Chronic Kidney Disease in Cats

Can we predict and diagnose early or are they aliens from outer space?

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On the Menu

1. **Pathogenesis of CKD (the great mystery)**
2. **Diagnosis of feline CKD in everyday practice (crystal ball?)**
3. **Early diagnosis and prediction: Revenge of AI and the biomarkers**
4. **Clinical signs, IRIS Staging: Why are we doing all of this?**
5. **Treatments, anything new?**

TRUE NORTH VETERINARY DIAGNOSTICS

Thank you!!!

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Sketch

- **11-year-old FS Calico**
- **Pre-dental exam: no concerns**
  - ”Getting older”
  - Weight 5.75kg (6.2kg 2y ago)
  - In-house labs:
    - USG 1.038
    - Creatinine 132umol/L (44-180umol/L)
    - BUN 8.5mmol/L (3.6-10.7mmol/L)
    - Phosphorus 1.3mmol/L (1.1-2.6mmol/L)

Poll: Does Sketch has evidence of CKD?

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What We Traditionally Do…

Well ☺

- **IRIS Stage Feline CKD**
- **Improve quality of life**
- **Diagnose once a patient is symptomatic**
- **Diet as therapy**
- **Proteinuria and hypertension**

Not Well ☹

- **Early diagnosis and treatment, acute kidney injury (AKI)**
- **We forget about post renal causes of azotemia**
- **Understanding the pathophysiology**
- **Still lots of grade 4 evidence-based treatments**

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Veterinary CKD Paradigm Shifts

Elliott J, et al., *J Small Anim Practice,* 2000: Cats with CRF fed the veterinary diet survived longer when compared with those that were not (633 days vs. 264 days).

Ross SJ, et al., *JAVMA,* 2006: CKD cats fed a renal diet survived longer and had fewer uremic crises.

Syme HM, et al., *JVIM,* 2006; King JN, et al., JVIM, 2007: Survival of cats with CKD is related to severity of proteinuria and it is a negative prognostic indicator.

King JN, et al., *JVIM,* 2007: Proteinuria significantly decreased with benazepril.

Jepson RE, et al., *JVIM,* 2009: High normal creatinine predicted development of CKD, and 30% of cats aged 9+ likely to develop CKD.

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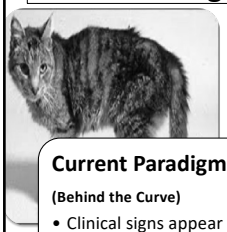
CKD Paradigm Shift in our Thinking



Current Paradigm

(Behind the Curve)

- Clinical signs appear
- Azotemia present
- Slow progression
- Treat symptoms
- Quality of life

New Paradigm

(Ahead of the Curve)

- Prior to clinical signs
- Prediction and early diagnosis
- Slow/prevent progression
- Early treatments

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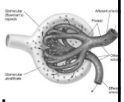
1. CKD = Permanent Decrease in GFR
CKD = Chronic + Kidney Disease

- **Decrease in GFR = increase in serum waste products that are supposed to be eliminated by the kidneys**
- **The problem… BUN and creatinine (the main waste products) are poorly sensitive as markers**
  - Creatinine MUCH more reliable than BUN
  - What about USG?



- **Another problem: we forget that CKD is about CHRONIC disease originating from the KIDNEYS**

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The end game is tubulointerstitial nephritis

But… What's the Cause?

- **Primary renal diseases**
  - Ex: congenital renal dysplasia (rare)
- **Viruses**
  - FIV
  - Paramyxovirus (feline morbillivirus)
- **Age**
  - Nope, not the cause (telomere study from CSU)
- **Extra-renal diseases**
  - Ureteroliths; more and more cats
- **Environment, diet**
  - Role unclear; phosphorus maybe?
- **Vaccinations**
  - Frequent vaccinations may be associated to CKD in cats
- **RAAS, hypertension**
  - Nope; activated in excess after development of CKD
- **Multiple active kidney injury**
  - Very likely in cats

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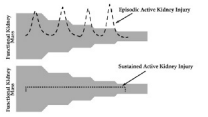
AKI Model of CKD

- **Acute, active kidney injuries (such as INFLAMMATION, TOXIC OR ISCHEMIA) likely cause maladaptive repair mechanisms**
  - Which then initiates CKD
  - Becomes more susceptible to damage, and repeated damage
  - Javard 2017 JVIM: CKD progression strongly associated with worsening inflammatory mediators
- **Mini damage progresses over time until we can finally diagnose it with our current methods**



Cowgill et al. Is progressive chronic kidney disease a slow acute kidney injury? Vet Clin Small Anim 46 (2016)

Poll: What % decrease in renal mass will lead to increased creatinine?

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2. Diagnosis and Prediction of Feline CKD:
How have we traditionally done this in everyday practice?

CKD?

Rule out post renal and acute azotemia

Decrease in renal function for at least 3 months

Renal azotemia and inappropriate USG	No azotemia but inappropriate USG	No azotemia, normal USG but structural changes
75% decrease of nephron mass	68-70% decreased renal function	Unknown

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So we have not been good at diagnosing kidney disease when…

- Creatinine is in normal range.
- There are no changes in urine specific gravity (USG).
- There are no clinical signs.

- **Early CKD (IRIS Stage 1-2) has been a "mystery"**
  - Is it real? And who cares, can't do anything about it?
  - Can we predict which cats will develop CKD?
  - 30% of cats in stage 1 will go into stage 2 within 1 year…
- **But CKD has a strong prevalence:**
  - Cats 30%–40% >10 years of age, also AKI model
  - Dogs 0.37%–3.74%

➢ **Hence the need for other tools**
Not just early diagnosis, but prediction

Stage 1? Boring. Just like cats.

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Early Diagnosis or Prediction is Good

Prediction models
More sensitive tests of GFR

- **Geriatric patients**
  - Yearly screening, prediction and earlier detection of kidney disease
  - Better preparation for anesthesia (dentals, mass removals etc.)
- **Any patient**
  - More sensitive for AKI, congenital disorders, non renal azotemia
- **CKD patients**
  - Monitoring of treatment outcomes, earlier detection of changes

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3. Early Diagnosis: Biomarkers

Biomarker	Indication	Advantages	Disadvantages	Methodology
Cystatin C	GFR, AKI	Good for CKD detection	Effect related to age and weight	Immunoassay
Retinol Binding Protein	AKI, CKD	Stable	Large variation with cats and CKD	ELISA, Western Blot
A1- microglobulin	AKI, CKD	Stable	Lower with hepatic disease	ELISA, immunoassay
B2-microglobulin	AKI, CKD	Good estimate of GFR in dogs	Non stable in acidic urine, less effective with disease progression	ELISA
Urinary clusterin	AKI	Early AKI, active AKI	Hemorrhage	Immunoassay
GGT	AKI	One urine sample	Unstable in acidic urine, hematuria, pyuria	Automated analyzer
NGAL	AKI, CKD	Urine, serum, plasma	Neoplasia, inflammation, hematuria, pyuria	ELISA

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Early Diagnosis: SDMA

- **Symmetric dimethylarginine**
  - Methylated form of the amino acid arginine
  - Produced by all cells and released into circulation during protein degradation
    - Excreted almost exclusively by the kidneys
  - Increases at **40% of renal dysfunction (20%–40%)**
    - Isosthenuria: 67-70% function loss
    - Azotemia: 75% function loss
  - Can identify CKD an average of **10 months earlier in dogs and 17 months sooner in cats**
- **DOES NOT REPLACE YOUR OTHER TESTS**
  - Synergistic approach

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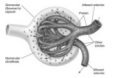
Serum Creatinine

- Increases at 75% loss
- Specific
- Not sensitive
- Decreases with muscle mass
- Decreases with hyperT4
- Biologic variability 15-20%
- Affected by hydration, diet
- Variable reference ranges



Serum SDMA

- Increases at 40% loss
- Specific
- More sensitive
- Not affected by muscle mass
- Less affected by hyper T4
- Biologic variability 15-20%
- Not affected by diet
- Less variable ref. range

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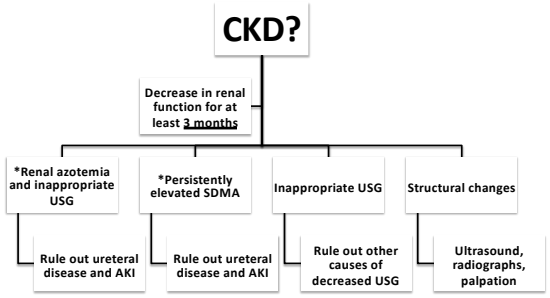
Poll: Can we predict which cats will develop CKD?

So: CKD Diagnosis



*** = most sensitive and more specific**

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Can We Predict CKD?

- **Association and development of CKD:**
  - Progressive weight loss (even small amounts)
  - Chronic renal proteinuria
  - Upper range creatinine
  - Evidence of chronic inflammatory diseases and ischemic events
  - High phosphorus (high protein?)
  - Frequent/annual vaccinations (cats)

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Coming Back to Diet?

Original Article

Effect of a high phosphorus diet on indicators of renal health in cats

Britta Dobenecker, Anna Webel, Sven Reese and Ellen Kienzle

Journal of Feline Medicine and Surgery
1–6

DOI: 10.1177/1098612X17710589
journals.sagepub.com/home/jfm
This paper was handled and processed by the European Editorial Office (iSFM) for publication in JFMS
SAGE

13 healthy cats fed phosphorus excess diet (HP) vs. 13 control diet for 30 days

- **High bioavailability, content similar to some commercial diets and treats**
- **9/13 HP cats had microalbuminuria and glucosuria**
- **Endogenous creatinine clearance decreased significantly for HP group**

STANDARD ARTICLE
Journal of Veterinary Internal Medicine ACVIM

Evaluation of phosphorus, calcium, and magnesium content in commercially available foods formulated for healthy cats

Stacie C. Summers | Jonathan Stockman | Jennifer A. Larsen | Loi Zhang | Anais Sanchez Rodriguez

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Is Phosphorus a Culprit?

ORIGINAL ARTICLE

WILEY

Observation about phosphorus and protein supply in cats and dogs prior to the diagnosis of chronic kidney disease

L. F. Bőswald | E. Kienzle | B. Dobenecker

State of the Art Review

The role of phosphorus in the pathophysiology of chronic kidney disease

Rebecca F. Geddes, MA, VetMB, MRCVS; Natalie C. Finch, BVSc, PhD, MRCVS; Harriet M. Syme, BSc, BVetMed, PhD, DACVIM, DECVIM-CA, MRCVS and Jonathan Elliott, MA, VetMB, PhD, DECVPT, MRCVS

- Links of excessive phosphorus intake being nephrotoxic in humans
- **Retrospective study:** 16 cats that developed CKD showed significantly higher P and protein intakes prior to diagnosis vs. control cats (home-made diets with P in excess of RDA)

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Journal of Veterinary Internal Medicine

Open A

Standard Article

J Vet Intern Med 2016;30:1661–1666

Evaluation of Weight Loss Over Time in Cats with Chronic Kidney Disease

L.M. Freeman, M.-P. Lachaud, S. Matthews, L. Rhodes, and B. Zollers

- **Median weight loss of -8.9% body weight in the 12 months prior to diagnosis of CKD**
- **Weight loss already present 3 years prior to diagnosis**
- **Accelerated weight loss after diagnosis, association with IRIS stage**

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Machine Learning?

STANDARD ARTICLE

Journal of Veterinary Internal Medicine ACVIM

Predicting early risk of chronic kidney disease in cats using routine clinical laboratory tests and machine learning

Richard Bradley[1] | Ilias Tagkopoulos[2,3] | Minseung Kim[3] | Yiannis Kokkinos[3] | Theodoros Panagiotakos[3] | James Kennedy[4] | Geert De Meyer[1] | Phillip Watson[1] | Jonathan Elliott[2]

- **>106,000 cats over 20 years EHR**
  - BUN, creatinine, USG, age
  - 3 CKD status: CKD, probable CKD, no CKD
- **SS 91%, SP 99% when near CKD dx**
  - 1y prediction: SS 63% SP 99%
  - 2y: SS 44% SP 99%
- **Machine model can lead to early prediction of CKD**

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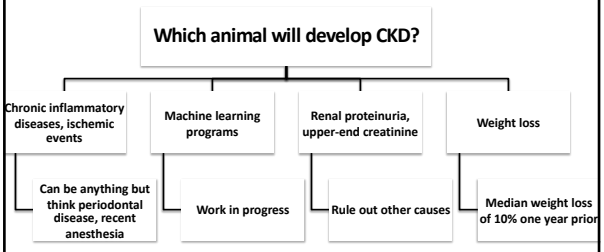
And Therefore: CKD Prediction



Prediction may mean we can limit CKD!

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4. Clinical Signs, IRIS Staging

- **Variable and depends on how advanced the disease is**
  - In general: dogs seem to have earlier clinical signs than cats
    - Cats seem to "tolerate" and hide azotemia better

Common clinical signs
Weight loss
PU/PD
Decreased appetite
Vomiting, nausea
Poor haircoat
Urinary tract infections (think: older animal with UTIs: rule out CKD
Rarely; hypertensive retinopathy
Lethargy
Rarely: heat-seeking behaviour

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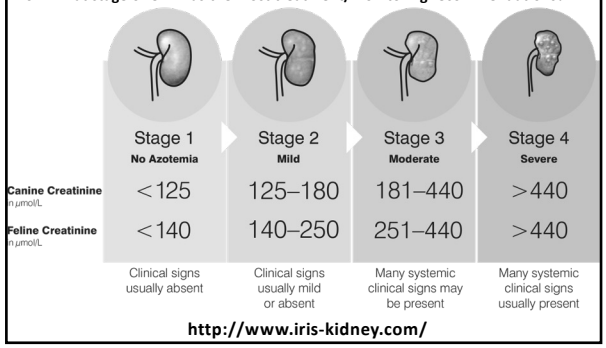
International Renal Interest Society (IRIS) Staging of CKD

Poll: What stage of CKD has the most treatment/monitoring recommendations?



http://www.iris-kidney.com/

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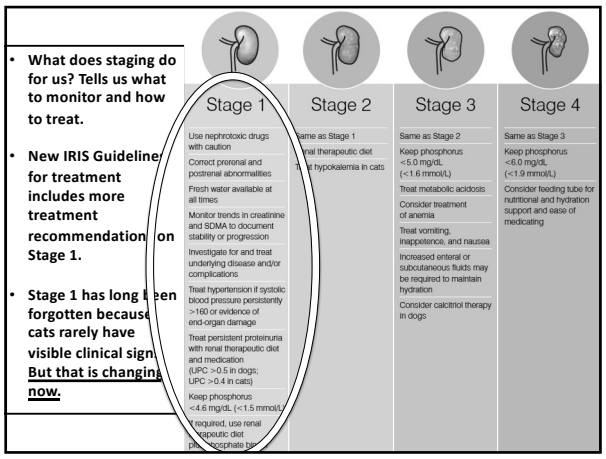

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IRIS Staging and SDMA

Remember: SDMA is more sensitive at detecting GFR changes and is not impacted by muscle loss

SDMA is useful for:

- **Early diagnosis**
  - Persistent SDMA > 14µg/dL (SS 90% but SP 50%)
    - >18µg/dL (SS 90% SP 83%)
- **Late staging**
  - Discrepancy between creatinine and SDMA from muscle loss

IRIS Staging of CKD (modified 2019)

1. Staging of CKD based on blood creatinine and SDMA concentrations

Staging is undertaken following diagnosis of chronic kidney disease (CKD) in order to facilitate appropriate treatment and monitoring of the canine or feline patient.

Staging is based initially on fasting blood creatinine or fasting blood SDMA concentration or (preferably) both assessed on at least two occasions in a hydrated, stable patient. The dog or cat is then substaged based on proteinuria and blood pressure.

Using these criteria, some empirical recommendations can be made about the type of treatment it would be logical to use for these cases. In addition, predictions based on clinical experience might be made about the likely response to treatment.

Stage	Blood creatinine[a] µmol/l mg/dl		Comments
	SDMA[a] µg/dl		
	Dogs	Cats	
1	<125 <1.4 <18	<140 <1.6 <18	Normal blood creatinine or normal or mild increase blood SDMA. Some other renal abnormality present (such as, inadequate urinary concentrating ability without identifiable non-renal cause (in cats not dogs), abnormal renal palpation or renal imaging findings, proteinuria of renal origin, abnormal renal biopsy results, increasing blood creatinine or SDMA concentrations in samples collected serially). Persistently elevated blood SDMA concentration (>14 µg/dl) may be used to diagnose early CKD
2	125–250 1.4 – 2.8 18 - 35	140 – 250 1.6 – 2.8 18 - 25	Normal or mildly increased creatinine, mild renal azotemia (lower end of the range lies within reference ranges for creatinine for many laboratories, but the insensitivity of creatinine concentration as a screening test means that patients with creatinine values close to the upper reference limit often have excretory failure). Mildly increased SDMA. Clinical signs usually mild or absent.
3	251 – 440 2.9 – 5.0 36 - 54	251 – 440 2.9 – 5.0 26 - 38	Moderate renal azotemia. Many extrarenal signs may be present, but their extent and severity may vary. If signs are absent, the case could be considered as early Stage 3, while presence of many or marked systemic signs might justify classification as late Stage 3.
4	>440 >5.0 >54	>440 >5.0 >38	Increasing risk of systemic clinical signs and uremic crises

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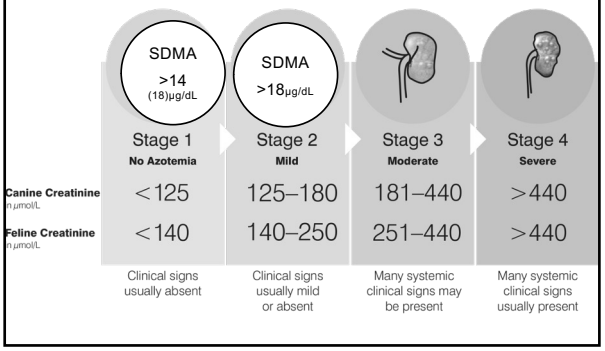
IRIS Staging of CKD and SDMA



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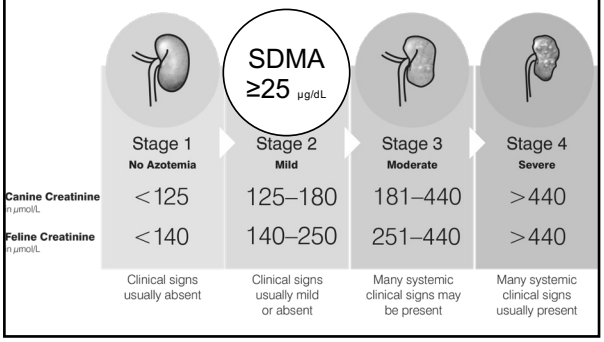
SDMA and Weight Loss Vs. Creatinine



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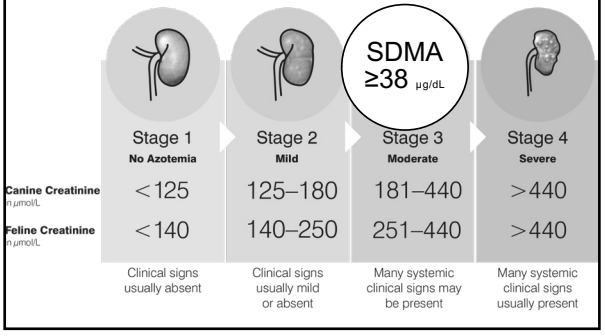
SDMA and Weight Loss Vs. Creatinine



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1-year-old cat:
- **Creatinine 300µmol/L**
- **SDMA 52 µg/dl**

What IRIS CKD stage is this cat?

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In-House Feline Serum Chemistry	Result	Range
Phosphorus	1.3mmol/L	1.1-2.6 mmol/L
Urea Nitrogen (BUN)	8.5mmol/L	3.6-10.7 mmol/L
Creatinine	132mol/L	44.2-180 mol/L
SDMA	16 µg/dl	<14 µg/dl

- **Evidence of early kidney disease**
- **Paradigm shift in our thinking**

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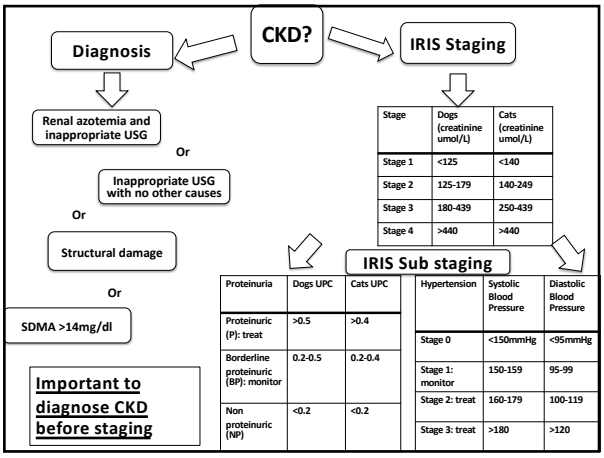

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Feline CKD Prognosis

(Dogs: likely faster disease progression)

- **Depends on how fast disease progresses**
  - Can have stable disease for years
- **IRIS Upper Stage 2: median survival time 1151 days**
  - IF not proteinuric or hypertensive (both negative prognostic indicators)
  - IF treated appropriately
- **IRIS Stage 3: 679 days**
- **IRIS Stage 4: 35 days**

Boyd, Langston 2008 JVIM

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Predicting Progression

J Vet Intern Med 2012;26:275–281

Clinicopathological Variables Predicting Progression of Azotemia in Cats with Chronic Kidney Disease

S. Chakrabarti, H.M. Syme, and J. Elliott

- **High phosphorus + UPC predicted progression in all stages**
- **Lower PCV, higher UPC predicted progression in stage 2**
  - UPC was 0.23 in progressive cases and 0.13 in stable cases
  - PCV was 33% in progressive cases and 36% in stable cases

Hence why it will be important to treat your patients accordingly

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5. Treatments

- **Goals**
  - Improve quality of life
    - Minimize uremic syndrome
  - Prolong life
  - Slow progression of disease
    - As disease progresses, more complications from azotemia + uremia
  - Prevent the disease?
  - Owner's quality of life

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Primary CKD Treatments

Treatment	What	When	Why
Renal diets	Multiple; split into early and later CKD diets	• Stage 1, early stage 2: early renal diets or geriatric diets • Stage 3: renal diet • Stage 4: renal diet, or anything they want to eat	Grade 1 evidence (stages 2-4); reduces uremic crises, prolongs life
Phosphorus binders	• Aluminum hydroxide • Calcium carbonate • Lanthanum carbonate	• See IRIS guidelines • If diet cannot get you to targets	Likely an important "killer" of the kidneys
Appetite stimulants	Mirtazapine	• Whenever; usually stage 3+4	Eating is important
Anti-nausea medications	Maropitant	Whenever; usually stage 3+4	Feeling good is important
SC fluids	LRS (does not sting)	Usually at stages 3+4	Only use when an animal cannot maintain hydration
Proteinuria, hypertension	• Benazepril • Telmisartan • Amlodipine	When present	Negative prognostic indicators

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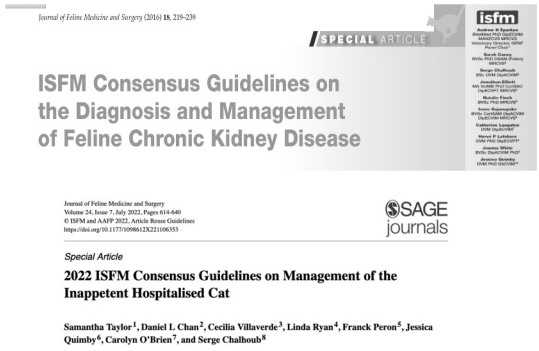
Consensus Statements to Help


Journal of Feline Medicine and Surgery (2016) 18, 219–239

SPECIAL ARTICLE

ISFM Consensus Guidelines on the Diagnosis and Management of Feline Chronic Kidney Disease

Journal of Feline Medicine and Surgery
Volume 24, Issue 7, July 2022, Pages 614-640
© ISFM and AAFP 2022, Article Reuse Guidelines
https://doi.org/10.1177/1098612X221106353

SAGE journals

Special Article

2022 ISFM Consensus Guidelines on Management of the Inappetent Hospitalised Cat

Samantha Taylor[1], Daniel L Chan[2], Cecilia Villaverde[3], Linda Ryan[4], Franck Peron[5], Jessica Quimby[6], Carolyn O'Brien[7], and Serge Chalhoub[8]

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Renal Diet

- **Cats**
  - 2006 Ross et al: Randomized study (24 months)
  - Cats in mid-stage 2 or 3
  - Uremic crisis 0% vs. 26%
  - Death from renal cause 0% vs. 22%
  - No change in LBM

Clinical evaluation of dietary modification for treatment of spontaneous chronic kidney disease in cats

Sheri J. Ross, DVM, PhD, DACVIM; Carl A. Osborne, DVM, PhD, DACVIM; Claudia A. Kirk, DVM, PhD, DACVN, DACVIM; Stephen R. Lowry, PhD; Lori A. Koehler; David J. Polzin, DVM, PhD, DACVIM

Elliott et al 2000: Cats lived 2.5y longer at IRIS stage 3 on RD
Plantinga et al 2005: RD survival 16 months vs. 7 months

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So, When You First Diagnose CKD:

Do:	Do not:
• Worry about hydration • Stimulate their appetite • Treat for nausea • Check for hypertension • Let them eat what they want, gradually introduce renal diet • Screen for proteinuria	• Treat for hyperphosphatemia (recheck 1 month later) • Treat blindly for proteinuria • Give them treatments with little to no evidence • Start famotidine or sucralfate (or omeprazole)

Get them feeling better (i.e. treat as a GI patient) usually for first month, then recheck phosphorus and gradually switch to just renal diet

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What If We Could Treat Prior to Clinical Signs (Stage 1)?

Positive Impact of Nutritional Interventions on Serum Symmetric Dimethylarginine and Creatinine Concentrations in Client-Owned Geriatric Cats

- 80 cats aged over 9 years age, all had normal creatinine at start
  - Renoprotective test food vs. owner-choice food
- Over 6 months: SDMA did not change for cats fed renal diet vs. increase in SDMA in owner-fed diet
- 30% started at or developed stage 1 CKD based on SDMA
  - SDMA increased in most cats on owner-fed diet
  - SDMA decreased/stayed stable on renoprotective diet

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New Paradigm: Early diagnosis + intervention has benefits:

- May slow CKD progression
- Early diagnosis = earlier intervention for proteinuria, phosphorus disorders and hypertension
- Stage 1: either a "renal friendly" diet: moderate or modified protein, lower phosphorus and sodium, higher omega-3 fatty acids, not acidifying, anti-oxidants (geriatric diet), or an early-stage renal diet

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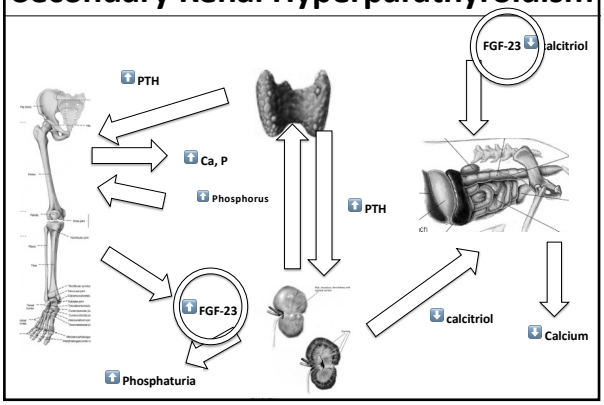
Secondary Renal Hyperparathyroidism



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Secondary Renal HyperPTH

- **Studies have shown:**
  - Secondary renal hyperparathyroidism common in CKD 76-84% dogs/cats, certainly in stage 4
  - Increased PTH and FGF-23 predicted the development of CKD *(Finch 2012, 2013)*
  - Increasing PTH and FGF-23 also predicted which cats progressed faster when in CKD *(Geddes 2013, 2015)*
    - **So… what about an FGF-23 test?**

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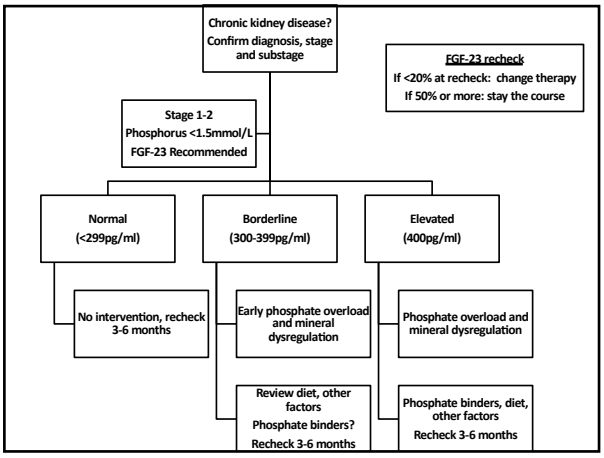

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Phosphate Binders

VERY IMPORTANT to control hyperphosphatemia

- **Renal diet: not a binder but one of your best treatments! Try renal diet for one month first to see if this controls your phosphorus**
- **Aluminum hydroxide**
  - Aluminum containing phosphate binder
    - Aluminum toxicity:
      - Anemia
      - Neurologic manifestations
- **Calcium carbonate**
  - Evidence of efficacy stage 1-2
  - Chitosan
- **Lanthanum carbonate**
  - Works but expensive
  - Studies on healthy cats

An online survey of dietary and phosphate binder practices of owners of cats with chronic kidney disease

Sarah MA Coney

Evaluating Sucralfate as a Phosphate Binder in Normal Cats and Cats with Chronic Kidney Disease

Jessica Quimby, DVM, PhD, DACVIM, Michael Lappin, DVM, PhD, DACVIM

- **Normal cats vomit with sucralfate**
- **CKD cats vomit even more with sucralfate**

Poll: When do we use antacids? …s in phosphorus (study stopped)

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Uremic Gastropathy

Received: 1 August 2018 | Accepted: 5 September 2018
DOI: 10.1111/jvim.15337

Journal of Veterinary Internal Medicine ACVIM

CONSENSUS STATEMENT

Consensus Statements of the American College of Veterinary Internal Medicine (ACVIM) provide the veterinary community with up-to-date information on the pathophysiology, diagnosis, and treatment of clinically important animal diseases. The ACVIM Board of Regents oversees selection of relevant topics, identification of panel members with the expertise to draft the statements, and other aspects of assuring the integrity of the process. The statements are derived from evidence-based medicine wherever possible and the panel offers interpretive comments when such evidence is inadequate or contradictory. A draft is prepared by the panel, followed by solicitation of input by the ACVIM membership that may be incorporated into the statement. It is then submitted to the *Journal of Veterinary Internal Medicine*, where it is edited before publication. The authors are solely responsible for the content of the statements.

ACVIM consensus statement: Support for rational administration of gastrointestinal protectants to dogs and cats

Stanley L. Marks[1] | Peter H. Kook[2] | Mark G. Papich[3] | M. Katherine Tolbert[4] | Michael D. Willard[4]

- **Acid suppressors not recommended for CKD in cats or dogs in stages 1-3**
- **Chronic acid suppression leads to decreased calcium absorption and increased PTH activity, worsening mineral bone loss**

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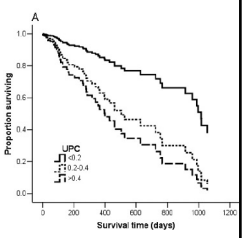
When to Treat Renal Proteinuria?

- **IRIS currently recommends UPC >0.4 once azotemic**
  - Syme 2006: survival 1000d with UPC<0.2, 500d with UPC 0.2-0.4, 400d with UPC > 0.4
  - Chakrabarti 2012: UPC was 0.23 in progressive cases and 0.13 in stable cases
  - Jepson 2009: Group that developed azotemia had proteinuria at entry but in low levels (UPC 0.14 vs. 0.19)



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ACEi vs. ARB

Vet Intern Med 2015;29:1479–1487

Comparison of Efficacy of Long-term Oral Treatment with Telmisartan and Benazepril in Cats with Chronic Kidney Disease

U. Sent, R. Gönd, J. Elliott, H. M. Syme, and T. Zimmering

- **Non-inferiority study**
- **ARBs likely improve proteinuria more efficiency and significantly**
- **Survival not looked at**

J Vet Intern Med 2006;20:1054–1064

Tolerability and Efficacy of Benazepril in Cats with Chronic Kidney Disease

Jonathan N. King, Danielle A. Gunn-Moore, Séverine Tasker, Allison Gleadhill, Günther Strehlau, and the BENRIC (BENazepril in Renal Insufficiency in Cats) Study Group

Benazepril significantly decreases proteinuria but does not seem to effect survival in cats (vs. dogs)

J Vet Intern Med 2014

The Effect of Chinese Rhubarb, *Rheum officinale*, with and without Benazepril on the Progression of Naturally Occurring Chronic Kidney Disease in Cats

A.S. Hanzlicek, C.J. Roof, M.W. Sanderson, and G.F. Grauer

Benazepril did not seem to slow progression of CKD

Case Report

J Vet Intern Med 2014;28:1071–1074

Telmisartan Treatment of Refractory Proteinuria in a Dog

A.C. Bugbee, A.F. Coleman, A. Wang, A.D. Woolcock, and S.A. Brown

Key words: Cardiology; Cardiovascular; Hemodynamics; Hypertension; Kidney; Pharmacology; Protein-losing nephropathy; Renal; Urinary tract.

- **Dog with GN refractory to benazepril**
- **ACEi decreased to SID and telmisartan added**

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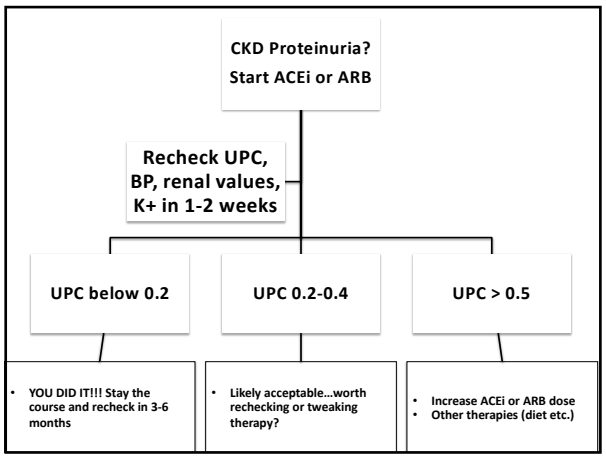

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Appetite Stimulants, Nausea

The Veterinary Journal

Mirtazapine as an appetite stimulant and anti-emetic in cats with chronic kidney disease: A masked placebo-controlled crossover clinical trial

J.M. Quimby

Significant increase in appetite, activity, and weight; decrease in vomiting

Drug exposure and clinical effect of transdermal mirtazapine in healthy young cats: a pilot study

Kellyi K Benson, Lara B Zajic, Paula K Morgan, Sarah R Brown, Ryan J Hansen, Paul J Lunghofer, Luke A Wittenburg, Daniel L Gustafson and Jessica M Quimby

Works despite variability in topical gel compounds

Chronic use of maropitant for the management of vomiting and inappetence in cats with chronic kidney disease: a blinded, placebo-controlled clinical trial

Jessica M Quimby, William T Brock, Kelsey Moses, David Bolotin and Kayla Patricelli

Significant decrease in vomiting over 2 weeks

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Hypertension

ACVIM consensus statement: Guidelines for the identification, evaluation, and management of systemic hypertension in dogs and cats

J Vet Intern Med. 2018;1–20.

Mark J. Acierno | Scott Brown | Amanda E. Coleman | Rosanne E. Jepson | Mark Papich | Rebecca L. Stepien | Harriet M. Syme

Normotensive (minimal TOD risk)	SBP <140 mm Hg
Prehypertensive (low TOD risk)	SBP 140-159 mm Hg
Hypertensive (moderate TOD risk)	SBP 160-179 mm Hg
Severely hypertensive (high TOD risk)	SBP ≥180 mm Hg

Treatments: amlodipine, telmisartan, ACEi

- 20-60% of cats with CKD
- Further kidney damage
- Cardiac compromise
- Ocular damage
- CNS damage
- 3X more likely to die or have progression

Section IX Blood Pressure

157 Pathophysiology and Clinical Manifestations of Systemic Hypertension

Serge Chalhoub
Douglas Palma

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Hypertension

- **Calcium Channel Blockers (#1 for cats?)**
  - Reduce afterload
  - Amlodipine
    - 0.625-1.25 mg per 5 kg daily for cats
  - Effective as single agent in 60% of cats
  - Chewable form works
- **ACE Inhibitors (dogs?)**
  - Reduce preload and afterload
  - But often BP not controlled, can use amlodipine
- **ARBs now have FDA approval for hypertension in cats**
  - Telmisartan effective 2mg/kg/d
  - Likely better also for dogs + GN + proteinuria

Journal of Veterinary Internal Medicine

Standard Article

Factors Influencing the Relationship Between the Dose of Amlodipine Required for Blood Pressure Control and Change in Blood Pressure in Hypertensive Cats

E.S. Bijsmans, M. Doig, R.E. Jepson, H.M. Syme, J. Elliott, and L. Pelligand

Evaluation of orally administered telmisartan for the reduction of indirect systolic arterial blood pressure in awake, clinically normal cats

Amanda E Coleman, Scott A Brown, Marcus Stark, Lawrence Bryson, Alicia Zimmorman, Tonja Zimmering and Anne M Trass

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What About Giving Fluids?

- **Dehydration**
  - No studies… but a no brainer? One old study: dehydration lowers GFR
- **Cooley, Caney, Sieberg, Quimby, ACVIM 2016 abstract**
  - Subcutaneous fluid practices in 468 cats stages 2-4; 95% recommended fluids
  - Most gave SC fluids, 79% easy/ok to learn
    - Food, warmed fluids* helped a lot
    - Needle size and time to administer affected tolerance
  - Only 42% received educational material

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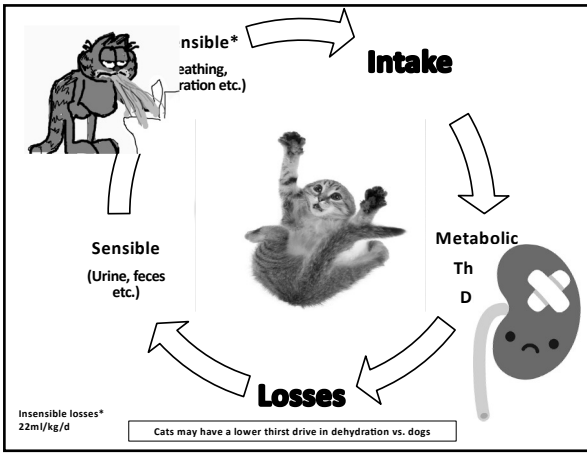

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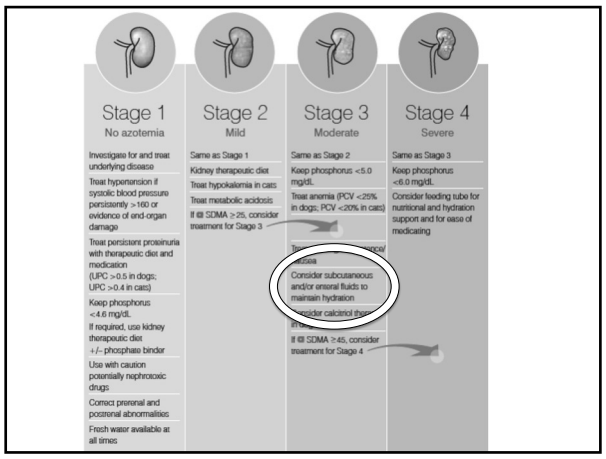

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Hi. My name is Sketch. I'm a Calico. Impatient. And strange.

SQ Administration

LRS preferable, can add potassium

- **Up to 12 hours of <u>maintenance</u> needs at a time SQ**
  - Anything more requires different route
- **Typically deliver 10-20ml/kg per site**
  - Deficits not corrected if > than 5%

Other strategies needed: organic osmolytes?

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Nutrient-Enriched Water: Purina Pro Plan Veterinary Supplements: <u>Hydra Care™</u>

- **<u>Nutrient-enriched water</u>** to improve hydration indices
- **<u>Organic osmolytes</u>** derived from whey protein isolates and glycerin
- Intracellular water regulation and also osmoregulation
  - Absorption and retention of water
- **<u>Paradigm shift</u>** in helping to balance water intake

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Meloxicam and… CKD?

jfms

Retrospective case–control study of the effects of long-term dosing with meloxicam on renal function in aged cats with degenerative joint disease

Richard A Gowan, Amy E Lingard, Laura Johnston, Wibke Stansen, Scott A Brown, Richard Malik

A retrospective analysis of the effects of meloxicam on the longevity of aged cats with and without overt chronic kidney disease

Richard A Gowan, Randolph M Baral, Amy E Lingard, Melissa J Catt, Wibke Stansen, Laura Johnston and Richard Malik

- **38 cats with DJD with 22 cats with CKD (mostly stage 2)**
  - Controls: cats with and without CKD, and not on meloxicam
  - 300+days of treatment; median dose 0.02mg/kg/d
- **No progression of CKD; cats with CKD may have progressed more slowly**
  - Slower creatinine increase but no change in stage for either group
  - Decline in BCS in all groups
- **Conclude safe for cats aged 7y+ at this dosage (selection bias? Selected cases, no cats had ACEi)**
  - Other study concluded no change in survival time for CKD cats on meloxicam

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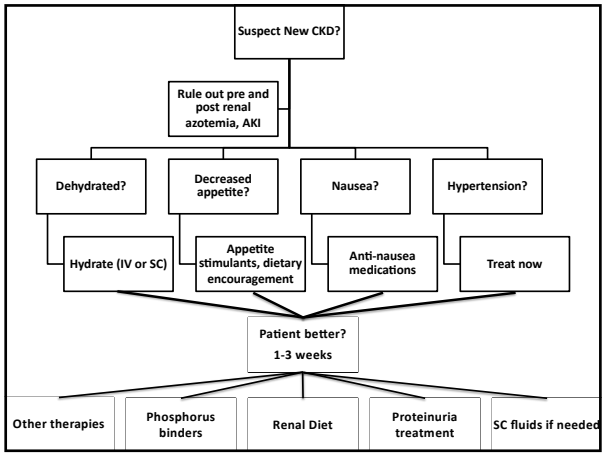

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CKD Monitoring

Test	Stage I-II Frequency	Stage III Frequency	Stage IV Frequency
Physical	q 6 months	q 3 months	Monthly
Biochemistry/SDMA	q 6 months	q 3 months	monthly
CBC	q 6 months	q 3 months	q 1-2 months
Urinalysis/UPC	q 6 months	q 6 months	q 3 months
Culture	q 12 months	q 6 months	q 3 months
BP			
Ultrasound			

How would have Sketch's care changed?

- Ruled out post renal causes
- Early renal diet
- Closer monitoring of UPC, BP
- More care with anesthesia, medications

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Conclusion

- CKD is a progressive, serious disease
- Lots that we know, even more we don't know
- Early diagnosis and prediction important
- New treatments aimed at slowing disease down, and new approach aimed at protecting the kidneys
- Change in paradigm from diagnosis/treatment when clinical signs are present, to earlier diagnosis/treatment and maybe prevention with prediction

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THANK YOU!

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