The CKD lifecycle: take it one “stage” at a time

+ Update on IDEXX FGF-23
Learning Outcomes/Objectives

• Recall essential components of kidney function markers
• Describe the importance & limitations of GFR
• Describe current kidney diagnostics and practical application in health & disease
• Provide an overview on how CKD in cats can be seen as an independent lifecycle
• Review the standard methods for diagnosing, staging, treatment and monitoring of CKD patients
• Visit each stage of CKD as defined by the IRIS CKD guidelines: explore detailed assessment, treatment choices, prognosis, and client communications.
• Understand how early, and comprehensive care at each point in the Lifecycle of CKD can improve morbidity and mortality of cats with CKD
• Discern the right clinical case and timing to run an IDEXX FGF-23
Kidney biomarker evolution over time in medicine

Proteinuria
Described by Hippocrates
400 B.C.

Creatinine
Jaffe reaction
1886

Glomerular Filtration Rate
Cockcroft-Gault equation for estimating GFR in 1973

SDMA
SDMA first discovered in brain tissue 1971 (Nakama et al)
ADMA → SDMA noted to be associated with GFR clearance (Mcdermot et al 1976)

FGF-23
Identified in early 1980’s (Brown et al)
Extensive research in cancer, Vit D dysregulation, CKD, and cardiac disease.

Acute Kidney Injury
Extensive human literature from 1940’s to now. Detects both active and acute kidney injury
NGAL, VGEF, Clusterin, Inosine, mRNA, RBP…
**Veterinary adoption and application of kidney biomarkers**

- **Proteinuria**
  - UA chemistry evaluation
  - UPC ratio
  - Reference Laboratory or Point-of-Care

- **Creatinine**
  - Jaffe reaction + Enzymatic (Lab Dependent)
  - Reference Laboratory or Point-of-Care

- **Glomerular Filtration Rate**
  - "GFR not a gold, but a gold-plated standard"
  - Body size, GFR may be influenced by age, gender or breed. While some studies have demonstrated an influence of age on GFR (Quex et al, Hiac et al 2007, Bexfield, 2008)
  - Surrogate markers can represent GFR at points in time with moderate accuracy (CREA, BUN) (Gleadhill 1994, Finco et al 1995)

- **IDEXX SDMA**
  - Surrogate marker for GFR in normal and abnormal function
  - Specific use case expansion

- **IDEXX FGF-23**
  - Validated at RVC in 2013 for felines focused on CKD and phosphate reduction treatment (Finch et al 2013, Geddes et al 2013 & 2015)
  - Renal Management Marker - Launched in North America for felines with chronic kidney disease 2022

- **Acute Kidney Injury**
  - Many, many, active kidney injury markers have been investigated – primarily tubular and some glomerular
  - NGAL is a primary area of focused discovered in the 1940’s and has continued to be used in research though with limited commercial application.
  - In veterinary medicine the focus has been on NGAL, urine clusterin, Kim-1, and Cystatin B

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Level set on the importance of the kidney for daily function

- Blood pressure control
- Control of vascular volume
- Excretion of waste
- Endocrine functions
- Drug metabolism and excretion
- Acid/base balance
Kidney function is defined by GFR and the methods in which we measure it in clinical practice.

- Measure of GFR is always indirect (Iohexal, Inulin...)
- Surrogate or further indirect markers (Creatinine, SDMA, BUN)
- Urinalysis (USG) + UPC
- Electrolytes, Minerals (Ca+, Phos), Albumin, HCT
- PTH, Vit D, Aldosterone
“GFR not a gold, but a gold-plated standard”

- **60+ GFR measurement publications for cats and dogs**
  - 1991 - 2022
  - Renal & Plasma Inulin clearance
  - Creatinine Clearance
  - Plasma iohexal
  - Plasma inulin
  - Estimated GFR iohexal
  - Renal Scintigraphy

- **15+ methods of measurement**
  - N Value from 5 -97 (control & CKD/AKI)
    - *majority < 30

- **Renal Populations**: Controls CKD/AKI (natural & induced)
  - Convenience Samples
  - GFR in CKD (cats & dogs)
    - Diagnostic Capacity
    - Comparison of Surrogate markers
    - GFR + Disease + Therapy
    - GFR in AKI

There is no single protocol or methodology for measurement of GFR

Methodology can affect the results and can cause substantial differences in measured GFR
- 1.38 to 4.85 mL/min/kg for dogs
- 0.85 to 3.05 mL/min/kg for cats

Measuring GFR is often cumbersome in clinical practice
“GFR not a gold, but a gold-plated standard”

Definition for control can vary
• Clinical Healthy
• Convenience Sample
• Senior Patients (Cats)

Methodology of GFR varies
• Iohexal
• Inulin
• Scintigraphy

Methodology of surrogate marker measurement varies
• Creatinine (Jaffe versus Enzymatic)
• SDMA (LCMS, Immunoassay, ELISA)

N Value from 5 -97 (control & CKD/AKI)
*majority < 30

Renal Populations:
Controls
CKD/AKI (natural & induced)
Convenience Samples

• GFR specific (method)
• GFR & Disease State
• GFR & Disease State & Treatment

• GFR in CKD (cats & dogs)
• Diagnostic Capacity
• Comparison of Surrogate markers
• GFR + Disease + Therapy
• GFR in AKI
• Retrospective more common
My lightbulb moment for understanding GFR

Volume of blood in the animal IE dehydration or volume expansion with fluids

Rate at which blood is moving into the kidney and glomerulus IE hypertension

The size of the cat or dog IE larger has lower and smaller has higher baseline GFR
Additive value of diagnostics for the kidney function dampen the limitations of individual components

Surrogate Biomarkers
Urinalysis + Protein (UPC)
Electrolytes Mineral HCT
Repeated Evaluation “Trending”
Ultrasound CT
Fluoroscopy
Blood Pressure
FGF-23 PTH Aldosterone

To get the most consistent repeated evaluation
Subject Specific – Individualized care
Early diagnosis & intervention

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Continuum of Kidney Health
Kidney function and disease is defined by risk factors, injury, and outcomes

Risk Factors
- Breed
- Age
- Sex
- Diet
- Drugs
- Hypertension
- Metabolic Disease
- Cardiac Disease

Disease Modifiers
- Severity of AKI
- Stage of CKD
- No. of Events
- Duration of injury (AKI)
- Proteinuria


Outcomes
- Cardiovascular events
- Kidney Events
- Diminished quality and quantity of life
- Cost events
Acute Kidney Event/Insult – Recurrent versus Sustained

- Infection, Infectious Disease
- Toxicities
- Anesthesia
- Obstructive Disease (Urethral)
- Comorbidities – pancreatitis, chronic GI disease

Recurrent or Acute Kidney Events

- Infection Recurrent/unresolved
- Infectious Disease
- Toxicities – medications (NSAIDs)
- Obstructive Disease (Ureteral)
- Comorbidities – Cardiac Disease

Sustained Injury
Comorbidities or disease states can heavily impact kidney health and management.

**Heart Disease**
- NT-proBNP
- Troponin
- SDMA

**Liver disease**
- CRP
- Iron

**Gastrointestinal Disease**
- CRP
- Microbiome

**Endocrinopathy**
- Aldosterone
- PTH
- Vitamin D
- Iron

**Infectious**
- Regional infectious testing
- Leishmaniasis
- Ehrlichiosis
- Lyme Disease

**Cardiorenal or Renocardial Syndrome**
- Hepatic Disease, Congestion

**Inflammatory effect, hypoproteinemia**

**Hormone imbalance, catabolic state**
Kidney injury markers could provide a more holistic understanding of kidney health in combination with current biomarkers.

<table>
<thead>
<tr>
<th>Analyte Concentration</th>
<th>Early Disease</th>
<th>Late Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>SDMA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Creatinine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BUN</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proteinuria (multiple trajectories in disease)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>USG</td>
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</tr>
</tbody>
</table>

*support citation listed in bibliography
CKD - Lifecycle
Over the lifetime of animal key timepoint analysis could help individualize and improve patient care.
Over the lifetime of animal key timepoint analysis could help individualize and improve patient care.
The high points of CKD Diagnosis

Physical Exam
- Kidney Palpation
- Muscle Mass
- Cardiac Auscultation

Medical History
- Appetite
- Weight loss
- Energy
- Water consumption

Diagnostics: Lab work
- Chemistry
- Urinalysis

Imaging
- Radiographs
- Ultrasound

Clinical Decision Points
Biochemistry
- Trended Values
- Persistent SDMA
- Value above the reference interval

Urinalysis
- Feline 1.035 – 1.008

<table>
<thead>
<tr>
<th>OTHER</th>
<th>CYSTOCENT...</th>
<th>CYSTOCENT...</th>
<th>CYSTOCENT...</th>
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<tbody>
<tr>
<td>YELLOW</td>
<td>YELLOW</td>
<td>YELLOW</td>
<td>STRAW</td>
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<tr>
<td>CLEAR</td>
<td>CLEAR</td>
<td>CLEAR</td>
<td>HAZY</td>
</tr>
<tr>
<td>1.030</td>
<td>1.030</td>
<td>1.049</td>
<td>1.039</td>
</tr>
<tr>
<td>5.5</td>
<td>5.5</td>
<td>6.0</td>
<td>6.0</td>
</tr>
<tr>
<td>1+</td>
<td>TRACE</td>
<td>NEGATIVE</td>
<td>NEGATIVE</td>
</tr>
</tbody>
</table>

Imaging
- Radiographs
- Ultrasound

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Staging CKD using the IRIS guidelines

Diagnosis

Therapy

Stage 1 considerations:

- Can still use USG, imaging proteinuria, to diagnose just biomarkers to stage

*persistent and stable

**Stage 1**

- **No azotemia**
  - Normal creatinine

<table>
<thead>
<tr>
<th>Creatinine in mg/dL</th>
<th>Stage based on stable creatinine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canine</td>
<td>Less than 1.4 (125 μmol/L)</td>
</tr>
<tr>
<td>Feline</td>
<td>Less than 1.6 (140 μmol/L)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SDMA* in μg/dL</th>
<th>Stage based on stable SDMA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canine</td>
<td>Less than 18</td>
</tr>
<tr>
<td>Feline</td>
<td>Less than 18</td>
</tr>
</tbody>
</table>

- Blood Pressure
- Proteinuria

**Treatment:**

- Pre/Post Renal
- Comorbidities
  - UPC > 0.4 x 2
  - BP > 160 mmhg
  - Phos > 4.6
  - Free water

- Review Anesthetic Choices
  - Avoid Nephrotoxic Drugs

**Monitor**

- CREA/SDMA
- Phosphorus
- Urinalysis
- Serial Weights

Diet?
Let’s take a second to dig into the diet discussion
Stage 2 considerations:

- Can still use USG, imaging proteinuria, to diagnose just biomarkers to stage

*persistent and stable

<table>
<thead>
<tr>
<th>Blood Pressure</th>
<th>Proteinuria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood Pressure</td>
<td>Proteinuria</td>
</tr>
</tbody>
</table>

**Treatment:**
- Pre/Post Renal
- Comorbidities
- UPC > 0.4 x 2
- BP > 160 mmhg
- Phos > 4.6
- Hypokalemia
- Free water
- Review Anesthetic Choices
- Avoid Nephrotoxic Drugs

**Monitor**
- CREA/SDMA
- Phosphorus
- Urinalysis
- PCV/TS
- Serial Weights
- Diet?
Some additional Stage 2 notes

Trending:
- Phosphorus
- Potassium
- Calcium

Progressive, Irreversible
- Recheck every 6 months
- Renal Profile & PCV

<table>
<thead>
<tr>
<th>GFR</th>
<th>Early</th>
<th>Late</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1.6</td>
<td>2.8</td>
</tr>
<tr>
<td></td>
<td>18</td>
<td>25</td>
</tr>
</tbody>
</table>

- +/- Diet (early) Monitoring +/- hypertension
- Diet/Appetite HCT Phosphorus Calcium Hypokalemia Monitoring +/- hypertension
Sidebar on Managing Hypertension

**When to treat:**
- Systolic pressure >160mmHg (repeated)
- Evidence of organ damage
- Retinal Changes
- Increasing kidney biomarkers

**How to treat:**

**Hypertension Alone (no proteinuria):**
- Amlodipine (0.625mg PO Q24)
- Telmisartan (Semintra™) – off label for hypertension alone (1.5-2mg/kg/day)

**Hypertension + proteinuria:**
- Telmisartan
- Amlodipine + ACEI (Benazepril, Enalapril)

- Amlodipine maybe more appropriate for cats >200mmHg (acute presentation)
- Telmisartan increases in effectiveness over 28 days

**How to monitor:**

**Blood Pressure**
- Acute Hypertension Hospitalization:
  - Amlodipine Q2-4hrs after initial administration
  - Q12 once stabilized in hospital
  - Recheck at 48 hours post discharge

- Starting Parental Therapy
  - Amlodipine +/- ACEi 48hr-7 days
  - Telmisartan 14 and 28 days
  - Every 3-4 months

- Renal Profile
  - 2-4 weeks after starting therapy
  - Every 6 months on therapy

**How to treat:**

- Systolic pressure >160mmHg (repeated)
- Evidence of organ damage
- Retinal Changes
- Increasing kidney biomarkers

- Cardiac
- Neurologic

- Amlodipine maybe more appropriate for cats >200mmHg (acute presentation)
- Telmisartan increases in effectiveness over 28 days

**How to monitor:**

- Acute Hypertension Hospitalization:
  - Amlodipine Q2-4hrs after initial administration
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- Starting Parental Therapy
  - Amlodipine +/- ACEi 48hr-7 days
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  - Every 3-4 months

- Renal Profile
  - 2-4 weeks after starting therapy
  - Every 6 months on therapy
Sidebar on proteinuria in cats

**When to treat:**
- 2x samples > 0.4 IRIS

**How to monitor:**
- Recheck UPC 10-14 days after starting or changing
- UPC every 6 months

**How to measure UPC?**
- Uncontaminated samples are appropriate – don’t need to be pooled
- Free-catch, cystocentesis
- Microscopic blood contamination won’t affect
- UPC > 0.4, serial sample within 2-4 weeks
- 2x samples >0.4 IRIS
- Rule out: neoplasia, infectious disease
- Significant UPC >1.0 should be followed up with more haste

**How to treat:**
- Hypertension Alone (no proteinuria)
  - Benazapril
  - Telmisartan (Semintra™)
- Both are well supported by literature
- Looking for 25-50% reduction in UPC if < 2.0

**How to monitor:**
- Renal Profile
  - 2-4 weeks after starting therapy or changing therapy
  - Every 6 months on therapy

---

**Sidebar on proteinuria in cats**


As you approach Stage 3 – several categories of medication to consider

<table>
<thead>
<tr>
<th>Appetite Stimulant</th>
<th>Anti-emetic</th>
<th>Phosphate binder</th>
<th>Potassium supplementation</th>
<th>RBC stimulant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mirtazapine</td>
<td>Mirtazapine</td>
<td>Aluminum Hydroxide</td>
<td>OTC formations</td>
<td>Darbepoetin</td>
</tr>
<tr>
<td>5HT2c receptor antagonist</td>
<td>5HT2c receptor antagonist</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Capromorelin (Elura®)</td>
<td>Maropitant (Cerenia®)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ghrelin receptor agonist</td>
<td>NK-1 Emetic center, CRTZ, GI</td>
<td></td>
<td></td>
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<tr>
<td>Cyproheptadine</td>
<td>Ondansetron</td>
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</tr>
<tr>
<td>serotonin and histamine antagonist</td>
<td>5HT3 CRTZ and GI afferent</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>
Stage 3 considerations:

- **Blood Pressure**
- **Proteinuria**

### Stage 3 Moderate azotemia

<table>
<thead>
<tr>
<th>Creatinine in mg/dL</th>
<th>Canine</th>
<th>Feline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage based on stable creatinine</td>
<td>2.9–5.0 (251–440 μmol/L)</td>
<td>2.9–5.0 (251–440 μmol/L)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SDMA* in μg/dL</th>
<th>Canine</th>
<th>Feline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage based on stable SDMA</td>
<td>36–54</td>
<td>26–38</td>
</tr>
</tbody>
</table>

*persistent and stable

### Treatment:
- Pre/Post Renal
- Comorbidities
- UPC > 0.4 x 2
- BP > 160 mmhg
- Phos > 5.0
- Hypokalemia
- Free water
- Review Anesthetic Choices
- Avoid Nephrotoxic Drugs

### Monitor:
- CREA/SDMA
- Phosphorus
- Urinalysis
- Potassium
- HCT/PCV
- Serial Weights
Stage 3, managing comfort and acute on chronic events

**Maintenance**
- Appetite Stimulant
- Phosphorus
  - Food & Binders
- Potassium
  - Supplements
- Acidosis
  - Supplements

**SQ fluids**
- Case dependent
- Risk Factors
  - Cardiac
- ¼ shock dose
  - IE 5kg cat (90ml x kg)
  - 315mls so 80mls at least
- Fluid choice
  - LRS or 0.45% Nacl (+ K+)
- Exceed animal’s patience
- Quality animal owner bond

**RBC support**
- Acute on Chronic
  - Transfusion is one the best things you can do – appetite, oxygen, energy level
- Blood Transfusion
  - Type
  - pRBC, WB (4 hours)
  - Xenotransfusions
- Darbepoetin
  - If you need to transfuse you likely need to treat
  - <20% but downward trend < 30 or <25 acute presentation
Stage 4 considerations:

- **Blood Pressure**
  - **Canine**
    - Greater than 5.0 (440 µmol/L)
  - **Feline**
    - Greater than 5.0 (440 µmol/L)

- **Proteinuria**
  - **Canine**
    - Greater than 54
  - **Feline**
    - Greater than 38

**Treatment:**
- Acute on Chronic
- Comorbidities
  - UPC > 0.4 x 2
  - BP > 160 mmhg
  - Phos > 6.0
  - Hypokalemia
  - Free water
  - Review Anesthetic Choices
  - Avoid Nephrotoxic Drugs

**Monitor**
- CREA/SDMA
- Phosphorus
- Urinalysis
- Potassium
- HCT/PCV
- Serial Weights

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Nutritional and fluids support

Feeding Tube:
- Esophageal
- Gastric
IDEXX FGF-23 Feline Kidney Management Marker
Phosphorus and FGF-23 feedback loop but not a linear relationship

- Main action at kidneys
- PHOS and FGF-23 have a feedback loop
- PHOS is easily and routinely measured but slower to show disease change and influenced by other comorbidities or medications
- FGF-23 can be an earlier indication for intervention in CKD in cats

Parathyroid Hormone
Vitamin D
Calcium
Loss of renal mass, decline in GFR (CKD)

- Decrease in calcium reabsorption
- Decrease in phosphorus reabsorption

Bone remodeling

- Increase in FGF-23

Altered parathyroid signaling

- Increase in parathyroid hormone

Change in gut absorption

- Decrease in calcium reabsorption
- Decrease in phosphorus reabsorption

**Loss of GFR** leads to a **decrease in phosphorus excretion** and calcitriol production, leading to bone remodeling and **increases in circulating FGF-23**.

Mineral imbalances in calcium and phosphorus alter gut metabolism and mineral reabsorption, which further promote mineral bone disorder.

Decreased calcium absorption, a secondary increase in PTH is eventually seen, which leads to secondary renal hyperparathyroidism.

*αklotho – not mentioned here but important in signaling*
> 60% of cats may have changes in kidney function in their lifetime

Chronic kidney disease (CKD) is common in older cats and can be associated with mineral dysregulation and mineral bone disorder (MBD). Fibroblast growth factor 23 (FGF-23) is a phosphotonin peptide hormone that regulates renal phosphorus excretion and calcitriol formation. FGF-23 is a biomarker of interest in feline CKD.

Chronic kidney disease (CKD) is common in older cats and can be associated with mineral dysregulation and mineral bone disorder (MBD). Fibroblast growth factor 23 (FGF-23) is a phosphotonin peptide hormone that regulates renal phosphorus excretion and calcitriol formation. FGF-23 is a biomarker of interest in feline CKD.
What we know about phosphorus alone

Total serum phosphorus

• Serum or plasma inorganic phosphate only represents a small fraction of phosphate in the body IE not a sensitive reflection of total body stores

• Only 1% of total body phosphate (the rest in soft tissues, such as skeletal muscle)

• Especially relevant in early kidney disease where understanding phosphate management influences treatment

Total body phosphorus

• Total body phosphate is found mostly in bone (80-85%)

• Inorganic and Organic phosphate in body

• Organic phosphate is not measured by current assays

• Metabolism involves: PTH, Vitamin D, Calcium, FGF-23, Klotho and many other hormonal components
What we know about phosphorus with FGF-23

IDEXX FGF-23 renal management marker

- FGF-23 rises to control circulating “free phosphorus”
- More effective for understanding of mineral metabolism and early phosphate overload than total serum phosphorus
- Chronic kidney disease induces metabolic bone disease – dysregulation of phosphorus
- Demonstrates in cats earlier indication for phosphate overload leading to more actionable care evidence-based care.

- PTH, Vitamin D, Calcium relationship to FGF-23 in CKD
- Klotho impact and changes due to alterations in renal mass
- RAAS impact
Medical Positioning: In cats with diagnosed early IRIS stage CKD an increased FGF-23 supports starting target therapy to reduce phosphorus intake

The prevalence of CKD in cats is substantial (>60% in senior and geriatric)

Total body phosphorus measurement is often delayed in relation to cats’ medical and clinical needs.

Rising phosphorus is common in CKD, contributing to deleterious effects to the cat, causing clinical signs such as decreased appetite.

FGF-23 often identifies phosphorus overload (*CKD-MBD) in cats earlier than total phosphorus.

FGF-23 provides evidence-based medicine for dietary change in early IRIS stage CKD cats.

Diet & phosphate reduction is correlated to improved quality and quantity life for cats with CKD.
> 60% of cats may have changes in kidney function in their lifetime

Chronic kidney disease (CKD) is common in older cats and can be associated with mineral dysregulation and mineral bone disorder (MBD). Fibroblast growth factor 23 (FGF-23) is a phosphatonin peptide hormone that regulates renal phosphorus excretion and calcitriol formation. FGF-23 is a biomarker of interest in feline CKD.
When should IDEXX FGF-23 renal management marker be run?

Persistent Findings of CKD – IRIS Stage 1 or 2 Diagnosis

FGF-23 is a protein excreted in the body in response to increases in phosphorus and calcitriol.

FGF-23 can precede a rise in total serum phosphorus giving earlier insight to the need for phosphorus reduction.

Metabolic bone disease (CKD-MBD) and in totality describes a complex syndrome which involves fibroblast growth factor 23 (FGF-23), parathyroid hormone (PTH), 1,25-dihydroxy D3 (1,25 vitamin D₃, calcitriol), calcium, and phosphorus.
Elevated FGF-23 in early in feline CKD suggests mineral imbalance, phosphate overload

- CKD-MBD is not the same as CKD (chronic kidney disease – metabolic bone disease)
- MBD is likely dependent on multiple factors including CKD etiology, comorbidities, and current therapies
- The relationship between SDMA or CREA and FGF-23 is not linear
Subset of cats with early-stage CKD have elevated FGF-23

Key Takeaways

- Moderate overlap of FGF-23 in healthy cats and early-stage CKD cats
- Clear tail offers clinical insight for cats in need of therapy (phosphorus overload)

Claim: In cats with a clinical diagnosis of early CKD, elevated FGF-23 supports targeted therapies to reduce phosphorus overload.
IDEXX Feline FGF-23 ELISA at the Reference Laboratory

- Sandwich ELISA optimized for feline FGF-23
- Large biological range of FGF-23 values

**Assumption:** all samples submitted are post CKD diagnosis, feline values in this state are higher and require dilution to evaluate to upper end, we achieve this by diluting all samples 1:5
  - If we failed to dilute, highest values would be artificially low
- Precise values at low end of range are not clinically important, similar medical message
- We will report <300pg/mL for low end (limit of quantification)

Contraindications for performing:
- Systemic Inflammation
- Uncontrolled Hyperthyroidism
- Severe Anemia
### IDEXX FGF-23 reported ranges and clinical interpretations

#### Clinical Cutoffs:

<table>
<thead>
<tr>
<th>Range</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;299 pg/mL</td>
<td>Within normal limits. FGF-23 is within expected range for normal cats. For cats with IRIS Stage 1 or 2 CKD, recommend rechecking IDEXX FGF-23 in 6 to 12 months alongside kidney biomarkers to identify progressive disease or onset of phosphorus overload.</td>
</tr>
<tr>
<td>≥300-399 pg/ml</td>
<td>Borderline. This result is higher than expected for normal cats and most cats with IRIS Stage 1 or 2 kidney disease. In cats with diagnosed CKD, recommend rechecking IDEXX FGF-23 in 3 to 6 months alongside kidney biomarkers to identify onset of phosphorus overload. If indicated by clinical context and/or other kidney diagnostics, targeted therapies (such as diet changes) should be initiated.</td>
</tr>
<tr>
<td>≥400 pg/ml</td>
<td>Abnormal, elevated. Elevated result indicating phosphorus overload. Targeted therapy to reduce phosphorus levels should be added to existing CKD therapies.</td>
</tr>
</tbody>
</table>
A snapshot of how FGF-23 adds to IDEXX renal portfolio

Signalment: Neutered Male 9-year-old DLH
Presentation/PE: Senior Wellness Check, maybe increased thirst– PE no major findings
Plan: CBC, Chemistry with SDMA, UA, T4

CBC and T4: Within Normal Limits

Clinical Evidence of CKD
- PU/PD
- SDMA > 14 µg/dL x 2
- CREA > 1.6 mg/dL x 2
- USG < 1.035

BUT normal phosphorus, minimal history

SO WHAT do I suggest a diet change?
A snapshot of how FGF-23 adds to IDEXX renal portfolio

Signalment: Neutered Male 9-ear-old DLH
Presentation/PE: Senior Wellness Check, maybe increased thirst– PE no major findings
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<thead>
<tr>
<th>Chemistry</th>
<th>4/30/22</th>
<th>7/28/22</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>110</td>
<td>112</td>
</tr>
<tr>
<td>IDEXX SDMA</td>
<td>15</td>
<td>17</td>
</tr>
<tr>
<td>Creatinine</td>
<td>2.0</td>
<td>2.3</td>
</tr>
<tr>
<td>BUN</td>
<td>21</td>
<td>31</td>
</tr>
<tr>
<td>BUN: Creatinine Ratio</td>
<td>10.5</td>
<td>13.5</td>
</tr>
<tr>
<td>Phosphorus</td>
<td>3.4</td>
<td>3.2</td>
</tr>
</tbody>
</table>

CBC and T4: Within Normal Limits

FGF-23: 988 >300 pg/dL

YES, diet is warrant in this cat
Recheck in 3-6 months is recommended
Establishing individual kidney parameters can enable earlier diagnosis of CKD in cats.

FGF-23 is a renal management biomarker and run alongside kidney parameters every 3-6 months in CKD.

FGF-23 should be run after diagnosis of IRIS Stage 1 or 2 CKD in cats.
Discussion is Welcome

Thank You!

rebekah-mack-Gertig@idexx.com