Management of Chronic Kidney Disease in Cats

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Harvey

- 14 year old M(N) DLH
- Inappetance
- Bad breath
- Polydipsia

- Poor body condition
- Dehydrated
- Irregular small firm kidneys

Diagnostics

- **Physical & ocular examination**
- **Body weight & % weight change**
- **Systemic blood pressure**
- **Blood sample**
  - Biochemistry (&T_4)
  - Haematology
- **Urine sample**
  - Urinalysis
  - UPC ratio*
  - Culture & sensitivity

*Urine protein to creatinine ratio

Harvey – Results

Systolic blood pressure:
- **170 mmHg** (<150 mmHg)

Haematology:

PCV	22%	(30-45)

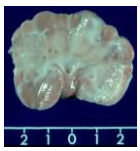
Serum biochemistry:

urea	30 mmol/l	(6.4-10.5)
creatinine	278 umol/l	(117-177)
phosphorus	2.5 mmol/l	(1.4-2.5)

Urinalysis:
- **SG** 1.012 (>1.035)
- **UPC ratio** 0.6 (<0.4)
- ***E.coli***

IRIS Classification of CKD

*Ref: 40-177 umol/l
0.45-2.0 mg/dl



↓ kidney function	Creatinine	USG	Urea, etc.	Cat ill	IRIS
Chronic kidney insufficiency:					
~ 67%	**<140 umol/l** (<1.6 mg/dl)	~ ↓	Normal	No	1
Azotaemia kidney disease:					
~ 75%	**140-249** (1.6-2.8)	↓	↑ + PO_4, ↓K^+	±	2
Uraemia kidney disease:					
~ 90%	**250-439** (2.9-5.0)	↓	↑ + PO_4	Yes	3
End-stage kidney failure:			↓K^+ + PCV		
> 95%	**>440** (>5)	↓	↑ + PO_4, ↓↑K^+ ↓PCV , ↓pH , ↓Ca	Yes	4

Syme et al JVIM 2006, 20: 528-535 King et al. JVIM 2007, 21:906-916

IRIS Guidelines

		Stage 1 No azotemia (Normal creatinine)	Stage 2 Mild azotemia (Normal or mildly elevated creatinine)	Stage 3 Moderate azotemia	Stage 4 Severe azotemia
Creatinine in mg/dL					
Stage based on stable creatinine	Canine	Less than 1.4 (125 µmol/L)	1.4–2.8 (125–250 µmol/L)	2.9–5.0 (251–440 µmol/L)	Greater than 5.0 (440 µmol/L)
	Feline	Less than 1.6 (140 µmol/L)	1.6–2.8 (140–250 µmol/L)	2.9–5.0 (251–440 µmol/L)	Greater than 5.0 (440 µmol/L)
SDMA* in µg/dL					
Stage based on stable SDMA	Canine	Less than 18	18–35	36–54	Greater than 54
	Feline	Less than 18	18–25	26–38	Greater than 38
UPC ratio					
Substage based on proteinuria	Canine	Nonproteinuric **<0.2**	Borderline proteinuric **0.2–0.5**	Proteinuric **>0.5**	
	Feline	Nonproteinuric **<0.2**	Borderline proteinuric **0.2–0.4**	Proteinuric **>0.4**	
Systolic blood pressure in mm Hg		Normotensive **<140**	Prehypertensive **140–159**		
Substage based on blood pressure		Hypertensive **160–179**	Severely hypertensive **≥180**		

Chronic kidney disease

- 10% of all cats
- 30% of cats >12 years

IRIS Guidelines

- Serum creatinine concentration
- Serum symmetric dimethylarginine (SDMA) concentration*
  - Creatinine normal but SDMA >14 ug/dl → classify as IRIS 1
  - IRIS 2 poor body condition SDMA ≥25 ug/dl → classify as IRIS 3
  - IRIS 3 poor body condition SDMA ≥38 ug/dl → classify as IRIS 4
- Serum FGF-23 & PO_4 concentration; systemic BP; UPC ratio

Prognosis – variable – all factors above

- **IRIS 2** >2 years; **IRIS 3** ~1 year; **IRIS 4** ~2 months

IRIS Guidelines - 2023 Updates

- **Breed specific RI for SDMA & Creatinine**
  - Healthy Birman cats have ↑serum creatinine **(~20%)** & SDMA v other breeds
- **Increase of SDMA for non-renal disease**
  - *e.g.* dehydration
  - Unlike in puppies, healthy kittens have the same SDMA concentrations as healthy adult cats

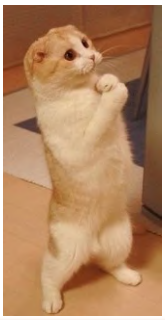
http://www.iris-kidney.com/pdf/2_IRIS_Staging_of_CKD_2023.pdf

Medical management of CKD

- **Remove underlying cause:**
  - **Treat bacterial infections with antibiotics**
  - *e.g.* Pyelonephritis, Leptospirosis?
  - **Remove nephrotoxins**
  - *e.g.* NSAIDS, lilies*, tulips, grapes
  - **Correct pre-renal problems**
  - *e.g.* dehydration or cardiac disease
  - **Correct post-renal obstruction**
- **Palliative treatment**
- **Renal dialysis**

*Most common cause of toxicity in cats

Palliative Tx of CKD



- **Renal diet**
  - **↓protein & phosphate**
  - **↑potassium**
- **Support food intake**
- **Maintain fluid intake**
- **Proteinuria - ACE-I & ARB**
- **↓hypertension**
- **Treat urinary tract infections** (UTIs)
- **Reverse anaemia**
- **Correct acidosis***
- **Long-term monitoring**

Diet - Cornerstone of management

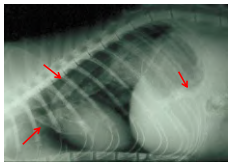
- **↑calories, ↑ K^+, ↑water soluble vitamins, ↓ Na^+, ↑omega-3 lipids, ↑anti-oxidants, alkalinisation**
- **Diet with ↓Pr & ↓ PO_4 → ↓urea & PO_4, ↓uraemic crises, ↑clinical improvement, ↑life span**
  - Average survival 633 vs 264 days - ~ 1 year more
- **Exact requirements unknown** - early renal food?
- **Do not too over restrict**
- **Multipurpose** - hypoallergenic
- **Wean gradually prior to onset of inappetence**

Harte et al (1994), Elliott et al (2000), Plantinga et al (2005) and Ross et al (2006)

Hill's

- **Added prebiotic fibres & betaine**
- **↓uraemic toxins in CKD patients**
- **Even in IRIS Stages 1-2**
- **Support hydration of renal cells & enterocytes**
- **Fibre change so wean over >7 days**
- **Multipurpose** – hypoallergenic, mobility

↓ dietary PO_4



- ↑ PO_4 in ~60% CKD
- PO_4 is a uraemic toxin
- ↓ PO_4 consumption → slow CKD progression of CKD
- Monitor plasma PO_4 [± PTH]

IRIS 2 Target PO_4 0.9-**1.5** mm/l (ref: 1.4-2.5)
IRIS 3 Target PO_4 0.9-**1.6** mm/l
IRIS 4 Target PO_4 0.9-**1.9** mm/l

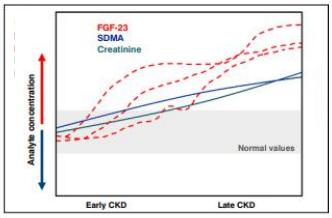
PO_4 controlled - median survival 799 days
PO_4 uncontrolled - median survival 283 days

Ross et al 1982, AJVR, 43:1023; Barber et al 1999, JSAP, 40:62; Elliott et al 2000, JSAP, 41:235

↓ dietary PO_4


- Feed ↓ PO_4 diet
- Intestinal PO_4 binders IN food
  - Aluminium hydroxide / carbonate
  - Calcium carbonate / acetate
  - Lanthanum carbonate
  - Pure carbon to trap uraemic toxins – Poros One
- FGF23 to assess need for P restriction
- Monitor: for response & for ↓ PO_4
  → weakness & anaemia

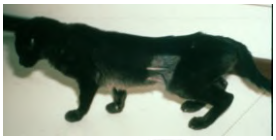

FGF-23



CKD-metabolic bone disease (CKD-MBD)

- **CKD-MBD complex interplay -** FGF-23, PTH, 1,25D_3, Ca + PO_4
- In early-stage CKD when total PO_4 is <1.50 mm/l FGF-23 identifies cats who need to ↓PO_4
- IDEXX FGF-23 when IRIS Stages 1 & 2
- ≤299pg/ml Normal
- 300-399pg/ml Borderline; recheck 3-6 months
- ≥400pg/ml Increased; give renal diet or PO_4 binders to ↓PO_4

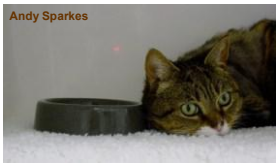
↑ dietary K^+



↓ K^+ with CRF:

- **Common in cats with CKD -** cause or effect?
- ↓ K^+ → CKD
- **Supplementation if ↓ K^+ → ↑ renal function**
- **Severe ↓ K^+ →** polymyopathy
  → generalised weakness + neck ventroflexion
- **Supplement if serum < K^+ 4 mmol/l**

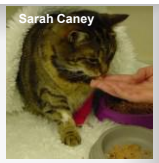

↑ food intake



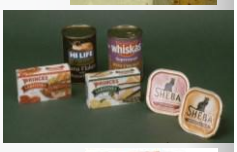
CKD → ↓ appetite due to:

- **Uraemic gastritis** (uraemic toxins & ↑gastrin)
- **Central effects of uraemic toxins → nausea & v$^+$**
- **GI bleed**
- **'Renal diets' less palatable**
- **↓ intake → protein malnutrition, endogenous protein catabolism & metabolic acidosis**

↑ food intake



- **Comfort –** warm bed, good nursing care, sit with the cat
- **↓ fear**
- **Small tempting meals**
- **Warm or aromatic foods**
- **Don't leave food with cat too long**
- **Don't overwhelm with food**
- **Choice of bowl type, raise it up**
- **Feliway Optimum, Cat nip**



THE UNIVERSITY of EDINBURGH
The Royal (Dick) School of Veterinary Studies

↑ food intake

Chemical appetite stimulants

- **Mirtazapine –** 0.5mg/kg po q3 days
- **Gabapentin –** 10-20mg/kg po q8-12h
- **Vitamin B_{12}**
- **Telmisartan & benazepril …**
- **Elura cat™** - Capromorelin, ghrelin receptor agonist for cats … licenced for CKD

Anti-emetic

- **Maropitant** 1mg/kg iv/sq; 2mg/kg po q24h

Feeding tube *e.g.* **oesophageal tube**

↑ fluid intake

- **Inadequate fluid intake →**
  - **Dehydration → ↓ renal perfusion**
  - **→ ↑ kidney disease**
- **Constant access to fresh water**
- **Feed moist diet**
- **Offer tempting 'soups'**
- **'At home' SQ fluids**
  - ~ 100-150 ml, q24h → q7d
  - Half strength Hartman's / 0.45% NaCl + K^+
  - Excess → over-hydration, ↑ Na^+

Raise food & water bowls for cats with arthritis

Proteinuria

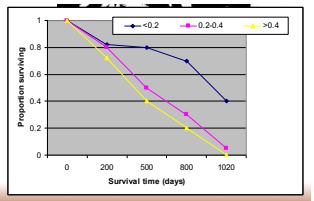
Proteinuria = independent risk factor for progressive renal disease; proteinuria → directly renotoxic → renal failure

- **↑UPC correlates with poor prognosis**

Cats less proteinuric v dogs: ~10% of cats with CKD → UPC >1.0

UPC >0.7 → **~4 months**
UPC 0.4-0.7 → **~9 months**
UPC <0.4 → **~15 months**

UPC >0.43 → **~9 months**
UPC <0.43 → **~2 years**



Syme et al JVIM 2006, 20: 528-535
King et al. JVIM 2007, 21: 906-916

Proteinuria

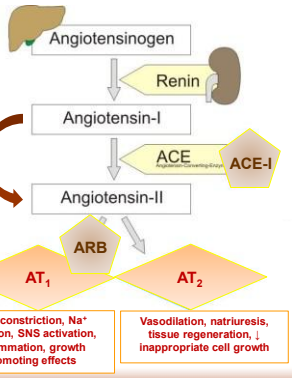
- **Dipsticks**

Dipsticks	Sensitivity	Specificity
Feline	90%; 60%	**11%; 31%**
Canine	81%; 54%	48%; 69%

- **IRIS** **<0.2** **non-proteinuric**
  0.2-0.4 **borderline …**
  >0.4 **proteinuric**
- **UPC** **Non-sterile urine**
  UPC dipsticks

Grauer JVIM 2004; Mardell + Sparkes JFMS 2006

Proteinuria



ACE-I
angiotensin converting enzyme inhibitors

ARB
Angiotensin II receptor blockers

ACE-I

- **In cats → experimental & natural CKD**
- **Benazepril → delayed progression of CKD & ↑ survival times**
- **BENRIC: 192 cats, 3y → ↓ proteinuria & ↑ quality of life**

Average duration

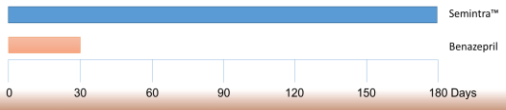
Placebo	391 days
Benazepril	501 days

- **Most significant effects in cats with ↑UPC & Persian cats**

King et al. JVIM 2007, 21: 906-916

ARBs

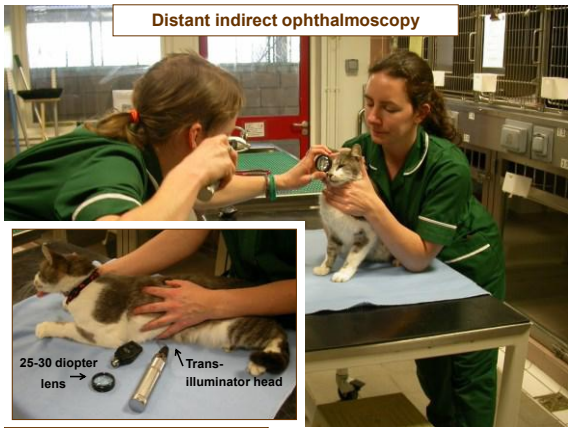
- Telmisartan = best sartan in cats & dogs → ↓BP
  224 cats with CKD, 6 months, telmisartan v benazepril
  As effective at → ↓BP, ↑appetite & survival, esp. if UPC ≥0.4
- 'ACE-escape' - benazepril → ↓ proteinuria for 30 days v telmisartan significantly more effective to 180 days

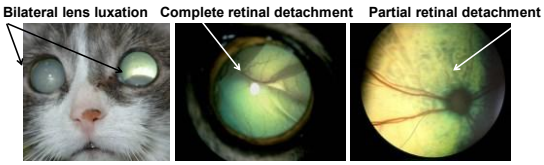


King et al, 2006; Sent et al 2015; Ebner et al 2012

↑BP

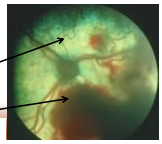
- ~20% → 60% cats with CKD have ↑BP
- Poor correlation: azotaemia & severity of ↑BP
- Kidneys → CKD "cause or effect"
- Heart → left ventricular hypertrophy → congestive heat failure
- Brain → cerebral vascular accidents → cognitive dysfunction
- Eyes → ocular changes …





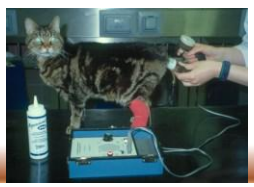
- Anterior chamber, vitreal or retinal haemorrhage
- Retinal oedema or detachment
- Arterial tortuosity
- Constriction & dilation of retinal primary venules
- Retinal degeneration
- Glaucoma
- Blindness

↑BP



↑BP: Diagnosis

- Indirect methods for measuring BP
- In cats, Doppler method is best
- Doppler - unpredictable at obtaining diastolic pressure



↑BP: Diagnosis

IRIS Guidelines

- Systolic:
  <140 mmHg (minimal*), 140-160
  160-180 (moderate), >180 (high ri
- Diastolic:
  <95 mmHg (minimal), 95-99 mmH
  100-119 mmHg (moderate), >120

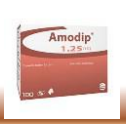
*Risk of Target Organ Damage

↑BP - Treatment

- **Calcium channel blockers** (CCB) (e.g. amlodipine)
- **ARB** (e.g. telmisartan) **v ACE-I** (e.g. benazepril)

Amlodipine:

- **Single agent of choice for treating ↑BP in cats**
- **More predictable & more effective in ↑↑BP**
- **Requires very small doses q24h**
- **Can double the dose in severe cases**



↑BP - Tx

ARB / ACE-I:

- **Both telmisartan & benazepril licensed in cats with CKD**
- **↓ progression of CKD, effect beyond ↓ BP & ↓ Pr loss …**
- **↑ appetite**
- **Telmisartan** 1-3 mg/kg po q24h → ↓ **systemic ↑BP**
- **In very severe ± refractory cases of ↑BP combine with amlodipine**
- ***Not in cats with dehydration or severe or unstable CKD***

Urinary tract infections (UTIs)

- **UTI in ~ 25-35% of cats with CKD**
- **75% in females & often recurrent**
- **UTI rarely → specific clinical signs**
- **But often → renal ↑ damage**
- **White blood cells not always present in urine**
- **Assess by urinalysis & bacterial culture**

Harvey

- **Moderate to severe CKD** - IRIS Stage **3**
- **Serum creatinine** (278 umol/l; 117-177 umol/l)
- **Serum PO_4** (2.5 mmol/l; 1.4-2.5 mmol/l; IRIS 0.9-1.6)
- **Hypertension** (170 mmHg; <150 mmHg)
- **UTI** (UPC 0.6; <0.4)

Treatment?

- **↓ protein, ↓ PO_4, ↓ Na diet**
- **2 weeks of amoxicillin / clavulanate**
- **Benazepril**
- **Monitor closely**

Harvey – Progress

	Visit 1	Ref. (IRIS)
Urea	**30**	6.4-10.5 mmol/l
Creatinine	**278**	117-177 umol/l
PO_4	**2.5**	1.4-2.5* mmol/l
PTH	**-**	2.5-25.5 pg/ml
SG	**1.012**	> 1.035
UPC	**0.6**	< 0.4
BP	**170**	< 150 mmHg
Other	**UTI**	
Tx	**Diet**	*0.9-1.6mmol/l
	Ab, ACEI	

Harvey – Progress

	Visit 1	+1 month	Ref. (IRIS)
Urea	**30**		6.4-10.5 mmol/l
Creatinine	**278**		117-177 umol/l
PO_4	**2.5**		1.4-2.5* mmol/l
PTH	**-**		2.5-25.5 pg/ml
SG	**1.012**		> 1.035
UPC	**0.6**	**0.1**	< 0.4
BP	**170**	**155**	< 150 mmHg
Other	**UTI**		
Tx	**Diet →**		*0.9-1.6mmol/l
	Ab, ACEI		

Harvey – Progress

	Visit 1	+1m	+ 6 months	Ref. (IRIS)
Urea	30		26	6.4-10.5 mmol/l
Creatinine	278		248	117-177 umol/l
PO_4	2.5		3.2	1.4-2.5* mmol/l
PTH	-		267	2.5-25.5 pg/ml
SG	1.012		1.016	> 1.035
UPC	0.6	0.1	0.1	< 0.4
BP	170	155	160	< 150 mmHg
Other	UTI			
Tx	Diet → Ab, ACEI		+ AI OH	*0.9-1.6mmol/l

Harvey – Progress

	Visit 1	+1	+ 6	+ 12 months	Ref. (IRIS)
Urea	30		26	29	6.4-10.5 mmol/l
Creatinine	278		248	268	117-177 umol/l
PO_4	2.5		3.2	2.0	1.4-2.5* mmol/l
PTH	-		267	170	2.5-25.5 pg/ml
SG	1.012		1.016	1.014	> 1.035
UPC	0.6	0.1	0.1	0.07	< 0.4
BP	170	155	160	180	< 150 mmHg
Other	UTI			UTI	
Tx	Diet → Ab, ACEI		+ AI OH	Ab Istin	*0.9-1.6mmol/l

Anaemia

- Progressive hypoproliferative anaemia
- Uraemia → ↓ RBC survival times & ↓ erythropoiesis
- ↓ EPO, GI bleed, renal bleeding (with renoliths)

Tx options:

- Iron supplementation, r-HuEPO, molidustat, anabolic steroids?, blood?
- Use of anabolic steroids:
  - Some clinicians advocate use *e.g.* nandrolone
  - Experimental support generally poor

Anaemia

Use of r-HuEPO:

- r-HuEPO → dramatic ↓ anaemia & ↑ in well being
- Tx if PCV < 20% & monitor
- Longer-acting darbepoietin sq q1 week → q3-4 weeks
- Complications - ↓ Fe, antibodies, ↑ BP & PCV
- Antibodies ~ 30% of cats → no effect, aplastic anaemia
- Side effects, cost & cost of monitoring (~£100/m)
- Give iron supplement too?

Molidustat *(muh-lid-eh-stat); Varenzin-CA1™ – oral suspension*

- Conditionally approved Tx of nonregenerative anaemia with CKD in cats
- ↑ endogenous EPO production → RBC production
- Hypoxia-inducible Factor Prolyl Hydroxylase (HIF-PH) Inhibitor is a reversible inhibitor of HIF-PH; HIF stimulates transcription of hypoxia-sensitive genes *e.g.*, EPO production, iron homeostasis

- 28 day licence (5mg PO q24h); 2-3 weeks to see effect
- 50-75% → ↑ HCT by 4% (*e.g.* 18 → 22%); 25% ↑ relative to baseline
- Side effects: Vomiting common (≈50%); stop if HCT or PCV exceeds upper RI
- Monitoring: HCT or PCV prior to Tx, weekly during Tx, start on 14th day of Tx & periodically after stopping Tx
- Repeat Tx after 7-days+ when HCT or PCV falls below lower RI
- Do not use in pregnant, lactating, or breeding cats; with seizures or thromboembolic Dz

Harvey – Progress

Following 2 years:

- Normotensive
- Not proteinuric
- 2 x UTI - *E.coli*

3 years after first diagnosis:

- Further ↓ weight & lethargy
- Progression of CKD
- Euthanasia

Summary

- CS can result from different & interacting disease processes
- Full diagnosis essential for correct treatment
- Each patient is different – prioritize Tx
- Monitoring essential
- ↑ UPC ratio important
- ↑ BP common
- UTI common

Questions?

catprofessional.com