Evaluation of novel ingredients for kidney and feline lower urinary tract disease (FLUTD): new findings

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Kidney disease & FLUTD:

- Kidney disease is a common cause of death in both dogs and cats & frequency increases with age
- Based on cat owner surveys, kidney disease and FLUTD (43%) were the most common feline health concerns identified by cat owners
- Both diseases have similar risk factors

Stages of chronic kidney disease (CKD) & goals of nutritional management

Stage	Serum creatinine*	Comments
1	<1.6 mg/dL	Non-azotemic
2	1.6-2.8	Mild azotemia
3	2.9-5.0	Clinical signs present
4	>5.0	Multiple clinical signs

*Cat

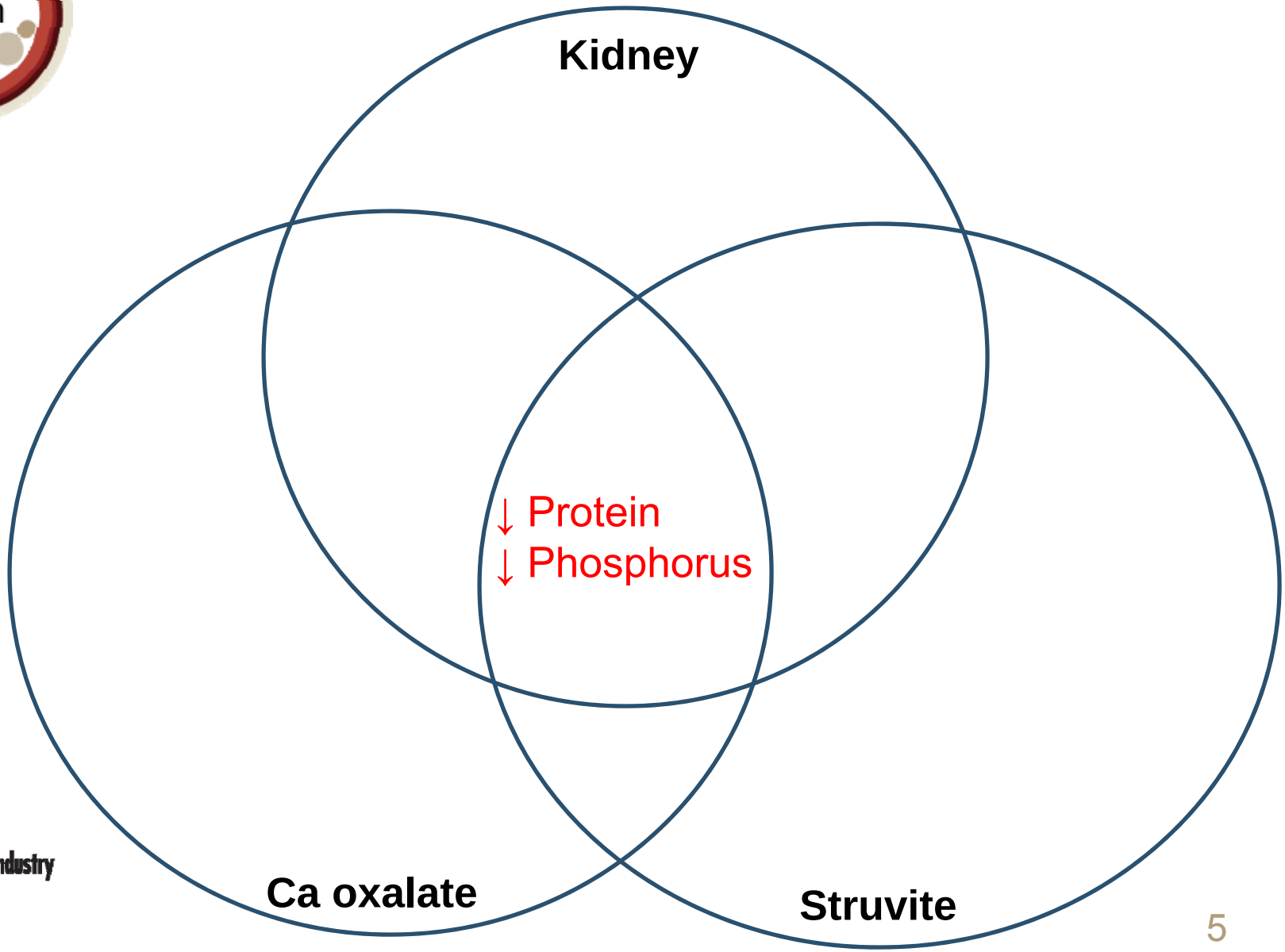
1) Control signs of uremia
2) ↓ disturbances of fluid, electrolytes & acid-base balance
3) Support adequate nutrition
4) Slow progression

Nutritional mgt of CKD & FLUTD:

- Kidney/renal
  - Decrease protein, phosphorus (P), sodium (Na)
  - Increase n3 fatty acids, potassium (K)
- Struvite (magnesium ammonium phosphate)
  - Decrease protein, P, magnesium (Mg)
  - Target urine pH (6.0-6.4)
- Calcium oxalate
  - Decrease calcium (Ca), P & oxalate
  - Target urine pH (>6.2)
  - Decrease animal protein (↑ kidney stones risk 250%*)

*Robertson et al. 1979; Curhan et al. 1996

Similar Dietary Strategies for CKD & FLUTD



Importance of a balanced diet & avoidance of nutrient excess

- Protein quality (Ideal amino acid (AA) profile) may be as important as protein quantity
- Lysine to energy ratio (mg Lys/100 kcal) & adequate calories also important
- Ash content (P, Ca, Mg, etc.) is generally correlated to protein content
- Protein source is also important
- P bioavailability is generally lower in vegetable protein vs animal protein

The "ideal protein" concept

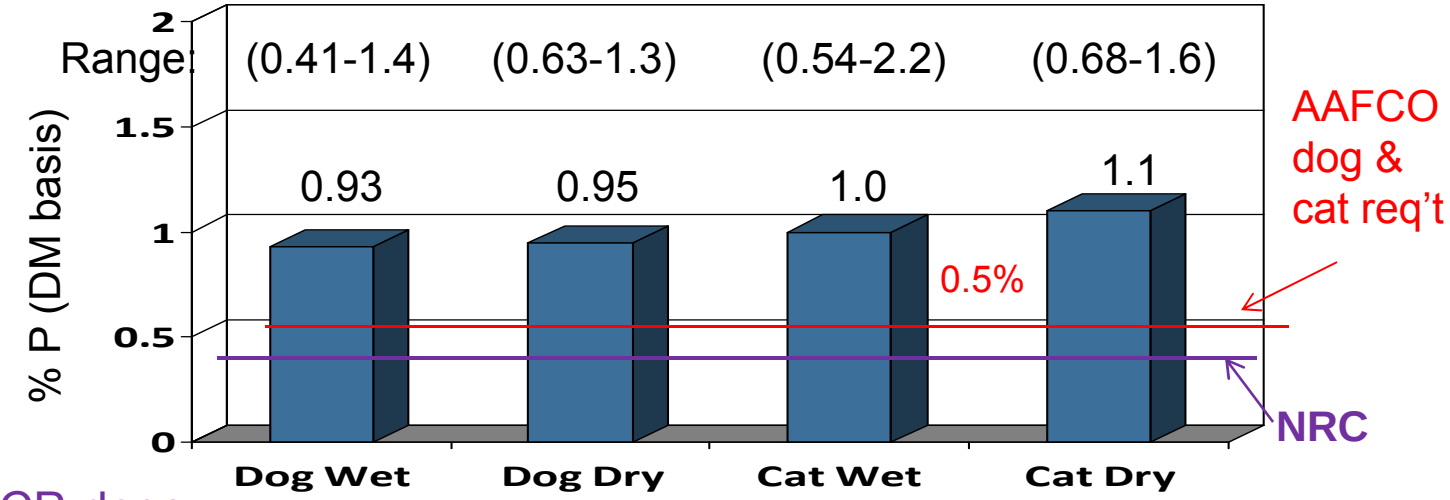
- Each species has specific needs for essential amino acid supply
- These needs can be expressed as ideal amino acid ratios
  - Relative to the AA that is typically most-limiting
  - Lysine for most mammals
- This approach published for cat, dog, pig, and chicken by Baker and Czarnecki-Maulden (1991)

Annu. Rev. Nutr. 1991. 11:239-253

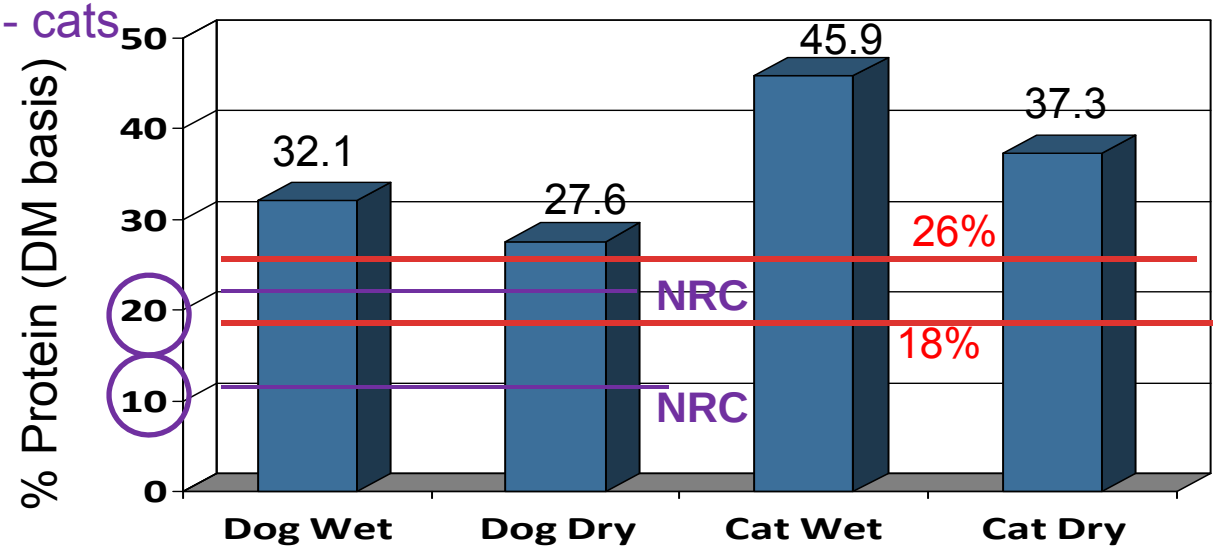
AA	Cat	Dog
Lys	100	100
Met+Cys	100	64
Trp	19	22
Thr	87	67
Arg	112	71
Ile	63	57
Val	75	75
His	38	29

Phosphorus & Protein Levels in Petfoods

Kidney diet recommended ranges: .3-.5% P



14-26% CP-dogs
28-35% - cats



Range: (18-47) (21-32) (35-59) (32-46)

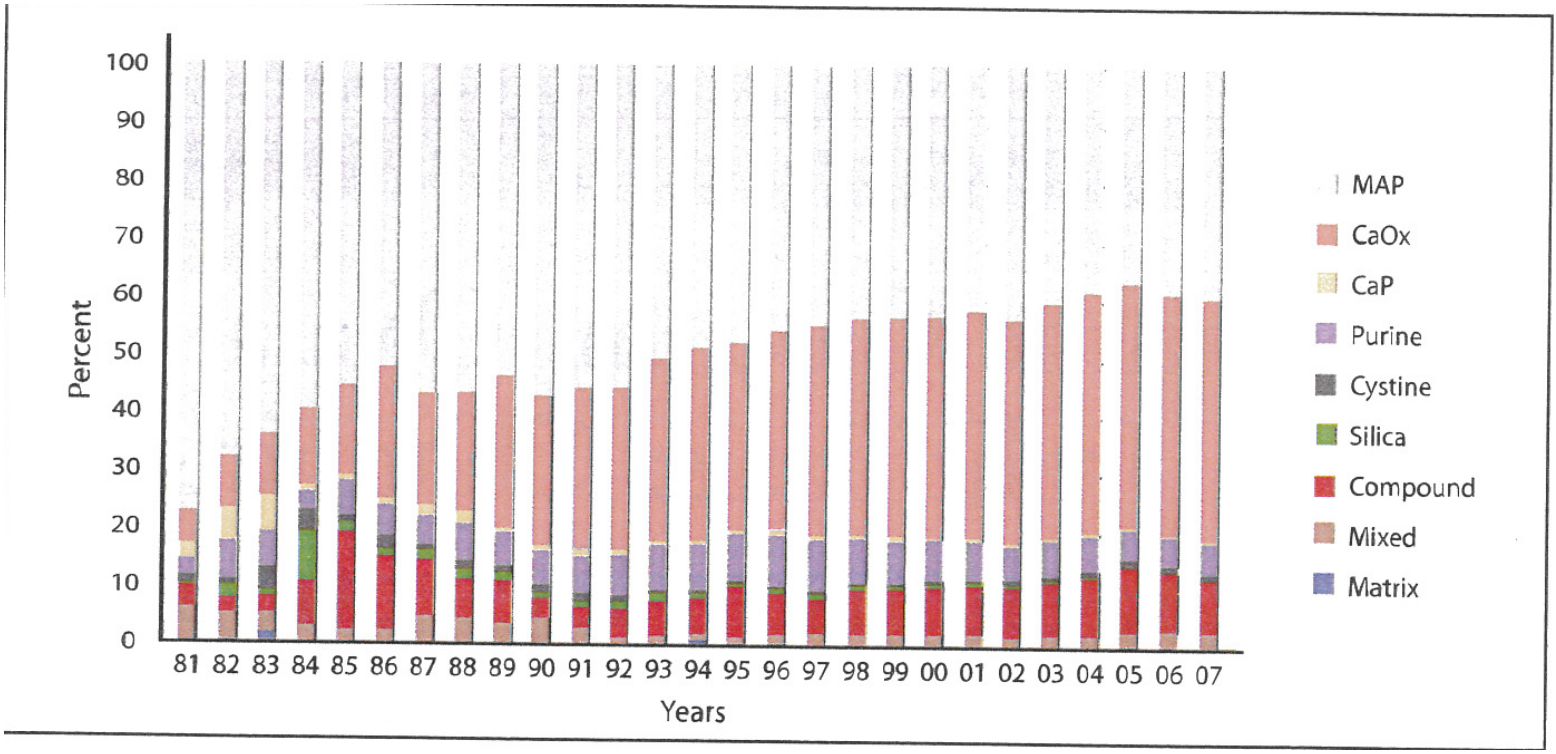
Comparison of National Kidney Foundation guidelines for maintenance dialysis patients

- 1.2-1.3 g protein/kg BW/d (≈ 13% CP for people)
- 70-90 g/d protein (60 kg BW)
- 4.64 g protein/kg $BW^{.67}$
- 19-23% CP (5 kg cat), similar to NRC minimum recommendation for CP (20%) for adult cats
- 1000 mg/d P equates to 0.19% P

- 2.5 g protein/kg BW/d (no UL DRI for humans)
(above is guideline for body-builder ≈ 26-33% CP)

AAFCO (cat)

Increased occurrence of Ca oxalate stones in dogs



- Similar pattern observed in people and cats (↑ CaOx stones)
- Inverse Ca:P ratio in people; high inorganic P intake from preservatives and additives found in processed foods & beverages

Phosphorus to Protein Ratio & P Digestibility in Petfood Ingredients

Ingredients	Protein (%)	P (%)	P-digest.* (%)	P-to-Protein ratio (%)
Animal protein				
Fishmeal	63.3	2.93	82	4.6
PBM	64.9	2.51	53	3.9
Poultry meal	64.7	1.94	62	3.0
Egg, spr. dr.	51.0	0.69	55	1.35
Egg, whole-fresh	12.2	0.18	--	1.5
Egg, yolk-fresh	16.5	0.51	--	3.1
Egg, white-fresh	10.3	0.01	--	**0.10**
Vegetable protein				
SBM-48%	47.7	0.71	48	1.5
Soy conc.-65%	65.2	0.82	48	1.3
Soy isolate-85%	84.8	0.75	48	0.9
Corn gluten meal	58.3	0.49	47	0.8

*Data from 2012 Swine NRC- total tract P digestibility

Kalantar-Zadeh et al. 2010

Evidence in cats that vegetable protein diets have renal-protective effects:

•Animal protein iodine concentrations approximately 10-fold higher than vegetable protein
•26 wk AAFCO maintenance trials with 8 healthy cats:

High vegetable protein catfood lowers serum creatinine*

Diet	Description	Initial	Wk 26	Chg
A	34% protein; 97% veg. protein	1.53	1.14	25% ↓
B	34% protein; 85% veg. protein	1.46	1.10	25% ↓

*Normal reference range = 0.8-1.8 mg/dL

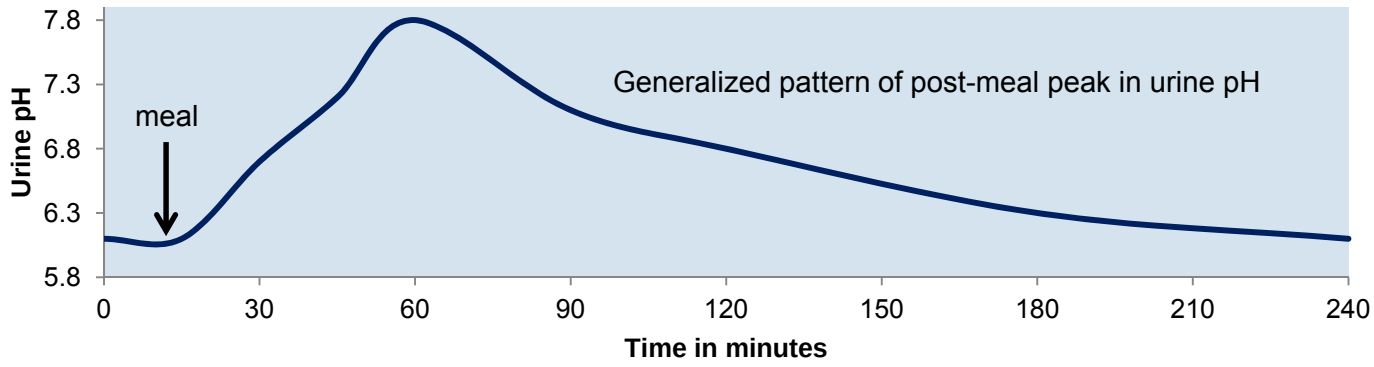
•In clinical trial evaluating efficacy of y/d prototype, observed 20% decrease in creatinine in hyperthyroid cats; many of these cats had concurrent renal/kidney disease

FLUTD- Feline Lower Urinary Tract Disease

- According to VPI Pet Insurance (USA), FLUTD is the most common reason pet owners filed a claim for their cat.
- Two most predominant uroliths or stones in cat urine are struvite (49%) & calcium oxalate (39%).
- Decreasing urine pH is the most reliable means of decreasing risk for struvite (< 6.5); for calcium oxalate, target pH is >6.2.

Urine pH fluctuates over time

- Normal healthy urine pH (fasted condition) ranges from 6 – 6.4
- Changes are driven by eating. A meal induces a spike in pH
  - Eating makes the stomach release acid internally
  - The “left over” alkaline ions are released into the blood
  - To maintain body pH, the alkaline ions are released in urine, increasing pH



Risk factors for FLUTD in cats

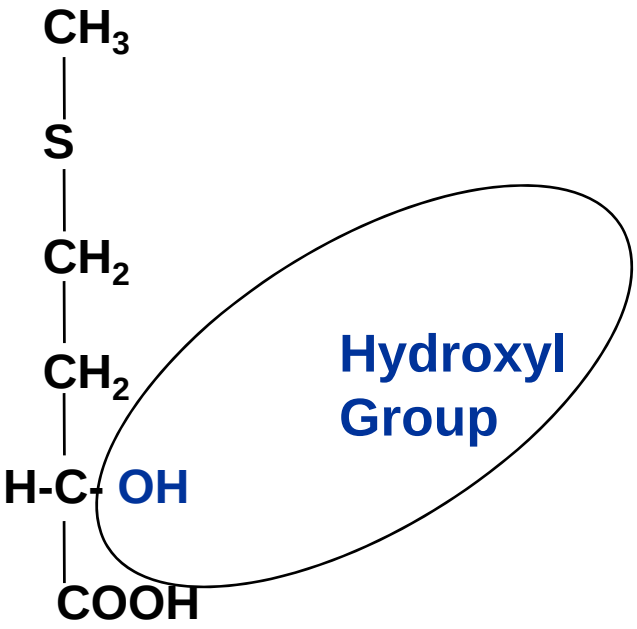
1. Urine pH
   - High pH (>6.4) allows for clumping of struvite to occur
   - Low pH (<6.0) allows for clumping of calcium oxalate to occur
2. Urine concentration (measured as specific gravity)
   - This is a measure of how much mineral the urine contains
   -- Urine with no mineral will have specific gravity close to 1.000 g/ml
   - High specific gravity is a risk because it promotes clumping
3. Residence time in the bladder
   - The longer urine remains in the bladder, the more opportunity the minerals have to find each other and clump
   - Residence time is usually increased in the fasted (non-fed) state

How to manage FLUTD in cats

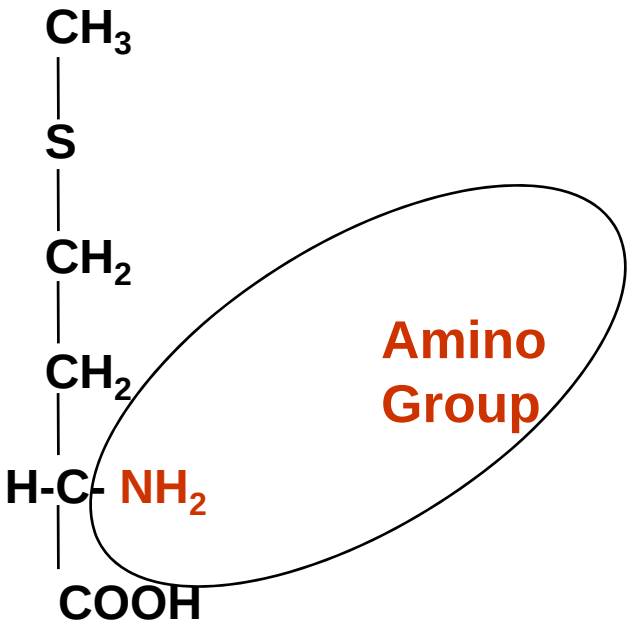
- Of the risk factors for urinary tract disease, the ones we can control the best nutritionally are
  - pH
  - Specific gravity
- Methionine has been traditionally used as a urine acidifier
  - DL-methionine (DLM)
  - DL-methionine hydroxy analog (MHA)
- Key difference between DLM and MHA
  - MHA does not contain nitrogen
  - Does not increase nitrogen load on the kidney – chronic high nitrogen loads are detrimental to health

MHA is Chemically Different

MHA



DL- Methionine



150 ← Molecular Weight → ***149***

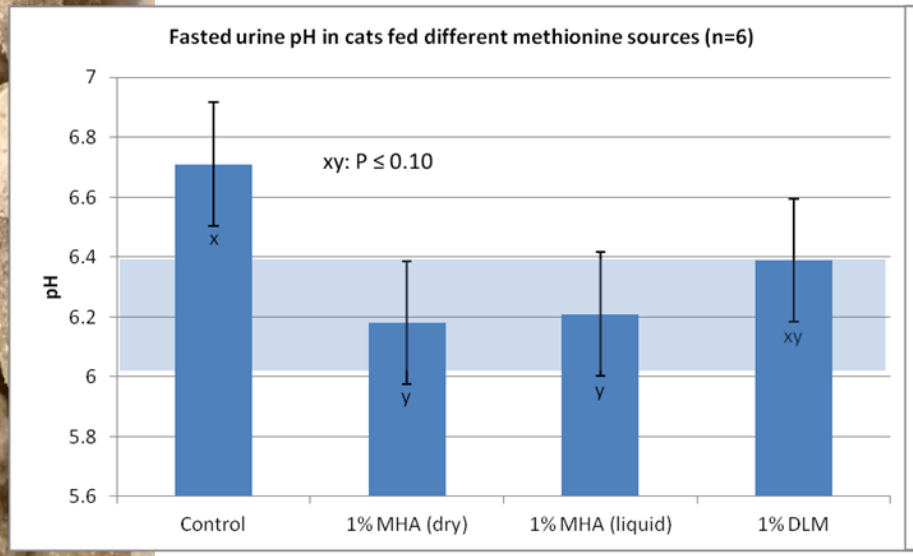
Key outcomes to look for in urine acidification

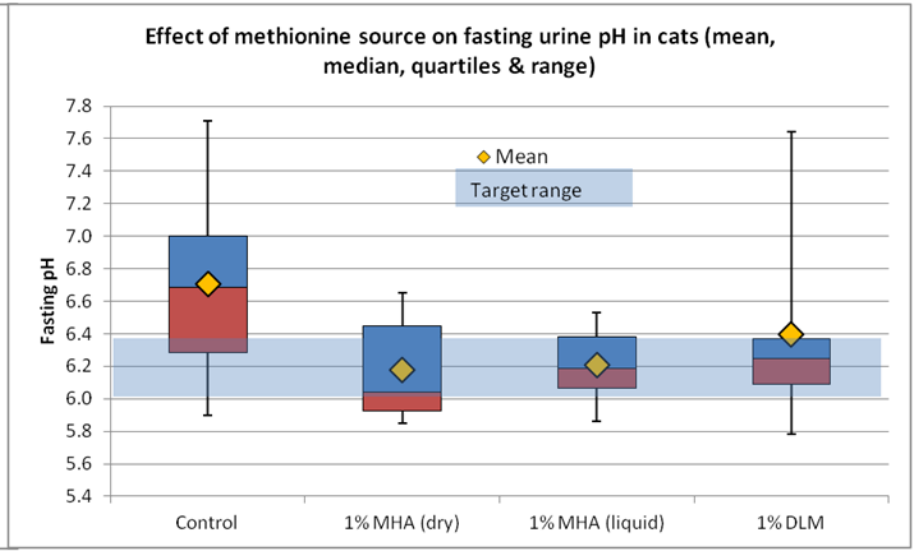
- Fasted (non-fed) urine pH, because
  - This state has a large contribution of the risk factor we cannot control (residence time)
  - Therefore we need to control the other risk factors as well as possible
- Fasted urine specific gravity, because
  - Again the contribution of residence time is significant
  - Lower specific gravity is beneficial
- What about fed state parameters?
  - They matter, too, but not as important as the non-fed parameters
  - In the fed state, residence time is usually much shorter

Feline urine pH experiment

- Dietary treatments
  1. Control diet (feline mtc food w/ chicken, corn, CGM, BR)
  2. As 1 + 1.0% methionine hydroxy analog (dry granule)
  3. As 1 + 1.0% MHA (liquid)
  4. As 1 + 1.0% DL-methionine (DLM)
- Animals
  - 24 cats (n=6 per treatment)
  - Randomly assigned
- Experimental
  - 14-day feeding
  - Fasting urine pH and specific gravity on day 7
  - Post-meal urine pH and specific gravity on day 14

Methionine source matters when controlling fasted urine pH



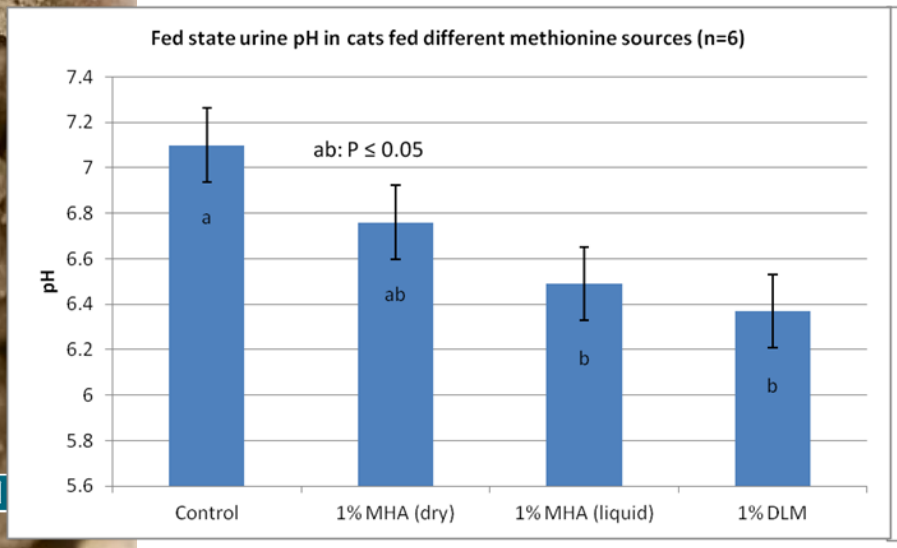


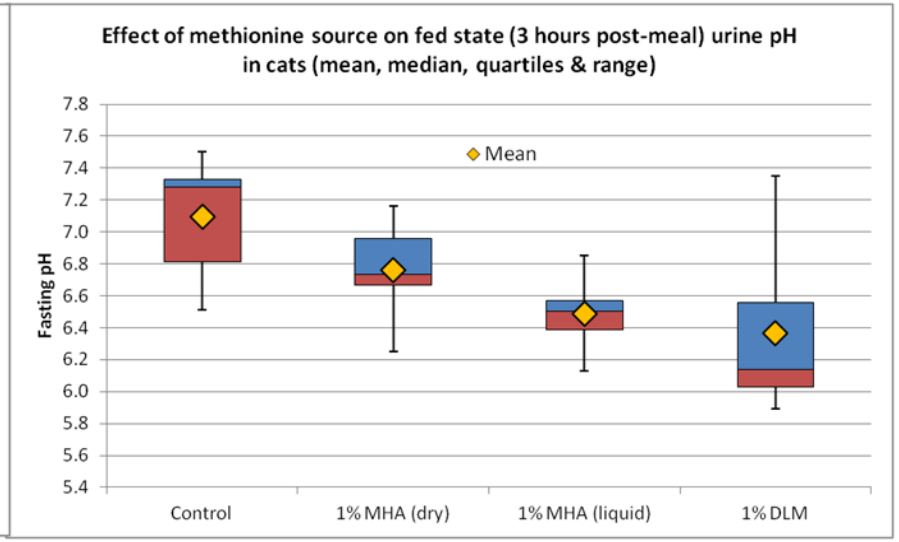
- MHA (liquid & dry) result in pH in the middle of the ideal range
  - -DLM not different from control
  - -Control is outside target range

- MHA (liquid & dry) result in much tighter pH range
  - -pH control is better for the entire population compared to DLM
  - -DLM range is similar to control

Methionine addition helps with post meal urine pH

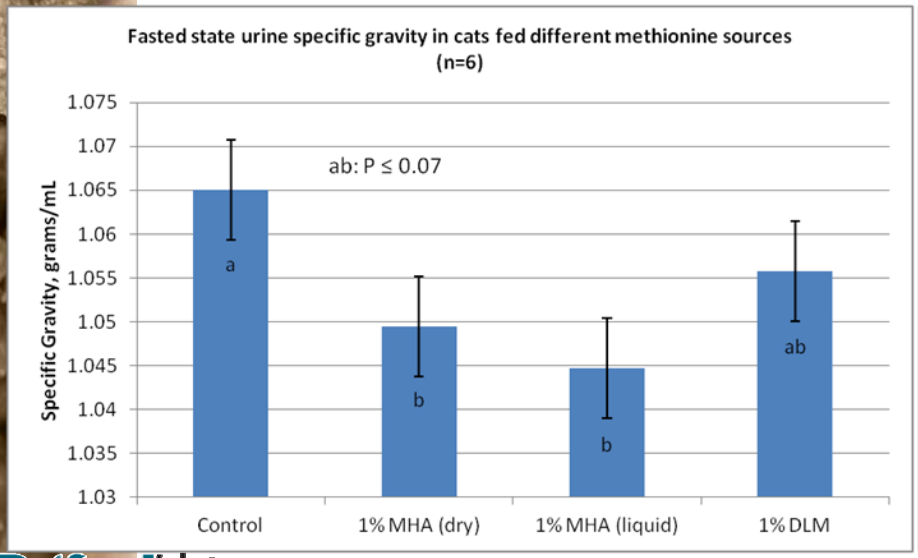
- Post meal data illustrate methionine helps
  - Post meal data more difficult to interpret
    - Meal size
    - Variability in digestion speed
    - pH recovery (where are we on the curve?)
- Post meal data still show tighter pH control with analog sources compared with DLM
  - More narrow ranges is more likely to benefit the overall population

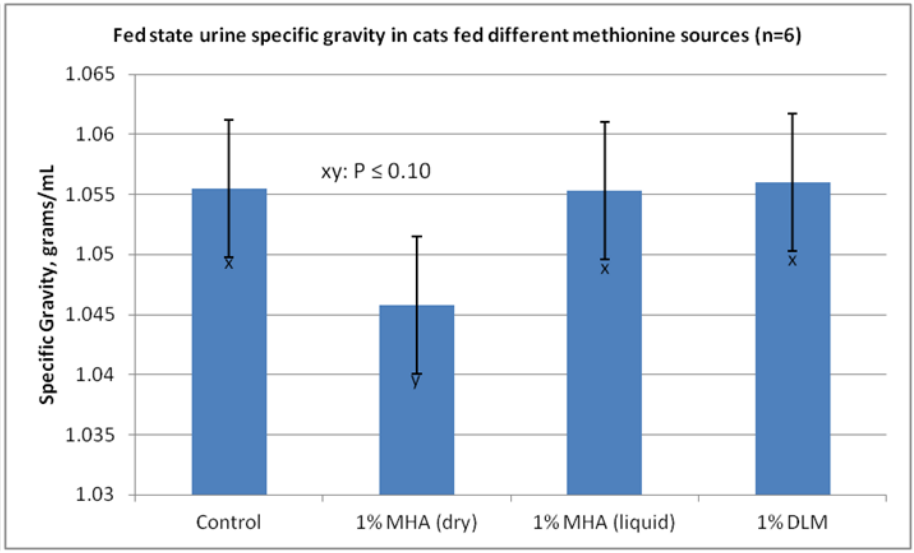




Analog methionine sources have a positive effect on urine specific gravity

- Positive effect on specific gravity most evident in fasted state
  - DLM not different from control (fed or fasted)





Summary

- Methionine helps control urine pH and urine specific gravity
  - Analog sources appear more efficacious than DLM
- Effects primarily seen where it matters, in the non-fed state
- Analog sources do not contain nitrogen, reducing excess nitrogen load on the kidney
- Analog sources are usually more economical than DLM

Summary:

- Over a dozen studies (humans & rats) have demonstrated renal-protective effects of vegetable protein (soy) & some evidence in cats supports this finding
- Egg products (whole or white) would have dual benefits in renal health: high protein quality and low P content
- Decreasing protein and minerals (P, Mg, Ca) has beneficial effects for both renal disease and FLUTD

Summary

- MHA (liquid and dry) was more effective than DLM in reducing urine specific gravity & pH and may offer other benefits to dogs and cats (e.g., anti-microbial, less toxic, lower N-load)

Thank You

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