM-CSF
Cyclosporine based tx but not CTLA4-Ig reduced IL10
High basal IL2 and IL10 in transplant recipients
Cyclosporine inhibits calcineurin, preventing activation of transcription factors that regulate the expression of cytokines/genes that cause allograft rejection
Corticosteroids also inhibit these cytokines but exact mechanism not understood
CTLA4-Ig successfully inhibited pro-inflammatory cytokines but spared those critical for allograft tolerance – worth investigating further clinically.

Schmiedt et al Vet Surg 2008: Survival, prognosis etc in renal transplant cats
78% survival to discharge
Median overall survival 613 days
Post op hypertension in 30% of cats
Acute rejection in 13%
Infection (mainly bacterial) in 37% of cats
CHF in 12% of cats
Delayed graft function in 5 cats

Paster et al. Vet Surg 2009: Hypophosphatemia in cats after renal transplants
86 cats, mean age 8 yrs
Hypophosphatemia in 37%
Median onset 2 days, median duration 4 days
Treatment needed in 56% of hypophosphatemic cats
No difference between survival and hemolysis frequency
No risk factors identified

Cohen et al. AJVR 2009: Urodynamics in female cats anesthetized with low and high levels of isoflurane and propofol
6 healthy female cats with 6Fr catheter for cystometrogram and UPP
Low dose propofol regime was easiest to titrate and maintain and yielded diagnostic quality detrusor reflexes in all cats
Maximal urethral pressure in skeletal muscle part, and maximal urethral closure pressure were higher with low dose than high dose propofol

Lulich et al. JAVMA 2009: efficacy and safety of lithotripsy for fragmentation and removal of urocystoliths and urethroliths in dogs
Cystoscopy performed and laser lithotripsy used to fragment liths
Basket retrieval and voiding urohydropropulsion to remove fragments
Urolith removal was complete in 82% of dogs
Incomplete in 18 dogs: 9 had >3 mm diam, 6 had 1-3, 3 had < 1 mm diam
More successful in female dogs
Median procedure time 72 mins

Complications:
Urinary tract obstruction in 2 dogs
Hematuria 53% dogs day 0, 84% (day 1), 13% (day 3), 3% (day 11)
Leukocyturia 13% day 0, 47% day 1, 0% day 3, 3% day 11

Smith et al. JAVMA 2010: Using cystoscopy to diagnose and treat ectopic ureter in 16 dogs
Cystoscopic transection of the membrane separating unilateral or bilateral ectopic ureters from the bladder
4/16 had complete resolution just with cystoscopic transection
5/16 had resolution with transection & phenylpropanolamine
4/16 had improvement in control but incontinence persisted
3 dogs couldn't be assessed (collagen injections x 2, nephrectomy x 1)
Complications were minor and easily managed

Runge et al. JAVMA 2011: Transvesicular percutaneous cystolithotomy for retrieval of cystic and urethral calculi in dogs and cats 23 dogs 4 cats
Ventral midline approach over bladder apex, screw cannula inserted at apex for normograde rigid and flexible cystourethroscopy, uroliths removed via stone basket device and retrograde flushing/suction
Median procedure time 66 minutes
All patients discharged within 24 hours
No post op complications at time of suture removal
Might decrease need for urethrotomy, serial transurethral endoscopy, and abdominal insufflation associated with other minimally invasive procedures currently available.

Berent JAVMA 2011: use of indwelling double pigtail stents for treatment of malignant ureteral obstruction in dogs – 12 cases
12 dogs, 15 ureters – all with trigonal urothelial carcinoma
11/12 had successful percutanous antgrade placement, 1 needed laparotomy
Median survival from date of diagnosis was 285 days
Median survival from stent placement 57 days
3 complications in one patient
7 patients needed concurrent urethral stents for urethral obstruction
All animals were discharged, median LOH post stent 18 hrs
All stents evaluated later were patent

North et al. JVIM 2010: congenital ectopic ureters in Entlebucher dogs (continent and incontinent)
20 dogs – 9 had signs of urinary tract disease
Both intravesicular and extravesicular ectopic ureters, also some had hydronephrosis

Zaid et al. JVIM 2010: Feline ureteral strictures – 10 cases
Median age 12 yrs, creat 3.7 mg/dl, size of renal pelvis 12 mm
6/10 had hyperechoic periureteral tissue on ultrasound around stricture
4/10 had circumcaval ureter
6 had ureteral stenting and 2 had traditional surgery
All survived, median survival > 294 days
6 cats had persistently improved creat and renal pelvis parameters.

Cunha et al. AJVR 2010: LRS vs NaCl in experimental FUO
Saline treated group had lower pH, bicarb and BE values up to 48 hrs

Saline group had hypocalcemia (2 hr) and hypernatremia (12 hr)
No difference K+ or Cl-
LRS has an alkalinizing effect because of lactate buffer (transformed to bicarb in the liver) which causes intracellular shift of K+ ions

Cooper et al. JAVMA 2010: Managing FUO without U cath
15 cats – Ace, buprenex, medetomidine, SQ fluids, decompressive cystocentesis, dark room
Success = urination within 72 hours and subsequent discharge
"success" in 11/15 cats
Remaining 4: 3 had uroabdomen, 1 had hemoabdomen (no evidence of bladder rupture in 3 which were necropsied)
Cats which failed treatment had significantly higher creatinine
"successful" cats didn't seem to have more recurrence than normally treated cats

Lee and Drobatz JVECC 2003: electrolytes, acid base, renal parameters in FUO
12% had severe hyperkalemia (> 8.0 mmol/L)
K+ was inversely correlated with pH, bicarb, pCO2, Na, Cl, iCa
K+ was positively correlated with BUN and creat
iCa was positively correlated with pH and bicarb
In cats with severe hyperkalemia, 75% had iCa < 1 mmol/L, 79% had pH < 7.2
74% of cats with pH < 7.2 had iCa < 1 mmol/L
Most cats had mild electrolyte changes and were relatively stable
94% survived to discharge

Drobatz et al. JVECC 2005: Serum PTH and 25- OH Vit D3 in FUO
PTH was inversely correlated with ionized calcium, positively correlated with phos
No relationship between 25 OH vit D3 and any other parameters
Lack of parathyroid response doesn't seem to be the underlying mechanism for hypocalcemia in FUO

Lee and Drobatz JVECC 2006: Predicting hyperkalemia in FUO
History: First time obstruction, outdoor status, anorexia, vomiting
PE: Rectal temp < 95, HR < 120 (2 most accurate predictors), RR, pulse quality, presence of arrhythmias
When rectal temp and HR in combination: specificity for hyperK was 98-100%

Sfiligoi et al. JVECC 2006: Uterus masculinus complication in FUO
Catheter was passed but urine was coming round the edge – imaging showed bicornuate structure entering urethra dorsally

Malouin et al. JVECC 2007: Blood pressure in FUO
28 cat prospective study
None were hypotensive, 71% were normotensive, rest hypertensive
Normotensive cats had lower heart rates and lower tCa
For all cats K and tCa were inversely correlated with blood pressure

Wisener et al. AJVR 2010: Risk factors for Ca ox or struvite urolithiasis in dogs
Nearly 8000 dogs

More likely Ca Ox if:
Individual level: age (older), sex (male), breed, neuter, BCS (obese), diet (moisture and type),
Community level (less impact than individual level): Major urban centre, median community family income
Previous study small breeds predisposed to Ca ox. Cocker, GSD, G Ret have reduced chance of Ca ox.

Albasan et al. JAVMA 2009: Rate and frequency of recurrence of uroliths after initial stone in cats
Nearly 4,500 cats
Ammonium urate (221 cats): 13% had a first recurrence (22 mths), 9% had a second (43 mths)
Ca ox (2400): 7.1% had a first (25 mth) , 0.6% a second (38) , and 0.1% (48) a third
Struvite (1800): 2.7% had a first (29 mth), 0.2% a second (40 mth)
Probably underestimated actual recurrence as many likely not resubmitted

Grant et al. JAVMA 2010: Complications after urolith removal in dogs
128 dogs that had a cystotomy for urolith/urethrolith removal
Effectiveness could be determined in 34% of dogs – of which 20% had incomplete removal of uroliths
Appropriate post op imaging in only 15% of dogs – of which 8/19 had incomplete removal
Dogs with uro AND urethro were more likely to have a failed cystotomy than dogs with one or the other
Complications in 4% of dogs
Cystotomy was safe but good proportion of dogs had incomplete removal

Low et al. JAVMA 2010: Trends in urolith composition, dogs
25,500 dogs
Increase in proportion of Ca ox uroliths over time
Probably multifactorial – diet changes, water consumption changes, increased popularity of breeds predisposed
Decrease in urate, silica and cysteine uroliths – possibly due to better breeding, increased genetic study awareness
Decrease in proportion of struvite uroliths
Ca ox, silica, cysteine – more from male dogs
Struvite and urate – more from female dogsthey have been formed within the circulation, but also within the glomerulum