Iris 2009 Treatment Recommendations

All treatments for chronic kidney disease (CKD) need to be tailored to the individual patient. The following recommendations are useful starting points for the majority of animals at each stage. Serial monitoring of these patients is ideal and treatment should adapted according to the response to treatment. Note that staging of disease is undertaken **following diagnosis of CKD** – an elevated creatinine level alone is not diagnostic of CKD.

Some of the suggested treatments are not authorised for use in dogs and/or cats and recommended dose rates are therefore empirical. It is the veterinarian's duty to make a risk:benefit assessment for each patient prior to administering any treatment.

Treatment recommendations for Dogs with Chronic Kidney Disease

Stage 1 Canine patients:

- Discontinue all potentially nephrotoxic drugs.
- Identify and treat any pre-renal or post-renal abnormalities.
- Rule out any treatable conditions like pyelonephritis (any urinary tract infection (UTI) should be regarded as a potential pyelonephritis and treated appropriately) and renal urolithiasis with radiographs and/or ultrasonography.
- Measure blood pressure and urine protein to creatinine ratio (UP/C).

Management of dehydration:

These patients have decreased urine concentrating ability and therefore

1) Correct clinical dehydration/hypovolemia with isotonic, polyionic fluid solutions (e.g., lactated Ringers) IV or SC as needed.
2) Have fresh water available at all times for drinking.

Systemic hypertension:

The blood pressure needed to prevent renal disease progression is unknown. Our goal is to reduce systolic blood pressure (SBP) to < 160 mm Hg and minimize the risk of systemic end organ damage (CNS, retinal, cardiac problems/damage). If there is no evidence of systemic end organ damage but SBP persistently exceeds 160 mm Hg, treatment should be instituted.

'Persistence' of elevation should be judged on multiple blood pressure measurements made over the following timescales:

- Moderate risk, SBP 160 to 179 mm Hg - 2 months
- Severe risk , SBP ≥180 mmHg – 1-2 weeks

If evidence of end organ damage exists, animals should be treated without the need to demonstrate persistence of elevated blood pressure.

It is recognized that some breeds (eg, sight hounds) tend to have higher blood pressure (see Appendix 1).

Reducing blood pressure is a long term aim when managing the patient with CKD and a gradual and sustained reduction in blood pressure should be the goal, avoiding any sudden or severe decreases leading to hypotension.

A logical stepwise approach to managing hypertension is as follows:

1) Dietary sodium (Na) reduction - there is no evidence that lowering dietary Na will reduce blood pressure. If dietary Na reduction is attempted, it should be accomplished gradually and be used in combination with pharmacological therapy.
2) Angiotensin converting enzyme inhibitor (ACEI) therapy at standard dose rate.
3) Double the dose of ACEI (in some patients, increasing the dose may improve the antihypertensive effect).
4) Combine ACEI and Calcium channel blocker (CCB; e.g. amlodipine) treatment
5) Combine ACEI, CCB (e.g. amlodipine) and hydralazine treatment

Monitoring response to antihypertensive treatment:
Hypertensive animals normally require life-long therapy and may require treatment adjustments. Serial monitoring is essential. After stabilization, monitoring should occur at least every 3 months.
SBP <120 mm Hg and/or clinical signs such as weakness or tachycardia indicate hypotension, which is to be avoided.

Plasma creatinine -reducing blood pressure may lead to small and persistent increases in plasma creatinine concentration (<0.5 mg/dl or 50 µmol/l increase), but a marked increase suggests an adverse drug effect. Progressively increasing plasma creatinine indicates progressive kidney damage/disease.

***Proteinuria*:**
UP/C > 2.0: investigate for the disease processes leading to proteinuria (see 1 and 2 below) and treat with anti-proteinuric drugs (see 3 and 4 below).
UP/C 1.0 to 2.0: requires thorough investigation and close monitoring (see 1,2 and 5 below).
UPC 0.5 to 1.0: requires close monitoring (see 1 and 5 below)

1) Look for any concurrent associated disease process that may be treated / corrected.
2) Consider kidney biopsy as a means of identifying underlying disease (see Appendix 2/consult experts)
3) ACEI plus dietary protein reduction.
4) Low-dose acetylsalicylic acid (0.05-0.5 mg/kg/day) if serum albumin is < 2.0 g/dl.
5) Monitor response to treatment / progression of disease:
   - Stable plasma creatinine concentration and decreasing UP/C = good response.
   - Serially increasing plasma creatinine concentration and/or increasing UP/C = disease is progressing.
   Therapy should ordinarily be continued for life, but if the underlying disease has been resolved dose reduction whilst monitoring UP/C might be considered.

Note: ACEI use is contraindicated in any animal that is clinically dehydrated and/or is showing signs of hypovolaemia. Correct dehydration before using these drugs otherwise glomerular filtration rate (GFR) may drop precipitously.

The intervention points for proteinuria differ according to the stage of CKD. In a non-azotaemic animal (Stage 1/early Stage 2) the number of filtering nephrons through which protein can be lost is high. Thus borderline & low level proteinuria (UP/Cs <2.0) are investigated and monitored closely whereas at Stages 2-4 treatment is recommended at lower UP/Cs.

Stage 2 Canine patients:

All of the above listed for Stage 1 plus the following

Proteinuria:

The intervention point for treatment of proteinuria should be reduced to UP/C 0.5 in azotaemic dogs

Reduction of phosphate intake:

Evidence suggests that chronic reduction of phosphate intake to maintain a plasma phosphate concentration below 1.5 mmol/l (but not less than 0.9 mmol/l) (<4.6 mg/dl but >2.7 mg/dl) is beneficial to patients with CKD. The following measures can be introduced sequentially in an attempt to achieve this:

1) Dietary phosphorus restriction.
2) If plasma phosphate concentration remains above 1.45 mmol/l (4.5 mg/dl) after dietary restriction, give enteric phosphate binders (e.g., aluminium hydroxide, aluminium carbonate, calcium carbonate, calcium acetate) to effect, starting at 30-60 mg/kg/day divided between meals and mixed with the food. The dose required will vary according to the amount of phosphate being fed and the stage of kidney disease. Treatment with phosphate binders should be to effect (as outlined above), with signs of toxicity limiting the upper dose rate possible in a given patient. Monitor serum calcium and phosphate concentrations every 4-6 weeks until stable and then every 12 weeks. Microcytosis and/or generalized muscle weakness suggests aluminium toxicity if using an aluminium containing binder – switch to another form of phosphate binder should this occur. Hypercalcaemia should be avoided – combinations of aluminium and calcium containing phosphate binders may be necessary in some cases.

Metabolic acidosis:

If metabolic acidosis exists (blood bicarbonate or total CO_2 < 18 mmol/l) once the patient is stabilized on the diet of choice, supplement with oral sodium bicarbonate or potassium citrate to effect to maintain blood bicarbonate / totalCO_2 in the range of 18-24 mmol/l.

Stage 3 Canine patients:

All of the above listed for Stage 1 and 2 plus the following:

Reduction of phosphate intake:

The realistic post-treatment target plasma phosphate concentration is <1.6mmol/l (5.0mg/dl).
Evidence suggests that judicious use of calcitriol prolongs survival in dogs (in Stages 3 & 4) where phosphate is controlled and ionized calcium and PTH are monitored.

Additional recommendations for stage 3 patients:

1) Appropriate dietary protein reduction in order to decrease blood urea and phosphate concentrations.
2) Consider treatment for anemia if it is affecting the patient's quality of life: typically this occurs when the PCV is ≤ 0.20 l/l (20%) Human recombinant erythropoietin is the most effective treatment but it is not approved for veterinary use: darbepoetin is preferable as it is less antigenic than epopoietin alfa. Anabolic steroids are of no proven benefit and may be detrimental.
3) Treat vomiting / decreased appetite / nausea with H_2 receptor blockers (e.g., ranitidine) and antiemetics (e.g., metoclopramide).
4) Give fluids parenterally as necessary to maintain hydration.

Drugs that rely predominantly on renal function for their clearance from the body should be used with caution in patients in stage 3 and above CKD. It may be necessary to adjust the dose of these drugs (depending on their therapeutic indices) to avoid accumulation.

Stage 4 canine patients:

All of the above listed for Stage 1, 2 and 3 plus the following:

Systemic hypertension / Proteinuria:

Take care not to introduce ACEI/CCB treatment to unstable dehydrated animals where GFR may drop precipitously if ACEI/CCB are introduced before the patient is adequately hydrated.

Reduction of phosphate intake:

The realistic post-treatment target plasma phosphate concentration is < 1.9 mmol/l (6.0 mg/dl).

Additional recommendations for stage 4 patients:

1) Intensify efforts to prevent protein / calorie malnutrition. One may need to consider feeding tube intervention (e.g., percutaneous gastrostomy tube).
2) Intensify efforts to prevent dehydration. Feeding tubes can be used to administer fluids as well as food.
3) Consider dialysis and/or renal transplantation.

Iris 2009 Treatment Recommendations

Treatment recommendations for Cats with Chronic Kidney Disease

Recommendations are similar to the same Stage in dogs, with the following exceptions:

Stage 1 Feline patients:

As for Stage 1 dogs with the following exceptions:

Systemic hypertension:
A logical stepwise approach to managing hypertension is as follows:

1) Dietary sodium (Na) reduction - there is no evidence that lowering dietary Na will reduce blood pressure. If dietary Na reduction is attempted, it should be accomplished gradually and be used in combination with pharmacological therapy.
2) Calcium Channel Blocker (CCB) e.g. amlodipine
3) Increase the dose of amlodipine up to 0.5 mg/kg daily
4) Combine angiotensin converting enzyme inhibitor (ACEI) and CCB treatment

***Proteinuria*:**
UP/C > 2.0: investigate for the disease processes leading to proteinuria and treat with anti-proteinuric drugs
UP/C 1.0 to 2.0: requires thorough investigation and close monitoring
UPC 0.4 to 1.0: requires close monitoring

Stage 2 Feline patients:

As for Stage 1cats / Stage 2 dogs plus the following:

***Proteinuria*:**
The intervention point for treatment of proteinuria should be reduced to UP/C 0.4 in azotaemic cats

Reduction of phosphate intake:
Many cats in stage 2 will have normal plasma phosphate concentrations but will have increased plasma PTH concentration.

Metabolic acidosis:
Metabolic acidosis should be considered at blood bicarbonate or total CO_2 < 16 mmol/l

Additional recommendations for stage 2 patients:
If the patient is hypokalemic, then potassium gluconate should be supplemented to effect (typically 1-2 mmol/kg/day).

Stage 3 & 4 Feline patients:

As for Stage 1 and 2 cats / Stage 3 or 4 dogs plus the following:

Reduction of phosphate intake:
The beneficial effects of ultra-low dose calcitriol have not been established in cats.