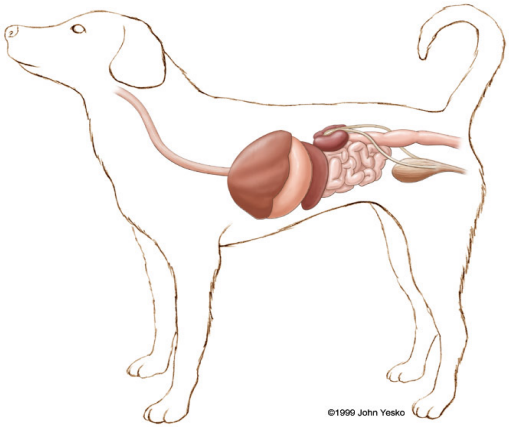
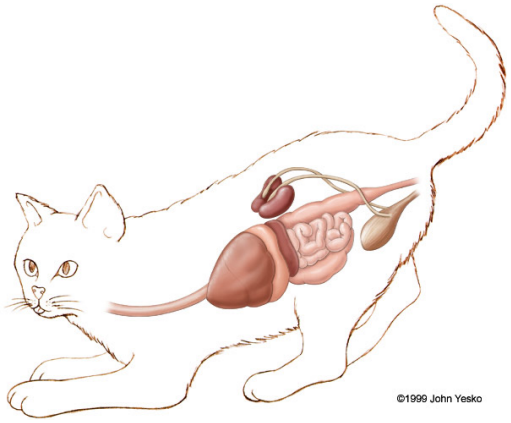

Fueling the Feline
When and how to make use of crystalline amino acids in commercial pet foods
UNIVERSITY OF GUELPH
Ontario Agricultural College

Felis catus

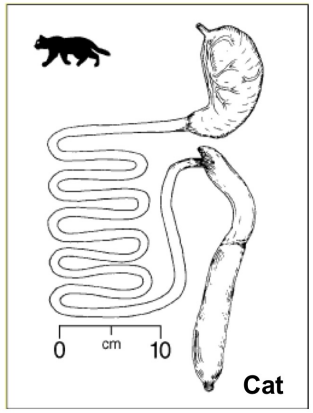
- Domestication started ~10,000 and co-dependence started ~3,000 years ago
- Key task: Hunting
- Self-domesticated as little controlled breeding and feral cats easily survive
- Domesticated from the Wildcat, *F. silverestris silvestris (European wild cat), F. silverestris lybica (African wild cat), and F. silverestris ornata*
- Obligate carnivore

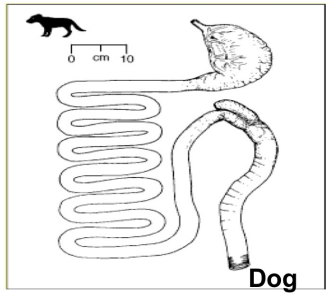


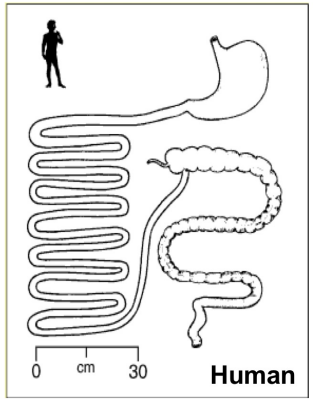


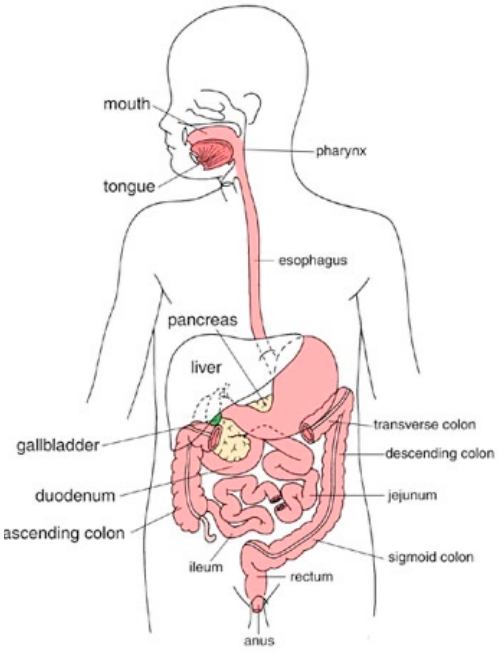
Carnivore

Omnivore









Organ	Cat	Dog	Human
Total tract transit time[1]	3,009 ± 1,220 minutes[1]	1,671 ± 513 minutes[1]	600 – 4,380 min range
Stomach	~70% digestive capacity Average pH ~ 2.5	~60% digestive capacity Fasting pH = 3.0 ± 1.4[1] Fed pH = 1.8 ± 0.3[1] *Older research suggests higher pH	~60% digestive capacity
Intestine	4x Body Length Small Intestine: 80% 15% of digestive capacity Taurodeoxycholic acid ~ 4.4 mg/mL	5x Body Length Small Intestine: 85% Large Intestine: 15% 23% of digestive capacity Taurodeoxycholic acid ~ 10.3 mg/mL	5x Body Length Small Intestine: 85% Large Intestine: 15%
Cecum	Small cecum	Small cecum	Vermiform Appendix
Colon	Short, tubular colon Unsacculated 16% of digestive capacity	Straight, tubular colon Unsacculated 13% of digestive capacity	Straight, tubular colon Sacculated
Fermentation Capacity	Some fermentation	Some fermentation	Some fermentation

[1]Tolbert MK et al. 2022, [2]Brosey et al. 2000

AA requirement terminology

INDISPENSABLE AMINO ACIDS	DISPENSABLE AMINO ACIDS
Arginine	Alanine
Histidine	Asparagine
Isoleucine	Aspartic acid
Leucine	Cysteine
Valine	Glutamic acid
Lysine	Glutamine
Methionine	Glycine
Phenylalanine	Proline
Tryptophan	Tyrosine
Threonine	Serine

Conditionally indispensable AA due to diet

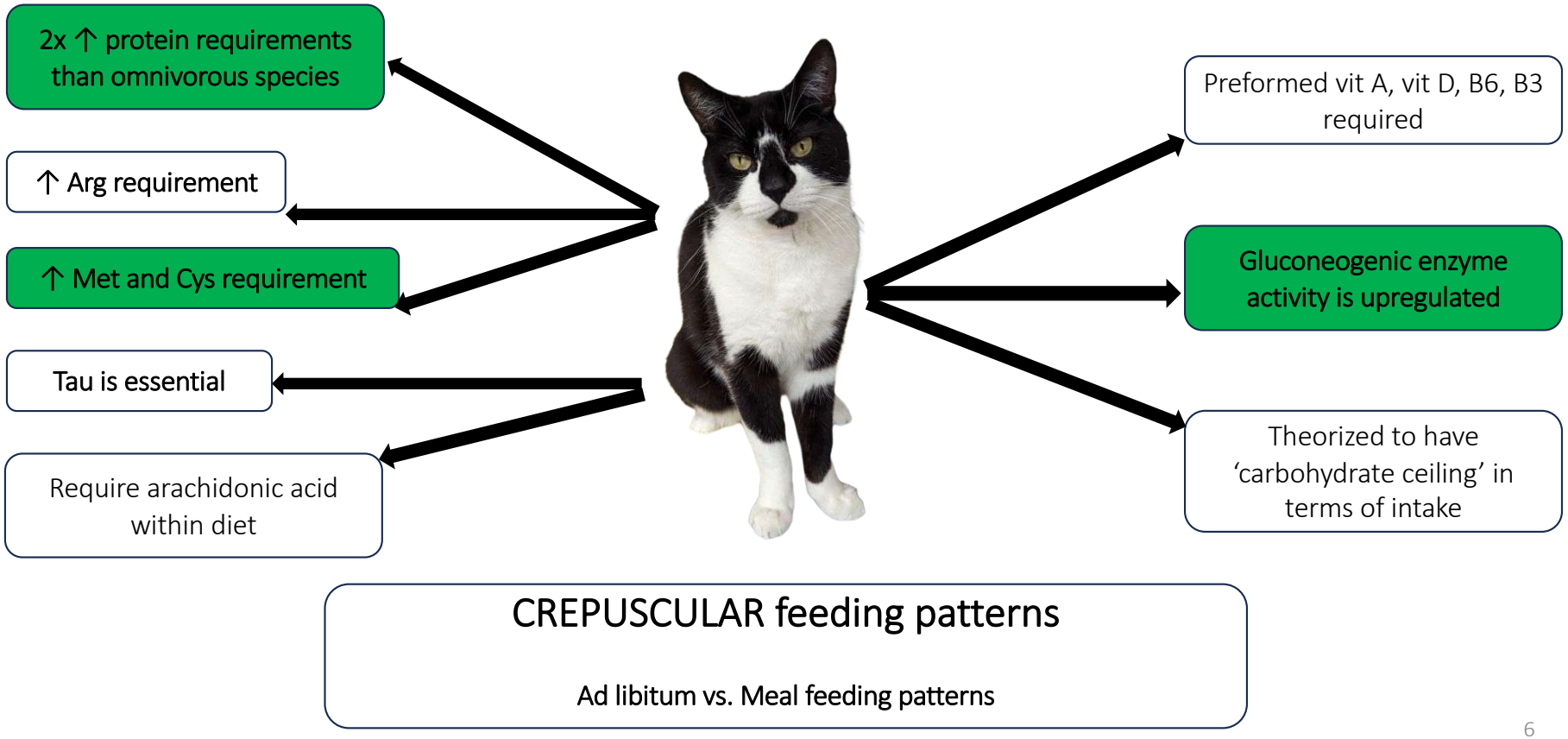
- Cysteine- TSAA
- Tyrosine- TAA

Conditionally indispensable AA due to physiological state:

Urine pH

Inflammation/infection

Feline Idiosyncrasies

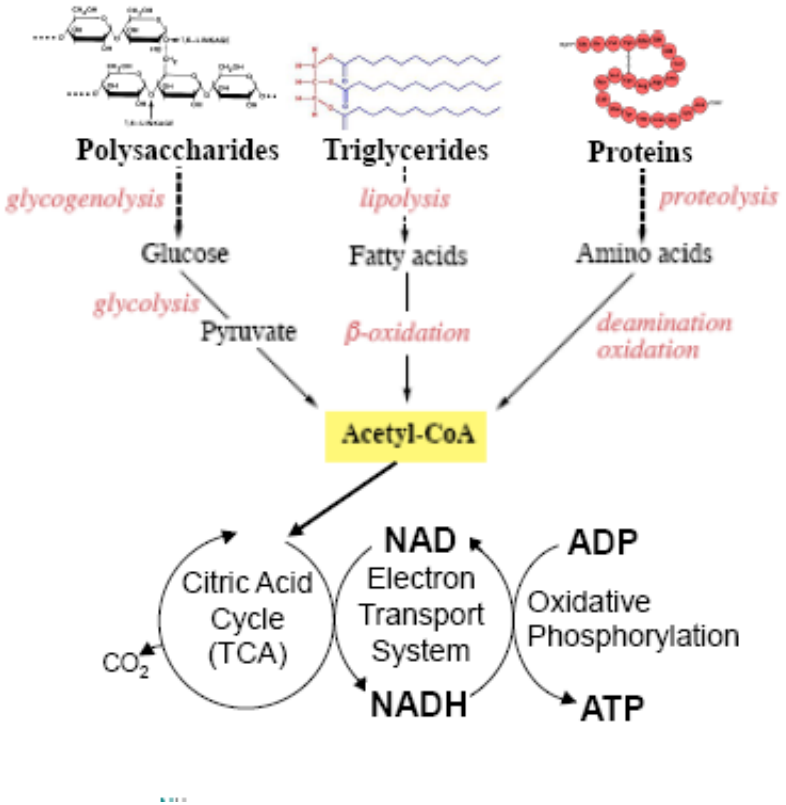


CREPUSCULAR feeding patterns

Ad libitum vs. Meal feeding patterns

Protein requirement

- Obligate carnivores cannot down regulate the enzymes that are involved in proteolysis and amino acid deamination and oxidation
- Other mammals down regulate these enzymes when they consume diets low in protein
- Kittens have ~2X the protein requirement than puppies



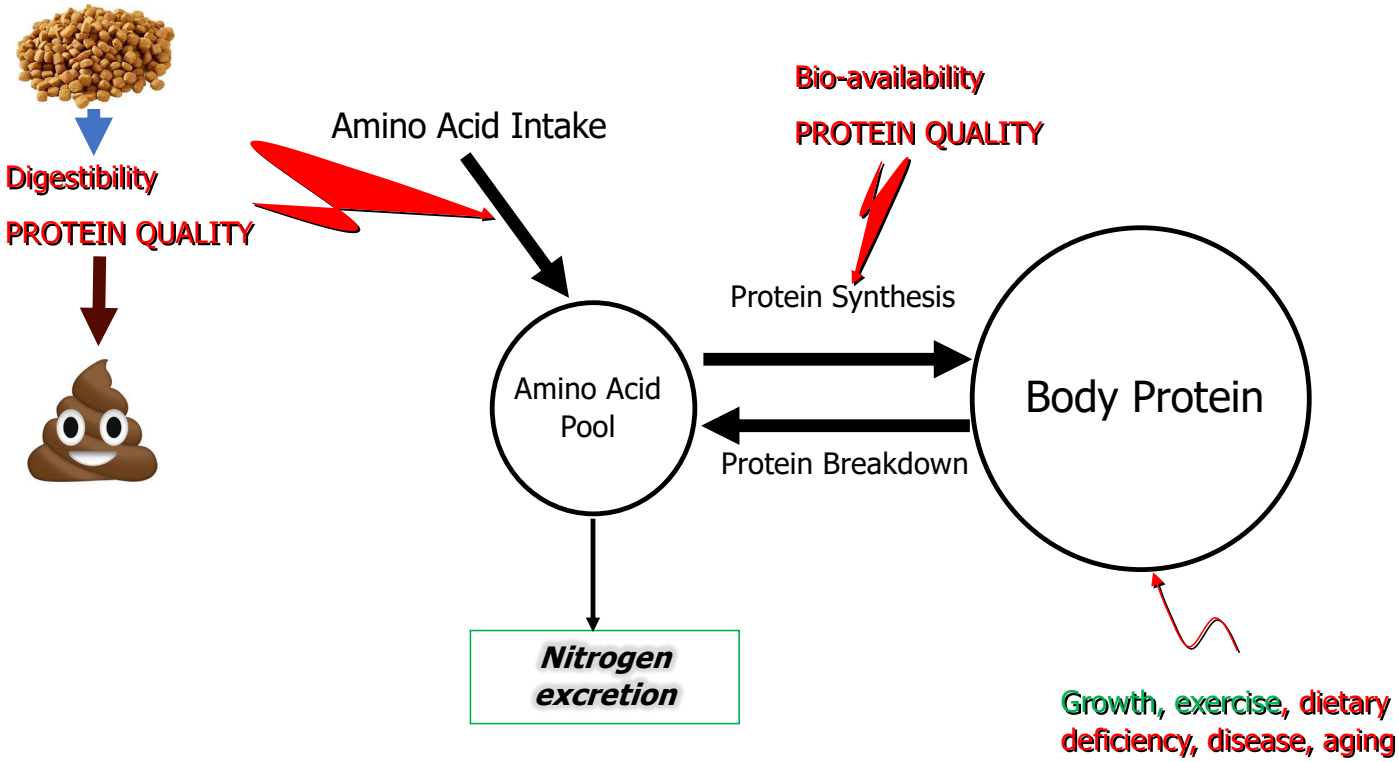
Protein quality

Protein quality is dependent upon:

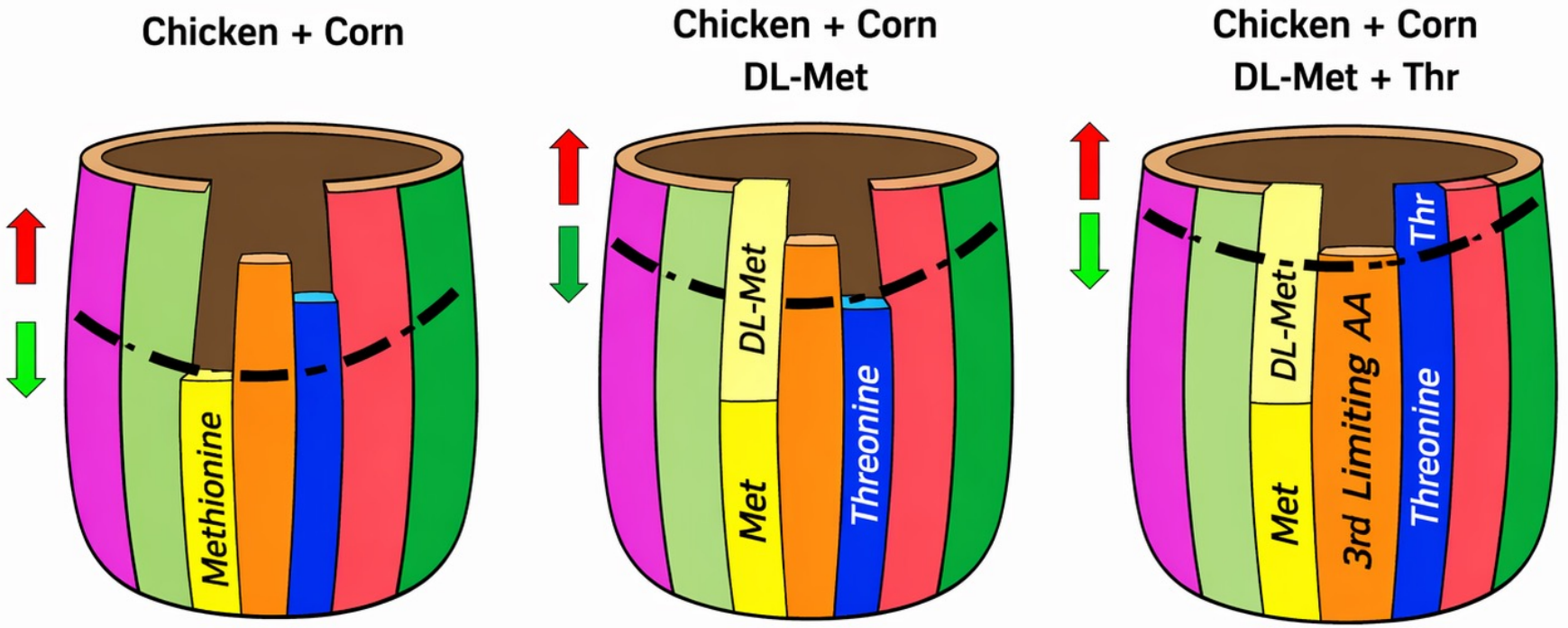
1. Protein content
2. Amino acid composition
3. Protein digestibility and amino acid availability

compared to the requirements of the species of interest.

Model of EAA metabolism and protein turnover



The limiting amino acid theory



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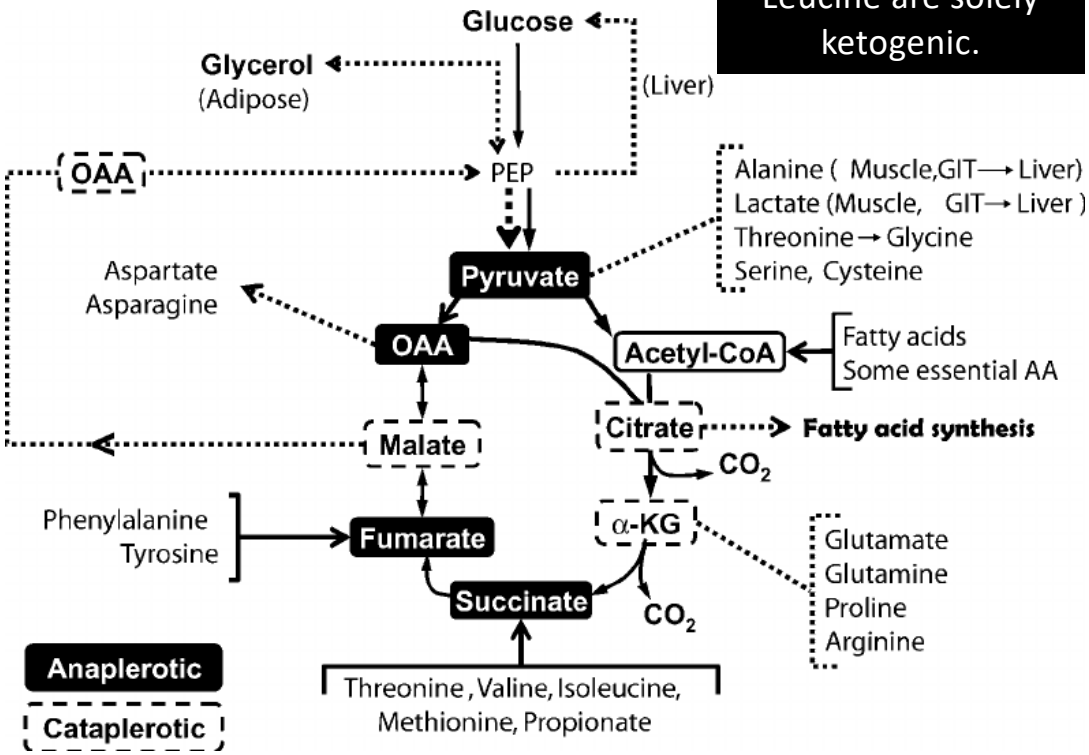
Glucose is precious and mostly self made, fundamentally affecting fuel use and energy metabolism

1) Cats have low hepatic glucokinase and limited regulation of other glycolytic enzymes
2) Cats have minimal salivary amylase and modest pancreatic amylase
3) Cats rely on gluconeogenesis, even in the fed state*
4) Protein and amino acids become the main substrate for glucose production, which is energetically costly *
5) Fat is preferred and rapidly used *

Only Lysine and Leucine are solely ketogenic.



Bequette et al. 2006. Application of stable isotopes and mass isotopomer distribution analysis to the study of intermediary metabolism of nutrients. Journal of Animal Science. 10.2527/2006.8413_supplE50x

Suggested minimum protein in the single format diets (% of diet on a DM basis)

	NRC[1]	AAFCO[2]	FEDIAF[2]
Cats			
Adult maintenance	20%	26%	25%
Growth and reproduction	21.3%	30%	28/30%

[1]Presumes an energy density of 4000 kcal ME/kg

[2]Presumes typical MER of 100 kcal * kg $BW^{0.67}$

*NRC Recommended allowance for adult cats for maintenance= 4.96 g/kg $BW^{0.67}$)

Let’s check our math

If we feed an ideal weight adult cat (5 kg as an example) to its energy requirement, would they meet their protein requirement being fed 20% CP (4,000 kcal ME/kg)?

100 kcal * kg $BW^{0.67}$

= 293 kcal ME

~73 g of food providing 14.7 grams of CP

CP requirement of lean adult cats =4.97 g * kg $BW^{0.67}$

= 14.6 grams of CP

Animal derived proteins result in greater nitrogen retention than vegetable proteins when fed to cats, but CGM resulted in lower urine pH, struvite activity products, and struvite crystals

Variable	MM	CM	CGM
N (g/kg of BW/d)			
Intake	0.64 ± 0.06	0.65 ± 0.05	0.66 ± 0.07
Feces	0.06 ± 0.01[b]	0.09 ± 0.01[a]	0.09 ± 0.01[a]
Urine	0.47 ± 0.06	0.48 ± 0.04	0.48 ± 0.04
Absorbed	0.57 ± 0.06	0.56 ± 0.05	0.57 ± 0.06
Retained	0.10 ± 0.02	0.08 ± 0.03	0.08 ± 0.05
Percentage of N intake			
Feces	10.0 ± 4.0[b]	14.0 ± 3.9[a]	14.1 ± 6.2[a]
Urine	73.6 ± 0.5	74.7 ± 0.5	75.6 ± 0.8
Absorbed	90.0 ± 4.0[a]	86.0 ± 3.9[b]	85.9 ± 6.2[b]
Retained	16.4 ± 3.9[a]	11.3 ± 4.0[a,b]	10.3 ± 6.4[b]
Percentage of N absorbed			
That was retained	18.3 ± 4.4	13.1 ± 4.6	11.8 ± 7.3

BW — Body weight

[a,b,c] Mean values which do not have a common letter in their superscripts differ at a significance level of $P < 0.05$

Funaba et al, Can J Vet Res. 2005; 69: 299-394.

Considering differences among the protein and AA provision for ingredients

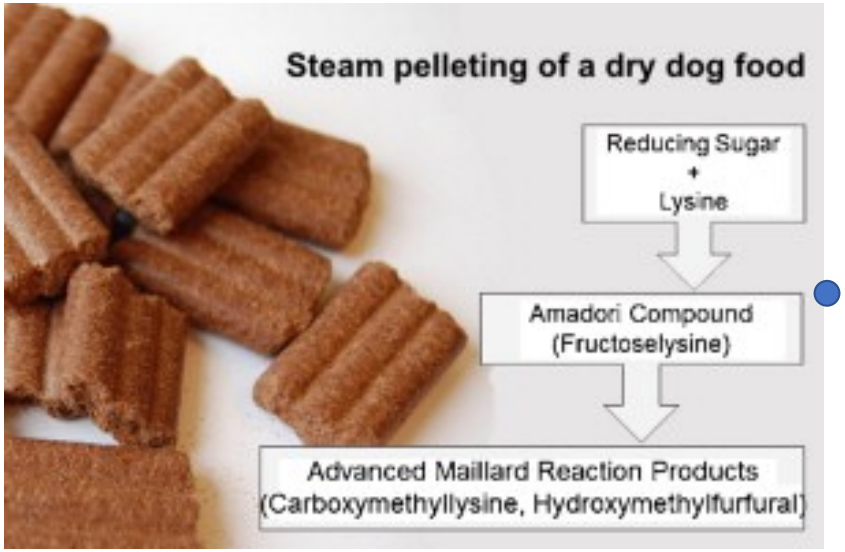
	Meat Meal	Chicken Meal	Corn Gluten Meal	Adult Cat requirement
CP (g/100g)	50	65	60	25
Arginine (g/100g)	3.5	4.8	1.8	1.07
Histidine (g/100g)	1.2	1.5	1.5	0.33
Isoleucine (g/100g)	1.8	2.5	3.5	0.54
Leucine (g/100g)	3.5	4.2	10.5	1.28
Lysine (g/100g)	2.5	3.8	0.9	0.85
Methionine (g/100g)	0.7	1.2	2	0.34
Cysteine (g/100g)	0.5	0.6	1	0.51
Phenylalanine (g/100g)	2	2.3	4.5	0.63
Tyrosine (g/100g)	1.5	1.8	3.8	0.63
Threonine (g/100g)	1.8	2.4	1.7	0.6
Tryptophan (g/100g)	0.3	0.5	0.3	0.2
Valine (g/100g)	2.5	3	4	0.68

FEDIAF adult cat maintenance amino acid recommendations on a diet basis (g/100 g DM) from the 2024 guidelines

Protein quality

$$\text{DIAAS} = \frac{(\text{mg digestible IAA / 1 g test ingredient crude protein})}{(\text{mg of same IAA / 1 g reference protein})} \times 100$$

Reference patterns? What happens when those are not accurate?



Van Rooijen et al. 2014

Analytical accuracy of measurements of AA in forms that mammals can utilize or compounds that may metabolically, but not digestively alter the use of AA for protein synthesis

Enabling calculations of protein quality …

> J Anim Sci. 2022 Nov 1;100(11):skac279. doi: 10.1093/jas/skac279.

Digestible indispensable amino acid scores of animal and plant ingredients potentially used in dog diet formulation: how this protein quality metric is affected by ingredient characteristics and reference amino acid profile

James R Templeman [1], Anna K Shoveller [1]

Affiliations + expand

PMID: 36029066 PMCID: PMC9624197 DOI: 10.1093/jas/skac279

Free PMC article

Mitacs

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Protein quality without digestibility correction

DIAAS – **LIKE**

Or AA Score

$$= \frac{(\text{mg IAA / 1 g test ingredient crude protein})}{(\text{mg of same IAA / 1 g reference protein})} \text{ x } 100$$

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Comparing protein quality scores

	Meat Meal	Chicken Meal	Corn Gluten Meal
Arginine	164	173	70
Histidine	182	175	189
Isoleucine	167	178	270
Leucine	137	126	342
Lysine	147	172	44
Methionine	103	136	245
Cysteine	49	45	82
Phenylalanine	159	140	298
Tyrosine	119	110	251
Threonine	150	154	118
Tryptophan	75	96	63
Valine	184	170	245

Suggested minimum total sulfur amino acid (TSAA) requirement in single format diets (% of diet on a DM basis)

	NRC[1]	AAFCO[1]	FEDIAF[2]
Cats			
Adult maintenance	0.34%	0.65%	0.85%

[1]Presumes an energy density of 4000 kcal ME/kg

[2]Presumes typical MER of 100 kcal * kg $BW^{0.67}$

*NRC Recommended allowance for adult cats for maintenance= 4.96 g/kg $BW^{0.67}$)

Let’s check our math

If we feed an ideal weight adult cat (5 kg as an example) to its energy requirement we will feed them 73 g of food and let’s assume that food contains 0.65% Met + Cys. Would they meet their total sulfur amino acid requirement?

~73 g of food providing 0.65% total sulfur AA with methionine providing 0.45%. **Methionine is the precursor cysteine, so methionine can supply the whole TSAA requirement and cysteine can “spare” or reduce the requirement for methionine.**

= 0.48 g Met+Cys

Total sulfur amino acid requirement of lean adult cats =0.076 g * kg BW

= 0.38 grams of Met+Cys

But people may restrict food to elicit weight loss

If we feed an overweight adult cat (6.5 kg, but ideal BW is 5 kg as an example) to 30% below its energy requirement we will feed them 55 g of food the same food (0.65% Met + Cys). Would they meet their total sulfur amino acid requirement?

~51 g of food providing 0.65% total sulfur AA with methionine providing 0.45%.

= 0.33 g Met+Cys

Total sulfur amino acid requirement of lean adult cats =0.076 g * kg BW

= 0.38 grams of Met+Cys

Grant *et al. BMC Veterinary Research* (2020) 16:426
https://doi.org/10.1186/s12917-020-02649-0

BMC Veterinary Research

RESEARCH ARTICLE Open Access

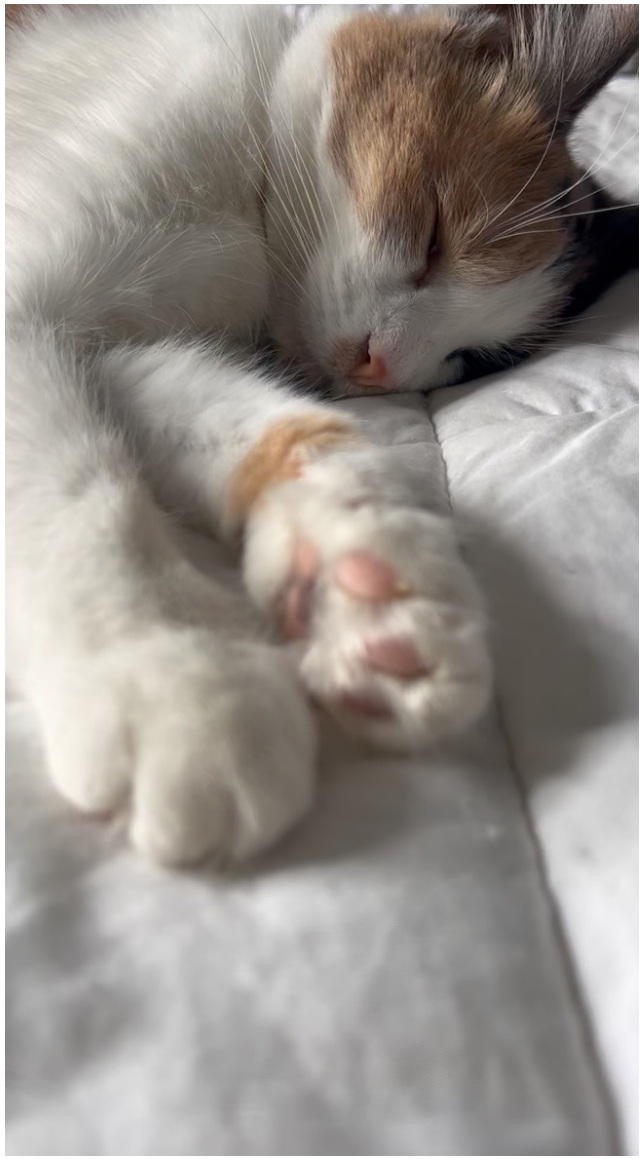
Dietary intake of amino acids and vitamins compared to NRC requirements in obese cats undergoing energy restriction for weight loss

Caitlin E. Grant[1], Anna K. Shoveller[2], Shauna Blois[1], Marica Bakovic[3], Gabrielle Monteith[1] and Adronie Verbrugghe[1*]

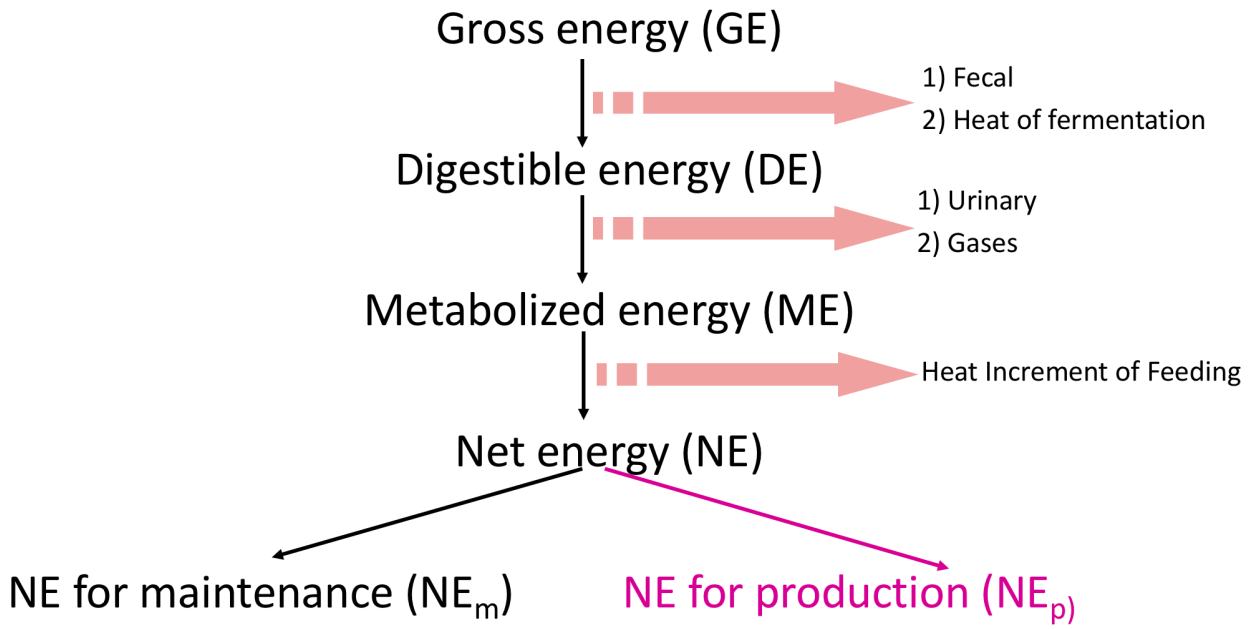
- *Cats were fed a therapeutic weight loss diet optimized for food restriction and **37% CP***
- *The optimal nutrient intake during energy restriction is not known, however some nutrients of concern have been identified in the present study and warrant further investigation*

Formulation guidance

- When you are formulating low protein diets, you must ensure that your digestible amino acid intakes are met
- To achieve this you can use protein sources that are highly digestible and of good quality, which are generally animal based ingredients with high digestibility.
- Using plant-based ingredients requires multiple ingredients to be used to “compliment” the amino acid profile OR the use of individual amino acids to ensure that all indispensable amino acid requirements are met or exceeded.
- Diets where all the indispensable amino acids are far above requirement will meet amino acid and nitrogen requirements and the excess amino acids will be utilized



Mammalian Energy Digestion and Metabolism



Net energy (NE)

$$NE = \frac{(energy\ intake - energy\ in\ feces - energy\ in\ urine - HIF) * 100}{energy\ intake}$$

- **Net energy for maintenance (60-70%)**
  - Basis of energy requirement recommendations to support basal metabolism in animal at rest, in a post absorptive state and thermo-neutral environment
- Net energy for production (up to 30%)

Whole body energy balance

Balance= energy ingested – energy lost

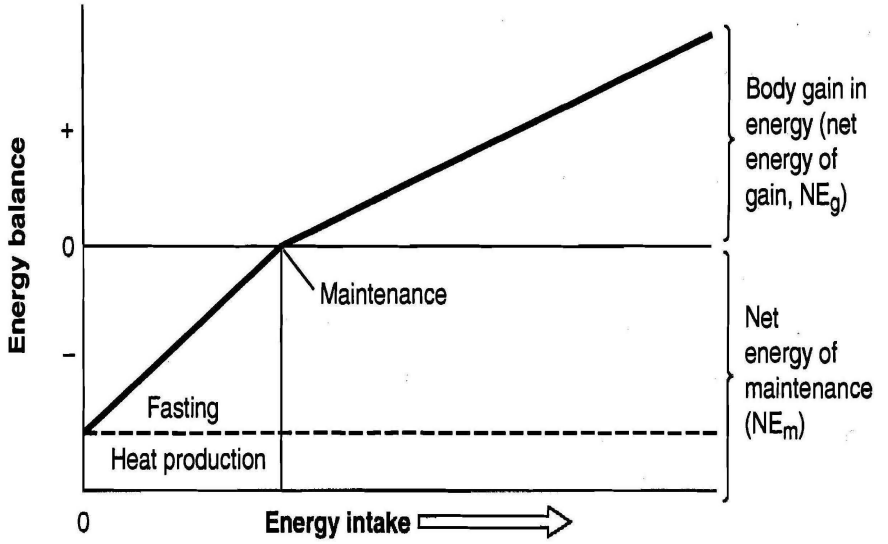


FIGURE 4.1. Illustration of the effect of energy intake on energy balance.

Davis and Drackley, 1998

Increasing dietary CP results in increases all types of energy available to the cat

Diet	23CP	25CP	26CP	29CP	36CP	41CP	SED	Linear *P*
GE (kcal/d)	299^{abc}	292^{a}	296^{ab}	300^{abc}	312^{c}	308^{bc}	5.07	<0.01
DE (kcal/d)	153^{a}	166^{ab}	169^{ab}	180^{b}	223^{c}	201^{bc}	24.0	<0.01
ME (kcal/d)	119^{a}	124^{ab}	129^{b}	130^{b}	170^{d}	148^{c}	20.8	0.02
NE (kcal/d)	89^{a}	95^{b}	115^{bc}	121^{c}	140^{d}	123^{c}	19.9	0.01

petcurean

NSERC CRSNG

Gluconeogenesis is constant

Brain glucose demand supported by gluconeogenesis in cats

Fed respiratory quotient in cats remain within 0.75-0.85 range

REVIEW

Hypercarnivory and the brain: protein requirements of cats reconsidered

Regina Eisert

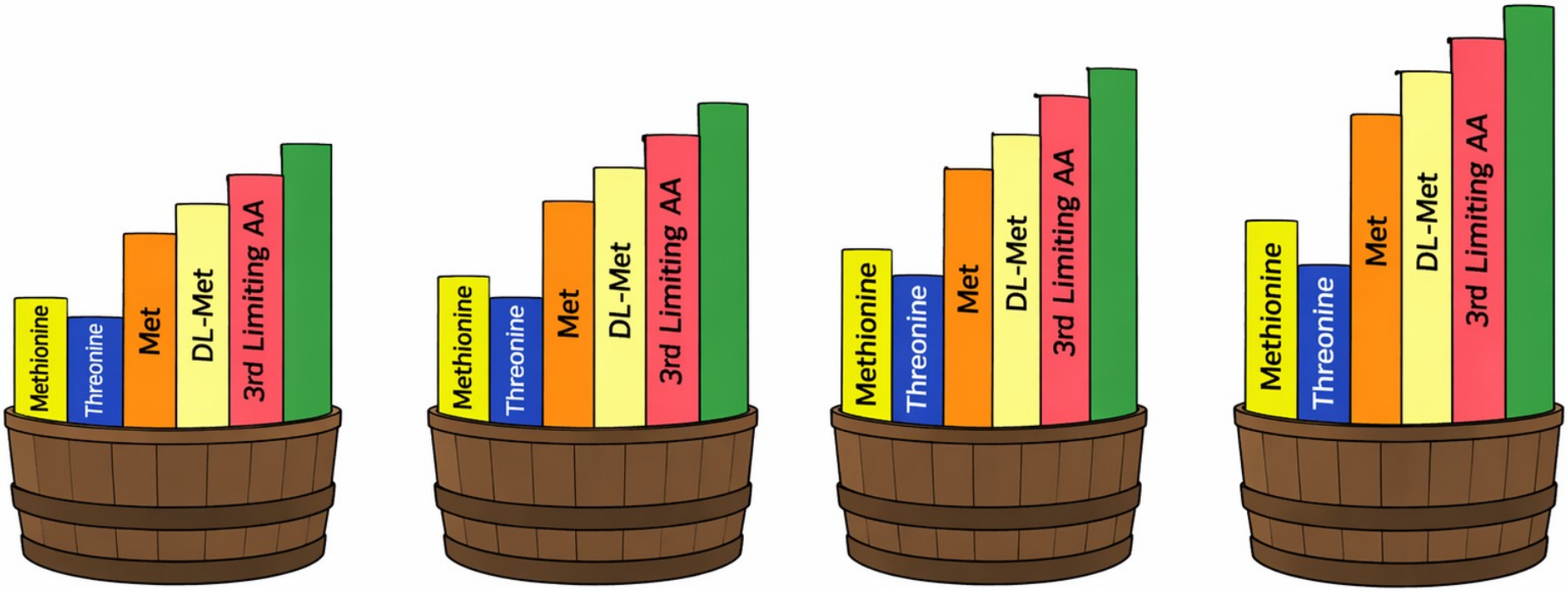
Oxygen consumption (VO_2), carbon dioxide production (VCO_2), heat of combustion ($-\Delta H_c$), and respiratory quotient (RQ) for amino acids and conventional food protein (modified and calculated from Livesey and Elia, 1988).

Oxidised substrate	VO_2 (l/g)	VCO_2 (l/g)	$-\Delta H_c$ (kJ/g)[1]	RQ
Alanine	0.75	0.63	18.28	0.83
Aspartic acid	0.50	0.59	11.25	1.17
Asparagine	0.51	0.51	11.37	1.00
Glutamic acid	0.69	0.69	14.99	1.00
Glutamine	0.69	0.61	15.11	0.89
Glycine	0.45	0.45	11.47	1.00
Proline	1.07	0.88	24.84	0.82
Serine	0.53	0.53	13.00	1.00
Cysteine	0.83	0.47	20.05	0.56
Tyrosine	1.18	1.05	25.27	0.89
Isoleucine	1.28	0.94	28.81	0.73
Leucine	1.28	0.94	28.82	0.73
Lysine	2.15	1.52	23.79	0.71
Methionine	1.13	0.68	25.34	0.60
Phenylalanine	1.36	1.15	29.44	0.85
Threonine	0.75	0.66	17.16	0.88
Tryptophan	1.32	1.09	26.86	0.83
Valine	1.15	0.86	26.26	0.75
Arginine	0.71	0.52	15.83	0.73
Histidine	0.72	0.65	17.64	0.90
Conventional food proteins			17.43-21.15	0.81-0.87

[1] Corrected for heat of combustion of urinary urea.

Diets	23CP	25CP	26CP	29CP	36CP	41CP	SED[1]	P Value
								Linear
RQ_{fasted}	0.774	0.775	0.777	0.778	0.768	0.764	0.01	0.06
$RQ_{total\ postprandial}$	0.828^{c}	0.816^{bc}	0.815^{bc}	0.807^{ab}	0.805^{ab}	0.799^{a}	0.01	<0.01

High protein diets



Increasing use of AA for GNG and with **greater** energetic efficiency

Summary of protein energetics

- Current AAFCO calculations for ME density underpredict energy density (kcal ME/kg)
- Energy efficiency positively related to dietary CP
  - **Big watch out for high protein diets in cats prone to weight gain and for feeding guidelines**
- Cats rely on protein for glucose, but dietary carbohydrate content is also related to satiety and gut health
- Need research to understand if protein efficiency and dietary protein intake are positively correlated in energy restriction

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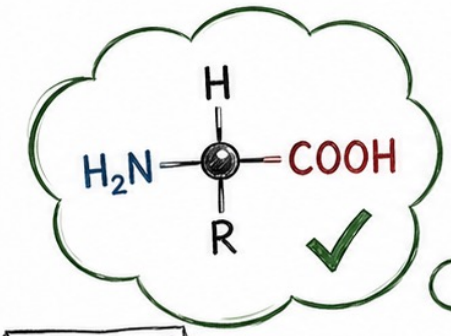
Amino acid supplementation cases in Cat food: Fact or fiction?



- ☑ Essential nutrients
- ☑ Support health
- ☑ Formulated with purpose

- ☒ Overhyped claims
- ☒ Instant miracles
- ☒ Lack of evidence

Science over myths. Nutrition over noise.

Efficacy of oral supplementation with L-lysine in cats latently infected with feline herpesvirus

David J. Maggs, BVSc; Mark P. Nasisse, DVM; Philip H. Kass, DVM, PhD

Primary conjunctival inoculation with FHV-1 of 14 young adult cats and viral reactivation on day 15 of L-lysine supplementation

400 mg of L-lysine per day for 30 days

Clinical signs and viral shedding by PCR and plasma AA

Results: Delayed clinical signs by 7 days and fewer shedding episodes; plasma lysine greater after meal eating and no effect on arginine concentrations.

TWO clinical studies: Both with phenotypic positive outcomes.

Effect of oral administration of L-lysine on conjunctivitis caused by feline herpesvirus in cats

Jean Stiles, DVM, MS; Wendy M. Townsend, DVM; Quinton R. Rogers, PhD; Sheryl G. Krohne, DVM, MS

Primary conjunctival inoculation with FHV-1 6 hours after first supplementation

500 mg of L-lysine per day for 21 days

Clinical signs and viral shedding by PCR and plasma AA

Results: Less manifestations of conjunctivitis in Lys; plasma lysine greater after meal eating and no effect on arginine concentrations.

Bol and Bunnik *BMC Veterinary Research* (2015) 11:284
DOI 10.1186/s12917-015-0594-3

BMC
Veterinary Research

RESEARCH ARTICLE Open Access

Lysine supplementation is not effective for the prevention or treatment of feline herpesvirus 1 infection in cats: a systematic review

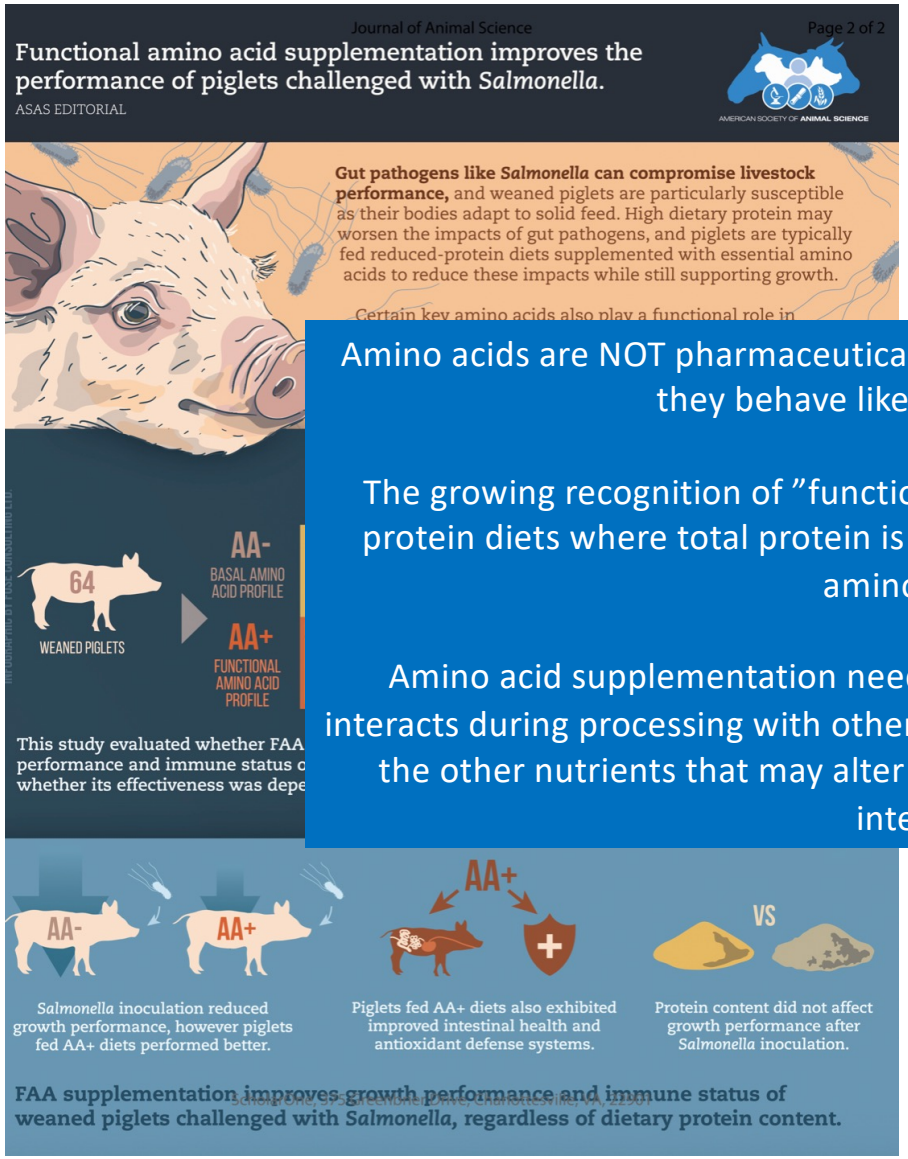
Sebastiaan Bol[1*] and Evelien M. Bunnik[2]

Lysine does not have anti-viral properties and does not antagonize arginine, reducing its concentrations intracellularly and inhibiting viral replication.

In vitro show no effect on viral replication

Clinical studies with cats have not shown any benefit to lysine supplementation, but the above two did.

No discussion about nutrient status, protein turnover or immune status.



Amino acids are NOT pharmaceuticals yet are often investigated as though they behave like pharmaceuticals.

The growing recognition of ”functional amino acids” best applies to low protein diets where total protein is often limited and as such, so are the amino acids.

Amino acid supplementation needs to consider how that amino acid interacts during processing with other nutrients and on a physiological basis, the other nutrients that may alter the availability of the amino acid of interest.

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Advance Access publication February 2, 2021
Received: 2 October 2020 and **Accepted:** 9 November 2020
Non Ruminant Nutrition

NON RUMINANT NUTRITION

Functional amino acid supplementation, regardless of dietary protein content, improves growth performance and immune status of weaned pigs

ález-Vega,‖
†,‡,1

AMERICAN SOCIETY OF ANIMAL SCIENCE

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https://doi.org/10.1093/jas/skae120
Advance access publication 30 May 2024
Gastrointestinal Biology

OXFORD

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Effects of supplemental citrulline on thermal and intestinal morphology parameters during heat stress and feed restriction in growing pigs

Sara K. Kvidera, Edith J. Mayorga, Carrie S. McCarthy, Erin A. Horst, Megan A. Abeyta, and Lance H. Baumgard[1]

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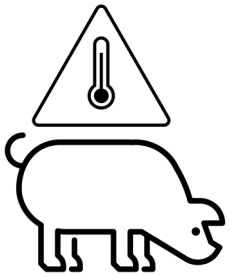

NOTE *Internal Medicine*

Effect of Supplementation of Dry Cat Food with D,L-Methionine and Ammonium Chloride on Struvite Activity Product and Sediment in Urine

Masayuki FUNABA[1)], Takayo YAMATE[1)], Yukako NARUKAWA[1)], Ken GOTOH[2)], Tsunenori IRIKI[1)], Yoshikazu HATANO[2)] and Matanobu ABE[1)]

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3% methionine, but not 1% methionine reduced urine pH and the presence of struvite activity products

While methionine is an effective urinary pH approach, considering mineral balance is most important to decrease struvite crystals.

The source of magnesium should also be considered since MgCl provides chloride, which acidifies the urine.

The diet format, macronutrient content, total feed intake, electrolyte intake, water source, and multiple behavior and physiological differences among cats also influence struvite formation.

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Different source … urinary parameters and acid-base balance

Efeitos da adição de diferentes fontes de enxofre na dieta de gatos adultos em parâmetros urinários e equilíbrio ácido-básico

…ionine or methionine …d in lower urinary pH.

This equates to approximately 12 g/kg of methionine.

Amino acid supplementation cases in cat food: Fact or fiction?

METHIONINE

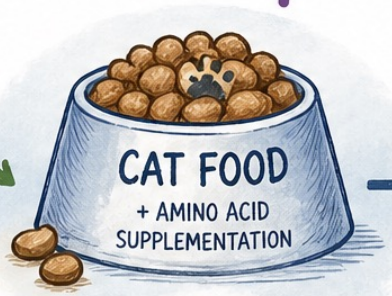
$H_3C-S-CH_2-CH_2-CH(NH_2)-COOH$

Essential sulfur amino acid

LYSINE

$H_2N-(CH_2)_4-CH(NH_2)-COOH$

Essential amino acid



?

FACT

Evidence-based benefits

FICTION

Limited evidence or no benefit

METABOLIC PATHWAYS

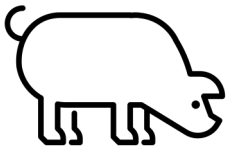
- Protein synthesis
- Methylation reactions (CH_3)
- Transsulfuration pathway (S → S)
- Energy production

POTENTIAL PHENOTYPIC OUTCOMES

- Improved growth & muscle mass
- Healthy skin & coat
- Immune support
- Appetite & palatability
- Better nitrogen utilization & stool quality

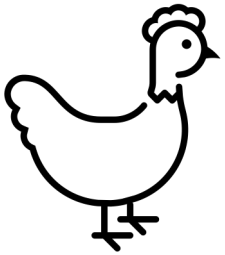
The truth lies in the evidence:
Dose, balance, bioavailability, and individual cat needs matter.
Science over stories.

Dietary glycine supplementation enhances postweaning growth and meat quality of pigs with intrauterine growth restriction



Wenliang He, Erin A. Posey, Chandler C. Steele, Jeffrey W. Savell, Fuller W. Bazer, and Guoyao Wu[1]

Dietary protein reduction with stepwise addition of crystalline amino acids and the effect of considering a minimum glycine-serine content in broiler diets



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Dietary glycine supplementation prevents heat stress-induced impairment of antioxidant status and intestinal barrier function in broilers

Chenxi Deng,[*,†,1] Jun Zheng,[*,†,1] Hua Zhou,[*,†] Jinming You,[*,†] and Guanhong Li[*,†,2]

ASN American Society for Nutrition

The American Journal of CLINICAL NUTRITION

journal homepage: https://ajcn.nutrition.org/

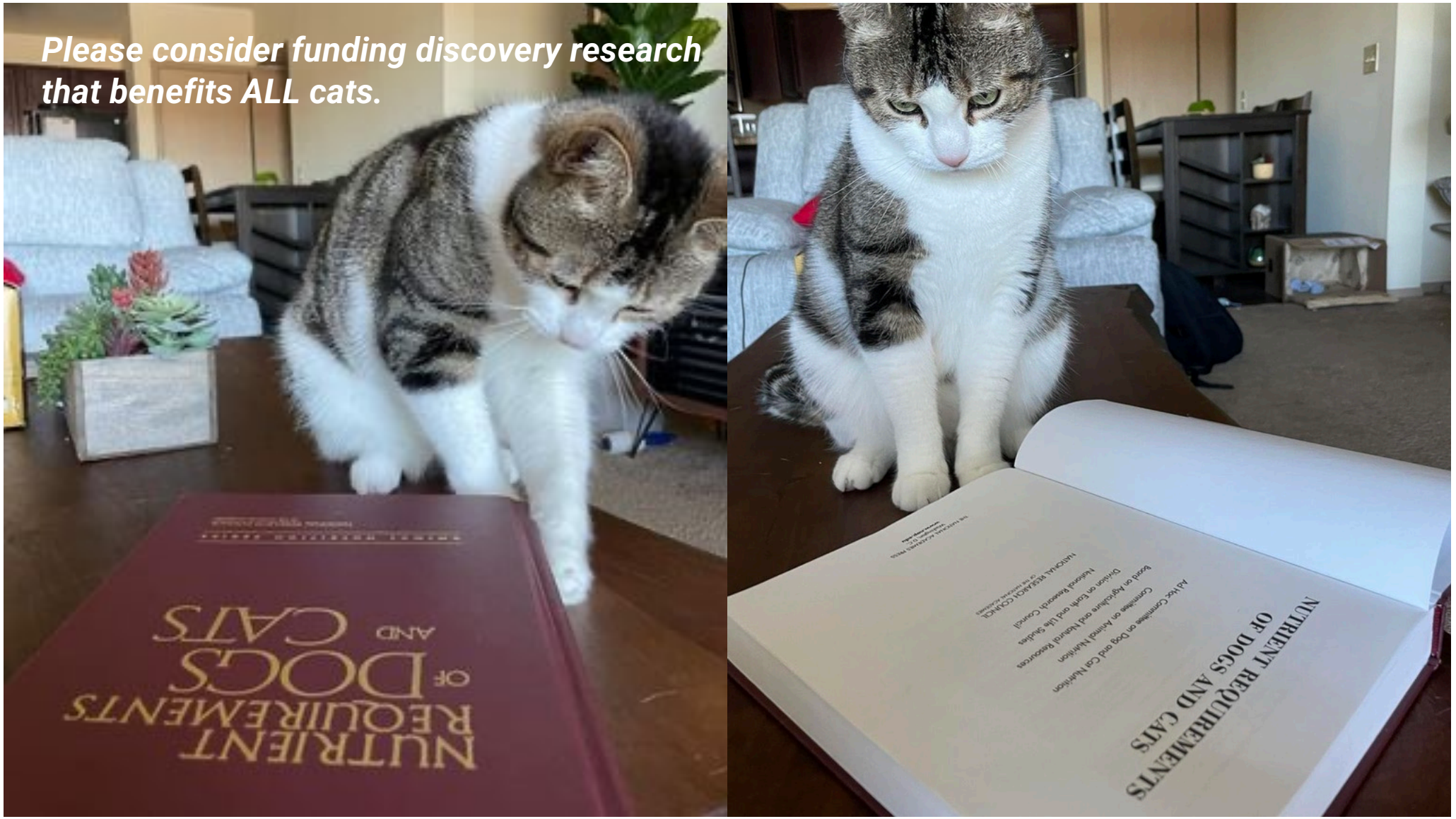
Original Research Article

Reduced plasma glycine concentration in healthy and chronically diseased older adults: a marker of visceral adiposity?

Lars NJ Deutz[1], Raven A Wierzchowska-McNew[1], Nicolaas EP Deutz[1,2], Mariëlle PKJ Engelen[1,2,*]

Bringing it all together

- Cats make glucose from protein and the CP content is related with greater energy efficiency, so the more protein, the better they are at harvesting the energy from the food
- Amino acid supplementation needs to be considered in the broader context of the diet and the animal investigated should be better understood before you consider amino acid supplementation
- To consider AA supplementation, you need to consider the individual role of the amino acids and its balance with other amino acids and nutrients.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