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FELINE CHRONIC KIDNEY DISEASE: RECENT ADVANCES IN UNDERSTANDING

CHRONIC KIDNEY DISEASE

- Consequences of CKD that lead to progression of CKD:
 - Polyuria ⇒ dehydration
 - Nausea ⇒ vomiting / inappetence
 - Hyperphosphataemia
 - Hypertension
 - Renal Proteinuria
 - Urinary tract infections
 - Hypokalaemia
 - Anaemia



MANAGING CKD

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MANAGING CKD

- What harm might this medication do?
- How will I get it into my cat?
- How will it affect my relationship with my cat?





CKD:TREATMENT DILEMMAS

What is the role of ARBs / ACE Inhibitors?

Dietary Management: What to feed and When to start?

Bacteriuria: What is the significance? When should we use antibiotics and for how long?



WHAT IS THE ROLE OF ARBS / ACE INHIBITORS?

Proteinuric CKD

Normal feline urine has very low protein content

Use UP:C not dip-sticks

- UP:C ≤ 0.2 Normal: No treatment required
- UP:C ≥0.4, with no active sediment
 Proteinuric: Treatment is required
- UP:C 0.2-0.4, with no active sediment
 Borderline: Monitor / treat

Persistent renal proteinuria is associated with more rapidly progressive kidney disease and significantly reduced survival



<u>Syme</u> et al, JVIM 2006 20:528



TREATMENT OF PROTEINURIA

Angiotensin II

- Vasoconstrictor
 - Increases blood pressure
 - Increases glomerular pressure
 - Improved GFR in the short term
 - Contributes to glomerular hypertrophy and fibrosis in the medium to longer term
 - Increases proteinuria
- Stimulates aldosterone release
 - Promotes sodium retention and increased blood pressure
 - Hypertension promotes proteinuria

TREATMENT OF PROTEINURIA

- Angiotensin Receptor Blocker (ARB)
 - Telmisartan (Semintra; Boehringer Ingelheim)
 - Specific to ATI receptor
 - I mg/kg (0.1 ml/kg) once daily; Liquid formulation
- Angiotensin Converting Enzyme Inhibitor
 - E.g. Benazepril
 - Non-specific, blocks AT1 and AT2 receptors
 - 2.5 mg once daily

















- Moderating Angiotensin has proven effect in reducing proteinuria
 - Proteinuria associated with increased mortality, increased risk of developing azotaemia, more rapid progression of CKD
- Does reducing proteinuria increase survival time?
 - IRIS recommendation: treat for proteinuria if UP:C persistently > 0.4, with inactive sediment
 - Increased monitoring if UP:C 0.2-0.4
 - "... borderline and even "normal" levels of proteinuria in cats have been associated with progressive disease." http://www.iris-kidney.com/education/ckd_assessment_levels.html





ADVERSE EFFECTS

- Reduced intraglomerular pressure
 reduced GFR
 Humans:
 - 35% develop û urea (usually mild)
- Reduction in GFR occurs when treatment started, then is stable
 - Do not start treatment in cats with IRIS stage 4 CKD
 - Can continue use in cats that progress to IRIS stage 4 CKD
- Monitor azotaemia after starting treatment



WHAT IS THE ROLE OF ARBS / ACE INHIBITORS?

Do they slow down progression of CKD in Non-Proteinuric cats?

- Humans:
 - Used early in the course of CKD to reduce progression of tubulointerstitial injury
- Cats:
 - Benazepril BENRIC study: No difference in survival times for benazepril treatment vs placebo treatment King JN et al - BENRIC Study Group (2006) J Vet Intern Med 20: 1054–64.
 - Telmisartan? watch this space publication pending



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WHAT TO FEED?

Prescription renal / reduced protein diets:

- Reduce uraemia
 - Improves well-being, appetite, activity
 - Reduces incidence of uraemic crises
 - Indicated in IRIS stage 3-4
- Control hyperphosphataemia
- Prolong life-span
 - Median 633 days vs 264 days Elliott et al (2000) JSAP 41 235-242





PRESCRIPTION RENAL DIETS

Very useful tool for management of CKD

- \square Protein $\Rightarrow \square$ Phosphate
- ♣ Sodium
- 爺 Potassium
- ☆ Water soluble vitamins
- ☆ Omega-3 fatty acids, FOS, antioxidants, Vit D etc
- Wet Foods
 - **Fluid Intake;** Energy from fat cf CH2O





PRESCRIPTION RENAL DIETS

- IRIS: Consider introducing "renal" diets in stage 2, recommended for use in cats in Stage 3 and 4
- Monitor energy intake
 - Owner to keep eye on food intake
 - Monitor bodyweight
- Offer additional tasty / favourite food as needed
 - Any food is better than no food
- Maintain / improve muscle condition
 - Ensure adequate calorie and protein intake



PROTEIN REQUIREMENT

- How much protein should be fed to cats with CKD?
 - Unknown
 - "Senior" cats (> | | y/o) may require more protein than younger cats
 - Some cats with CKD fed "renal diets" show decline in bodyweight, BCS and/or muscle condition score, others do not
 - Effect of protein restriction?
 - Effect of inadequate caloric intake (unpalatable food, poor appetite)?
 - Effect of CKD independent of diet?
 - Substantial loss of lean body mass is associated with increased mortality



PHOSPHATE BINDERS

- Poor compliance with renal diet
- Weight loss on low protein diets
- Inadequate control of phosphate (> I.4 mmol/L)
- ~10% reduction in serum phosphate
 - Introduce gradually Mix with food Give with all meals



Give with all meals Allow 4-6 weeks to take effect



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BACTERIURIA VS URINARY TRACT INFECTIONS

UTIs are common in elderly cats:

- Can cause incontinence / inappropriate urination
- Can cause pain, debilitation, "off colour"
- Can cause haematuria
- Can be asymptomatic
- Rarely cause classic signs of cystitis
- Treatment?





URINARY TRACT INFECTIONS

Treatment?

ISCAID guidelines for the diagnosis and management of bacterial urinary tract infections in dogs and cats. Weese et al, 2019

- No clinical signs: No treatment
 - Amount of bacteria (CFU's), abnormal odour and presence of inflammatory cells in urine are NOT considered indications for treatment
- Clinical signs of LUTD: Use 3-5 days antibiotics, based on C+S, or empirical use of amoxicillin / amoxicillin-clavulanate
- Equivocal clinical signs: Use 3-5 days treatment, cease after 3 days if no change
- Suspected pyelonephritis: 10-14 days treatment