Chronic Kidney Disease
Paradigm shift from late diagnosis and treatment to earlier detection/intervention

Serge Chalhoub, DVM, Dipl. ACVIM (SAIM)

On the Menu
1. Diagnosis and prediction of feline CKD in every day practice (crystal ball?)
2. Pathogenesis of CKD (the great mystery)
3. Early diagnosis: Revenge of the biomarkers
4. Treatments (without getting scratched)

Thank you!

Sketch
• 10 year old FS Calico
• Pre-dental exam: no concerns
  – “Getting older”
  – Weight 5.75kg (6.2kg 2y ago)
  – In-house labs:
    • USG 1.038
Feline Serum Chemistry Result Range

<table>
<thead>
<tr>
<th>Substance</th>
<th>Result</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phosphorus</td>
<td>1.3mmol/L</td>
<td>1.1-2.6 mmol/L</td>
</tr>
<tr>
<td>Calcium</td>
<td>2.75mmol/L</td>
<td>2-2.9 mmol/L</td>
</tr>
<tr>
<td>Total Protein</td>
<td>62g/L</td>
<td>54-78 g/L</td>
</tr>
<tr>
<td>Albumin</td>
<td>34g/L</td>
<td>25-39 g/L</td>
</tr>
<tr>
<td>Urea Nitrogen (BUN)</td>
<td>8.5mmol/L</td>
<td>3.6-10.7 mmol/L</td>
</tr>
<tr>
<td>Creatinine</td>
<td>132mol/L</td>
<td>44.2-180 mol/L</td>
</tr>
<tr>
<td>Sodium</td>
<td>152mmol/L</td>
<td>145-160 mmol/L</td>
</tr>
<tr>
<td>Potassium</td>
<td>4.2mmol/L</td>
<td>3.5-5.5 mmol/L</td>
</tr>
<tr>
<td>Chloride</td>
<td>124mmol/L</td>
<td>112-129 mmol/L</td>
</tr>
</tbody>
</table>

Brownie

- 12 year-old DSH MN, presents for weight loss over past year, on/-off anorexia for 3 months
  - Exam: mild dehydration, dental disease, muscle loss around thighs
  - Labs: Mild NR anemia, mild hypokalemia, creatinine 240umol/L, USG 1.024, 1+ proteinuria
    - Last year: creatinine 130umol, no urine collected

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
Paradigm shift in our thinking

**Newton and theory of motion**

**Copernicus and the solar system**

**Linnaeus and species concept**

**Darwin and natural selection**

**Mendel and genetics**

**Watson and Crick and DNA**

**Paradigm Shift**

*A fundamental change in approach or underlying assumptions, a new way of thinking*

**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 died vs. 264 died).
- **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.
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
• Early diagnosis with new biomarkers
• Slow/prevent progression
• Early treatments

1. Diagnosis and Prediction of Feline CKD:
   How do we do this in everyday practice?

   CKD?
   - 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

   Large change in GFR (early renal disease)
   Large change in P/K creatinine but little change in GFR (enhanced renal tissue)

   No azotemia but inappropriate

   68-70% decreased renal function
   Unknown
So we have not been good at diagnosing kidney disease when...

- Creatinine is in normal range.
- There is 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?

- But CKD has a strong prevalence:
  - Cats 30%-40% >10 years of age
  - Dogs 0.37%-3.74%

Hence the need for advanced biomarkers

**Diagnosis**
- Renal azotemia and isosthenuria
- Isosthenuria with no other causes
- Persistent proteinuria, or structural damage
- Persistent SDMA >14

**CKD?**
- Proteinuria, or structural damage
  - Persistent proteinuria
  - No other causes

**IRIS Staging**

### Dogs

<table>
<thead>
<tr>
<th>Stage</th>
<th>Urea Concentration (mg/dl)</th>
<th>Creatinine Concentration (mg/dl)</th>
<th>BUN/Creatinine Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>&lt;8.5</td>
<td>&gt;1.5</td>
<td>6</td>
</tr>
<tr>
<td>2</td>
<td>8.5-11.9</td>
<td>&gt;1.5</td>
<td>6</td>
</tr>
<tr>
<td>3</td>
<td>12.0-14.9</td>
<td>&gt;1.5</td>
<td>6</td>
</tr>
<tr>
<td>4</td>
<td>&gt;14.0</td>
<td>&gt;1.5</td>
<td>6</td>
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</tbody>
</table>

### Cats

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<tr>
<th>Stage</th>
<th>Urea Concentration (mg/dl)</th>
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<td>&gt;14.0</td>
<td>&gt;1.5</td>
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</table>

**Predicting CKD Prior to advanced biomarkers**

  - High protein, low potassium diet likely to be “real” diet

- Jeppson, Brodbelt, et al., *JVIM*, 2009:
  - 118 cats >3y, monazotemic, 12 months later 30% became azotemic
  - High end creatinine and UPC predicted

- Greene, Lefebvre, et al., *JVAM*, 2014:
  - Thin BCS, recent anesthesia, male cat
  - Dental disease, cystitis

- Finch, Syme, et al., *JVIM*, 2016:
  - 148 geriatric cats
  - Annual/Frequent (every 2 years) vaccination
  - Moderate/severe dental disease

- Piyarungsri and Pusoonthornthum, *J Fel Med Surg*, 2016:
  - 101 cats with CKD vs. normal cats >5y age
  - Increased risk: tap water, outdoor lifestyle, males
  - Decreased risk: eating commercial diet, filtered water, indoor lifestyle
Predicting CKD
Prior to advanced biomarkers

Take home messages:
• Hard to predict CKD
• Unclear if diet has a role
• Chronic inflammatory/ischemic diseases and CKD?
• Weight loss
• UPC and high-end creatinine

Journal of Veterinary Internal Medicine
Evaluation of Weight Loss Over Time in Cats with Chronic Kidney Disease

• Median weight loss of -8.5% 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

What IRIS stage are we talking about here?

The end game is tubulointerstitial nephritis

2. But... What’s the Pathogenesis?

Environment, diet, vaccinations
RAAS, Hypertension
Primary renal diseases
Extra-Renal Diseases
Viruses
Age
Multiple AKIs?
CKD progression strongly associated with worsening inflammatory mediators19

AKI can initiate CKD in people and dogs; why not cats? AKIs (such as INFLAMMATION, TOXIC OR ISCHEMIA) likely cause maladaptive repair mechanisms, which initiate CKD.

– Changes typical of ischemic AKI are present in experimental and naturally occurring CKD; AKI can lead to CKD in cats. (Brown, et al., Vet Path, 2015)15

• Link between AKI/CKD pathologic processes?
  – Likely interconnected entities
  – Progressive CKD associated to active episodic or ongoing AKI
  – AKI linked to CKD

Maladaptation repairs even if traditional markers return to “normal”

3. Early Diagnosis: Biomarkers

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>Indication</th>
<th>Advantages</th>
<th>Disadvantages</th>
<th>Methodology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cystatin C</td>
<td>GFR, AKI</td>
<td>Good for CKD detection</td>
<td>Effect related to age and weight</td>
<td>Immunoassay</td>
</tr>
<tr>
<td>Retinal Binding</td>
<td>AKI, CKD</td>
<td>Stable</td>
<td>Large variation with cats and CKD</td>
<td>ELISA, Western Blot</td>
</tr>
<tr>
<td>Protein</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>α1-microglobulin</td>
<td>AKI</td>
<td>Stable</td>
<td></td>
<td>ELISA, immunoassay</td>
</tr>
<tr>
<td>B2-microglobulin</td>
<td>AKI</td>
<td>Good estimate of GFR in dogs</td>
<td>Non-stable in acidic urine, less effective with disease progression</td>
<td>ELISA</td>
</tr>
<tr>
<td>Urinary clusterin</td>
<td>AKI</td>
<td>Simple, active site</td>
<td>Nonspecific</td>
<td>Immunoassay</td>
</tr>
<tr>
<td>GGT</td>
<td>AKI</td>
<td>One urine sample</td>
<td>Unstable in acidic urine, hemosiderin, pyuria</td>
<td>Automated analyzer</td>
</tr>
<tr>
<td>NGAL</td>
<td>AKI, CKD</td>
<td>Urine, serum, plasma</td>
<td>Nephritis, inflammation, hemosiderin, pyuria</td>
<td>ELISA</td>
</tr>
</tbody>
</table>
Wait...Why Early Diagnosis?

- *What’s the fuss?*
  - Undetectable or difficult to detect changes in early kidney disease
  - Weight loss
  - Inflammation
  - Changes in appetite, activity
  - Ongoing damage
    - Multiple mini AKI model, inflammation
    - Breaking out of our current paradigm
  - Can be tough...
- *Maybe we should care...*
  - 30% of stage 1 cats will go into stage 2 within a year

IRIS Stage 1

- *Has been a mystery*
  - Low sensitivity in previous biomarkers (creatinine, BUN) in detection
  - Little to no research
  - No clinical signs
- *Paradigm shift: we now have the ability to reliably diagnose early kidney disease (both acute and chronic)*
  - In-house and at reference laboratory

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%)\(^\text{(20)}\)
    - Isothenuria: 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
Serum Creatinine
- Increases at 75% function loss
- Specific
- Not sensitive 17%
- NPV 70%
- Decreases with age in cats
- Decreases with hyperthyroidism
- Biologic variability 15-20%
- Affected by hydration, diet (ex. meat)
- Variable reference ranges

Serum SDMA
- Increases at 40% loss
- Specific
- Sensitive 100%
- NPV 100%
- Not affected by age or muscle mass
- Less affected by hyperthyroidism
- Biologic variability 15-20%
- Can be affected by hydration, not by diet
- One reference range

What Does It Mean
- Detecting kidney disease in animals with poor BCS
  - Note: new reference range for dogs <2y (<16ug/dl)
- Detecting kidney diseases before azotemia or isosthenuria develops
- Monitoring of renal disease
  - Setting new guidelines for monitoring of IRIS Stage 1 patients
  - Setting the stage for monitoring of treatment outcomes
  - Developing earlier treatments and prevention
- Helpful with ARF/AKI
- BUT it does not tell you what disease you have (investigate, manage, monitor)

So SDMA helps with the diagnosis and the staging of CKD
More sensitive test of GFR (in-house or at lab)

Geriatric patients

Yearly screening and earlier detection of kidney disease

Better preparation for anesthesia (dentals, mass removals)

Any patient

More sensitive for AKI, congenital disorders, non renal anemia

Monitoring of treatment outcomes, earlier detection of changes

CKD patients

More sensitive for AKI, congenital disorders, non renal anemia

IRIS Staging of CKD and SDMA

**IRIS Staging of CKD (modified 2016)**

**Symmetric dimethylarginine (SDMA) and IRIS CKD guidelines**

IRIS CKD staging is based currently on finding total creatinine concentrations. Further are indications that SDMA concentrations in blood plasma or serum may be a more sensitive and early indicator of kidney function decline than current creatinine. The use of SDMA in staging of CKD is currently proposed.

A persistent increase in SDMA above upper limit suggests impaired renal function and may be a reason to consider a diagnosis of chronic kidney disease. The upper limit is set at 15 µmol/L (in WHO units 14 µg/dL). This cutoff is consistent with a 40% decrease in estimated GFR.

Stage 1: SDMA < 14 µg/dL

Stage 2: SDMA 15-25 µg/dL

Stage 3: SDMA 26-40 µg/dL

Stage 4: SDMA > 40 µg/dL

These comments are preliminary and based on early data from the use of SDMA in human patients. Further research is ongoing to apply this as routine practice. Following experience using SDMA alongside creatinine, the internationally validated in disease and mortality of acute and chronic KD risk.

SDMA assays are offered by a number of laboratories throughout the world. The methodology used may vary or be standardized and the measurements made above are based on the proprietary methodology offered by InterSystems

SDMA
SDMA and Weight Loss Vs. Creatinine

SDMA ≥25 µg/dL

SDMA and Progression of CKD with Weight Loss vs. Creatinine

Creatinine 300µmol/L
SDMA 52 µg/dl
So what stage is this cat in?
### In-House Feline Serum Chemistry Result Range

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<thead>
<tr>
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<th>Result</th>
<th>Range</th>
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<tr>
<td>Potassium</td>
<td>3.5-5.5 mmol/L</td>
<td></td>
</tr>
<tr>
<td>Chloride</td>
<td>129 mmol/L</td>
<td></td>
</tr>
<tr>
<td>SDMA</td>
<td>16 µg/dl</td>
<td>&lt;14 µg/dl</td>
</tr>
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### In-House Canine Renal Chemistry Result Range

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• Evidence of AKI; Suzie-Q is in trouble
• Real-time analysis can change our approach
• Utility for monitoring

Suzie-Q
SDMA can help detect AKI before creatinine, therefore can be used as a biomarker for early renal dysfunction (same as in humans)\textsuperscript{22}

43 cats with kidney stones vs. 21 healthy geriatric cats\textsuperscript{22}
- 39/43 had increased SDMA (92% vs. 17% azotemic)
- Only 18/43 had elevated creatinine at some point (42%)
- USG > 1.035 in 15/39
- 27 months before creatinine increased in these cases

CKD Prognosis\textsuperscript{24}

**Cats**
- 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

**Dogs**
- CKD cats usually live longer than CKD dogs
  - Proteinuric diseases more common in dogs and have worse prognosis
  - Arterial hypertension
- Stage 3 + 4
  - Usually more progressive
  - Months to years to death
  - Proteinuria and hypertension

Boyd, Langston 2008 JVIM
Predicting Progression

Clinicopathological Variables Predicting Progression of Azotemia in Cats with Chronic Kidney Disease
S. Chokrubari, H.M. Synec, and J. Elliott

- High phosphorus and UPC predicted progression in all stages
- Lower PCV and higher UPC predicted progression in stage 2
  - UPC was 0.23 in progressive cases and 0.13 in stable cases
  - PCV was 13% in progressive cases and 16% in stable cases

4. 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

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

Practical relevance: Chronic kidney disease (CKD) is one of the most commonly diagnosed diseases in cats, yet most cases, CKD is a slow progressive disease and can be accompanied by a wide range of clinical and clinicopathological changes. These ISFM Consensus Guidelines have been developed by an independent panel of clinicians and academicians to provide practical advice on the diagnosis and management of this complex disease.

Clinical challenges: Although CKD is a common clinical problem in cats, the manifestations of disease vary between individuals. Thus there is a need for careful and repeated evaluation of cases with CKD to determine whether and adjustment of therapy according to individual needs. In addition, it is challenging to define the exact point at which dialysis is necessary to slow the progression of disease and owners may be encouraged to delay starting dialysis until the final stages of the disease process. In our patients, this can be challenging when multiple therapies are indicated. It may be difficult to prioritize therapy and provide understanding of what is likely to benefit the individual patient, and prevent the disease from progressing further. Thus, the ISFM has recently revised the existing guidelines to reflect the latest evidence and has also provided a quality of evidence to different interventions to help provide practical recommendations in the management of cats with CKD. This is a dynamic document that will be updated from time to time as published clinical research and further research findings will undoubtedly modify the recommendations contained in these Guidelines in the future.
As you will see, all current treatments are for IRIS 2 and above

- Why???
  - Poor ability to diagnose earlier
  - No clinical signs so why treat?
  - Minimal research up to this point

- So what's the point of early diagnosis?

Stage 1 has long been forgotten because cats rarely have visible clinical signs. But that is changing now.

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

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
Renal Diet

- Nausea
- Appetite
- Hydration

Initially diagnosed CKD cats need to be treated as GI patients first

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

Jepson 2009: 30% cats in IRIS Stage 1 will progress within 1 year

- 80 cats aged over 9 years, 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
  - In renal diet: BUN and creatinine dropped

- 30% started at or developed stage 1 CKD based on SDMA
  - SDMA increased in most cats on owner-fed diet
  - SDMA decreased or stayed stable on renal diet

Journal of Animal Physiology and Animal Nutrition

- Current IRIS guidelines: feed renal diet at stage 2+
- Unknown if earlier benefit or if detrimental:
  - Prospective 12 month trial of 36 dogs IRIS Stage 1 fed renal diet (44 clinical sites):
    - 97% of dogs transitioned successfully, majority enjoyed the new diet
    - BUN, creatinine, SDMA significantly decreased from baseline at 3 months
    - 12/16 dogs with proteinuria had significant decrease
    - Owners: overall health and quality of life attributes, hair coat
The Diet Controversy
The Pro and Con View of Renal Diets at Stage 2-4

The Pro View

• Renal diets improve survival, decrease uremic crises
• Not just about the protein: phosphorus, sodium, omega-3, antioxidants, potassium, vitamin D, neutral effect on pH
• Protein restriction decreases uremia
• Phosphorus linked to CKD progression
• High protein leads to proteinuria and glomerular lesions
• Uremia causes weight loss, sarcopenia
• High protein diets untested and likely dangerous recommendation
• Promote eating

The Con View

• Obligatory carnivores that need high protein diets, lose LBM with lower protein diets
• Remnant kidney studies showed no association between high protein intake and renal lesions, proteinuria, or decreased GFR
• No study has looked just at protein CKD diet effect on proteinuria unclear (Ross 2006)
• Increased mortality with lower BW CKD
• Phosphorus restriction alone not studied
• Fatty acids?
• What about acid-base status correction
• Geriatric cats may need more than 32-34% of calories from protein

The New Paradigm: Early diagnosis and intervention has benefits:

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

Paradigm shift in our thinking

Appetite Stimulants

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

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Appetite Stimulants

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

• Works despite variability in gel compounds
• Significantly increased appetite
• Begging, activity, vocalization
• Lower dose and different frequency administration likely needed for CKD cat

Ghrelin Receptor Agonists

• Hormone mainly produced by stomach
  - “Hunger hormone”
  - Homeostasis and energy metabolism
    - Distribution and rate of energy usage
    - Increased GH, IGF-1
    - Increase in lean muscle mass
    - Negative feedback on its own secretion
    - Anti-inflammatory properties

• Ghrelin agonists
  - Capromorelin
    - Beagles increase in weight and appetite
    - 200 dogs field study: significantly increased appetite and weight 70%
    - 40 cats CKD pilot field study over 90 days; significant increase in weight vs. placebo

Nausea

Significant decrease in vomiting over 2 weeks

Julie Allen ACVIM 2016
Nausea

**Assessment of absorption of transdermal ondansetron in normal research cats**


**Abstract**

Objective: The objective was to assess the absorption of transdermal ondansetron in healthy cats.

Methods: Five regular cats with unanesthetized corneal scleral fornix were used. Ondansetron, a small molecule, was used for both single- and multiple-dose application studies. For single-dose application, a 1 ng/mL ondansetron was injected into the external jugular vein. Blood samples were collected via jugular catheter at 1, 10, and 30 minutes, and then hourly for 4 hours. For multiple-dose application, a 1 ng/mL ondansetron was applied for 5 consecutive days before blood samples were obtained in the same manner. Serum was collected and frozen in aliquots. Ondansetron was measured via high-performance liquid chromatography.

Results: Ondansetron was not detected in the serum of any cat at the time of application. Ondansetron was detected in the serum of any cat at the time of application.

No significant serum concentration achieved.

**Stem Cells**

**Assessment of intravenous adipose-derived allogenic mesenchymal stem cells for the treatment of feline chronic kidney disease: a randomized, placebo-controlled clinical trial in eight cats**

Jessica M Quinley*, Tanya L Hudock, Elizabeth Rickard, Angela Ward, Alex Vindel-Abadzic and Omer M Dweck

**No significant improvement in renal function when given IV+**

**Secondary Renal Hyperparathyroidism**

**PHOSPHORUS CONTROL IS A REAL PROBLEM**

• Secondary renal hyperparathyroidism common in CKD 76-84% dogs/cats, certainly in stage 4

• Geddes 2013 JVIM*: FGF-23 increases in cats with CKD and correlated with staging

• Finch 2012 JAVMA**: PTH higher in nonazotemic cats that developed azotemic CKD within 12 months and this prior to any changes in phosphorus

• Finch 2013**: FGF23 predicted development of azotemic CKD over 12 months

• Geddes 2015 JVIM**: FGF-23 associated with survival in azotemic CKD
Effect of a high phosphorus diet on indicators of renal health in cats

Brita Dohmen-Recker, Anna Weibel, Sven Reese, and Ellen Kneifel

- 13 healthy cats fed phosphorus excess diet (HP) vs. 13 control diet for 30 days
  - High bioavailability
  - 9/13 HP cats had microalbuminuria and glucosuria
  - Endogenous creatinine clearance decreased significantly for HP group

Paradigm shift in our thinking

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

Jessica Quinby, DVM, PhD, DACVIM, Michael Lappin, DVM, PhD, DACVIM

- Normal cats vomit with sucralfate
- CKD cats vomit even more with sucralfate
- No changes in phosphorus (study stopped)

Uremic Gastropathy

Relationship among Serum Creatinine, Serum Gastrin, Calcium-phosphorus Product, and Uremic Gastropathy in Cats with Chronic Kidney Disease

S.M. McLelland, K.F. Lunn, C.G. Duran, K.R. Refsdal, and J.M. Quinby

GI ulceration not found in any stage of CKD

But evidence of gastric mineralization especially in moderate/severe azotemia

Ca X P product associated with disease severity and mineralization
Anemia of Renal Disease

- Cats: renal anemia 30-65% of CKD patients
- Anemia independent predictor of progressive CKD, increased mortality
- Tx: Epogen, Darbepoetin
  - Darbe has MUCH lower pure red cell aplasia
  - <10% vs. 25-40% Epogen

When to Treat Renal Proteinuria?

- IRIS currently recommends UPC >0.4 once azotemic
  - Syme 2005: survival 1100d 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)

Paradigm shift in our thinking

Renal Proteinuria Treatments

![Graph showing Renal Proteinuria Treatments]
• Works as efficiently as benazepril in non-inferiority study51
• Likely improves proteinuria more efficiency and significantly
• Survival not looked at

My CKD Monitoring

<table>
<thead>
<tr>
<th>Test</th>
<th>Stage I-II</th>
<th>Stage III</th>
<th>Stage IV</th>
</tr>
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<tbody>
<tr>
<td>Physical</td>
<td>q 6 months</td>
<td>q 3-6 months</td>
<td>Monthly</td>
</tr>
<tr>
<td>Biochemistry/SDMA</td>
<td>q 6 months</td>
<td>q 3-6 months</td>
<td>monthly</td>
</tr>
<tr>
<td>CBC</td>
<td>q 6 months</td>
<td>q 3-6 months</td>
<td>q 1-2 months</td>
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<tr>
<td>Urinalysis/UPC</td>
<td>q 6 months</td>
<td>q 6 months</td>
<td>q 3 months</td>
</tr>
<tr>
<td>Culture</td>
<td>q 12 months</td>
<td>q 12 months</td>
<td>q 3 months</td>
</tr>
<tr>
<td>BP</td>
<td>q 6 months</td>
<td>q 3-6 months</td>
<td>q 3 months</td>
</tr>
<tr>
<td>Ultrasound</td>
<td>As needed</td>
<td>As needed</td>
<td>As needed</td>
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My Geriatric Cat Monitoring (age 8+)

<table>
<thead>
<tr>
<th>Test</th>
<th>Frequency</th>
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<tr>
<td>Weight</td>
<td>q 6 months</td>
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<tr>
<td>Biochemistry/SDMA</td>
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<tr>
<td>CBC</td>
<td>q 12 months</td>
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<tr>
<td>Urinalysis/UPC</td>
<td>q 12 months</td>
</tr>
<tr>
<td>BP</td>
<td>q 12 months</td>
</tr>
</tbody>
</table>

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
Conclusion

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

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