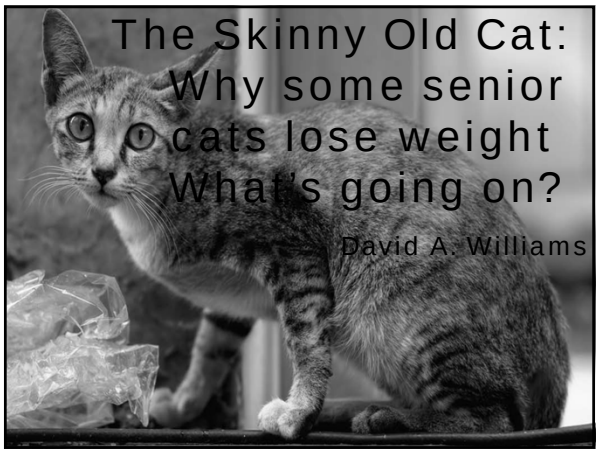


Skinny old cats

- **The Cat Fat Project**
  - **Thanks to Nestle-Purina for their support of my involvement in this project**
  - **Revisit long standing interest in intestinal microflora, cobalamin, tocopherol and bile acids in malabsorption**

Initial dietary study

- **Nestle study started in 2000 to evaluate changes in three groups of cats fed diets varying in fatty acid, tocopherol and prebiotic content for their entire remaining life span**
- **One diet did prolong life and delay physical decline significantly – tocopherol (vitamin E) is part of the picture**
- **Observed weight loss and steatorrhea in an increasing proportion of cats in each group beginning at 8-10 years**

Skinny old cats

- **Decline in body weight is common in cats older than 11 years of age**
- **In many cases there are no obvious signs of illness**
- **Routine diagnostic approaches fail to reveal evidence of an underlying problem**
- **Energy requirements of older cats do not decline as markedly as they do in dogs and humans**
- **Physical activity does not decrease as much with age in cats**

TABLE 1
Incidence of Feline Obesity and Underweight by Age[3]

Age Group	Body Weight (kg)	Obesity Incidence	Percent Under-weight Incidence
Adult (1–7 years)	3.7 ± 0.8	<1%	<1%
Mature (7–12 years)	4.4 ± 1.7	28%	<1%
Geriatric (>12 years)	2.9 ± 1.0	<1%	23%

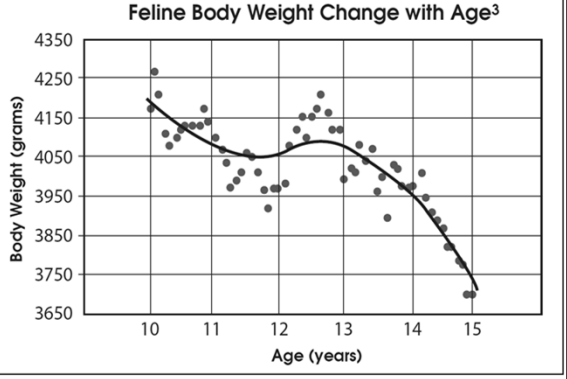
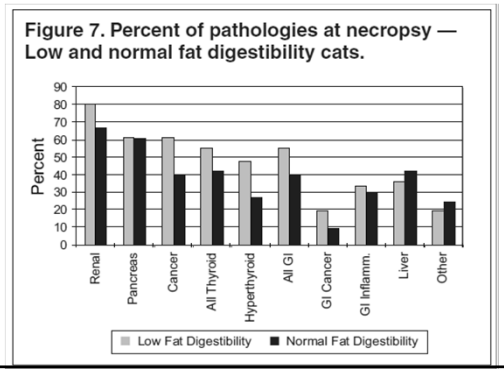


Figure 6. After 12 years of age, there is marked decline in body weight among cats, which supplants obesity as a common life-threatening condition.

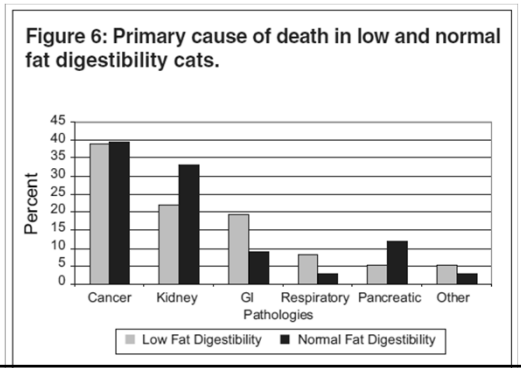
- **Maintenance energy requirement of older cats may actually increase**
- **Cats would be expected to regulate their energy intake to compensate for the various changes to maintain body weight, which clearly is not always the case**
- **Interspecies variation in age-related body composition changes may also contribute to these differences**
- **Protein and fat digestibility decrease in many apparently normal cats after 10 years of age**

- **The change is quite marked in some individuals and can be dramatic with regard to fat digestibility**
- **Progressive decline in body weight has been reported in the 2 years prior to death of cats from a variety of seemingly unrelated diseases**
- **As cats live increasingly long lives and receive attentive health care, this weight loss is increasingly recognized**
- **These changes are not readily apparent from observation of stool quality**

Weight loss in old cats



Weight loss in old cats



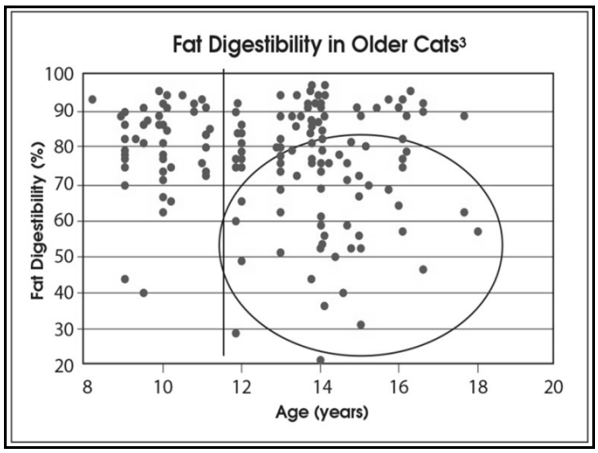
- **Obesity tends to be the predominant body-mass concern in cats between 7 and 12 years of age**
- **In cats older than 12 years, obesity is rare and being underweight is a far greater life-threatening risk factor**

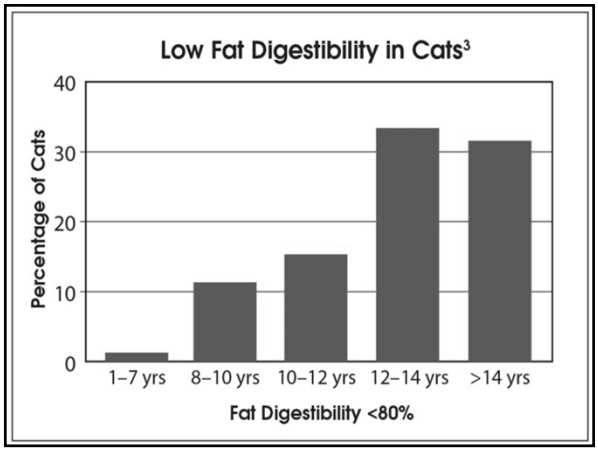
Attributable weight loss

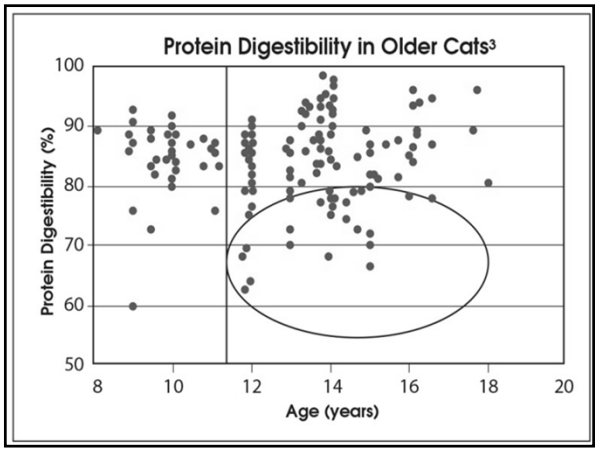
- **Causes of weight loss in old cats include chronic renal disease, diabetes mellitus, hyperthyroidism, IBD, EPI, and dental problems**
- **Serum thyroxine, TLI, cobalamin and folate, dental radiography, and GI endoscopy/biopsy may be necessary to identify problems**

Unattributed weight loss

- **Subtle weight loss may not even be noted unless cats are weighed regularly – monitor % change**
- **Moderate changes in food and water intake also probably often go unnoticed**
- **A substantial proportion of senior cats will experience weight loss, despite apparently otherwise good health and no detectable change in food intake**
- **Evidence exists to indicate that in these older cats there is an age-related decline in food digestibility**


Fat Digestibility in Older Cats[3]
Fat Digestibility (%)
100
90
80
70
60
50
40
30
20
8
10
12
14
16
18
20
Age (years)


Low Fat Digestibility in Cats[3]
Percentage of Cats
40
30
20
10
0
1–7 yrs
8–10 yrs
10–12 yrs
12–14 yrs
>14 yrs
Fat Digestibility <80%


Protein Digestibility in Older Cats[3]
Protein Digestibility (%)
100
90
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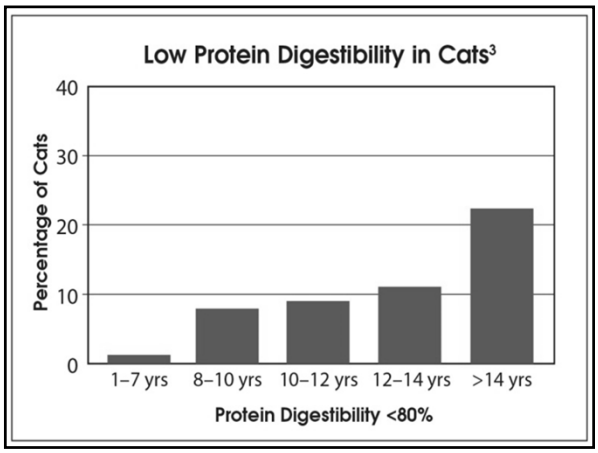
20
Age (years)



Unattributed weight loss

- **The incidence of low fat digestibility increases with age:**
  - **10% to 15% of mature cats**
    (8–12 years of age)
  - **30% of geriatric cats**
    (>12 years of age)
- **In some geriatric cats, fat digestibility was found to be as low as 30%**
- **Larger than normal stools (not frank diarrhea) and low body weight may be the only clinical signs**
- **May be "subclinical"**

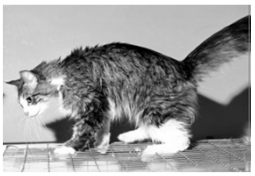
- **Approximately 20% of cats older than 14 years show protein digestibility lower than 77%**
- **Decreased fat and protein digestibility tend to occur in the same cats.**
- **Many cats show only subtle changes in stool characteristics (slightly larger volumes of stool with a more clay-like consistency), but not frank diarrhea, even when steatorrhea is marked**
- **These changes were correlated with several other measures of health including serum vitamin E (tocopherol), vitamin B12 (cobalamin), skin thickness, body fat, and body condition score**

Low Fat Digestibility Incidence

Normal Fat Digestibility

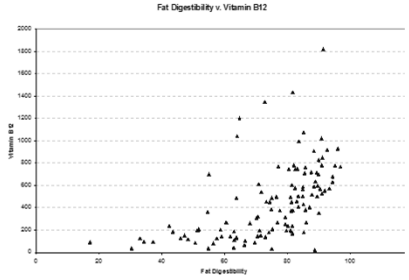
Low Fat Digestibility

Cobalamin deficient cats



Correlation Fat Digestibility & Vitamin B12 NT945

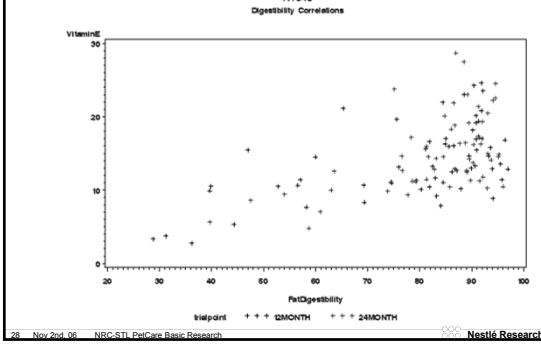
- Significant correlation (P<0.001, r=0.36) between Vit B12 and fat digestibility



Correlation Fat Digestibility & Serum Vitamin E NT945

Nestlé Good Food, Good Life

- Significant correlation (P<0.001, r=0.72) between Vit E and fat digestibility

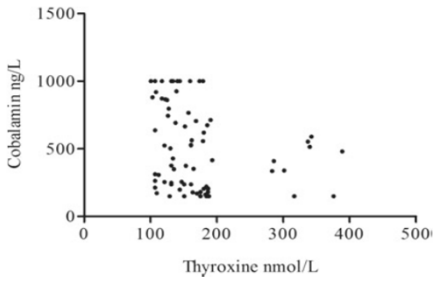


Hyperthyroid cats

- **More than 50% of hyperthryoid cats have abnormal serum cobalamin or folate at initial presentation**
- **Many also have abnormal fTLI and /or fPL**
- **Serum cobalamin subnormal in 40% hyperthyroid cats but only in 25% of geriatric control cats**

(Cats from Animal Medical Center, New York) JVIM 19:474-475, 2005
(Idexx Reference Labs Samples) J Small Anim Pract 52:101-106, 2011

Hyperthyroidism and Hypocobalaminemia



Cook *et al*. J Small Anim Pract 52:101-106, 2011

- **Many hyperthyroid cats are appropriately diagnosed and treated, but GI signs, especially weight loss, persist despite return to the euthyroid state**
- **Subsequent work up reveals evidence of enteric disease and cobalamin deficiency!**
- **If you think about testing for hyperthyroidism, evaluate possible pancreatic and intestinal abnormalities (fPL, fTLI, cobalamin and folate) too!**
- **Treat all abnormalities detected concurrently**

Skinny old cats

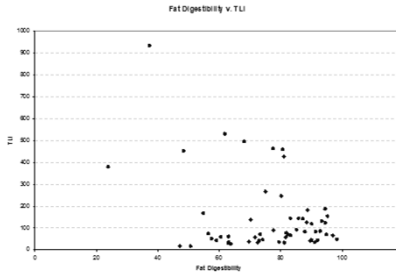
- **The cause(s) of this decline in nutrient digestibility remains unknown but presumably reflects enteropathy of some type**
- **In some cases, this intestinal dysfunction may overlap with what is commonly loosely classified as (idiopathic) IBD.**
- **Some cats may compensate by eating more and therefore exhibit minimal or no weight loss**

Small intestinal disease?

- **Is pancreatic function adequate?**
- **Is there dietary sensitivity?**
- **Is there specific GI infection?**
- **Is there malabsorption?**
- **Is there protein-losing enteropathy?**
- **Is there villous atrophy / inflammation?**
- **Is there small intestinal dysbiosis (SIBO)?**

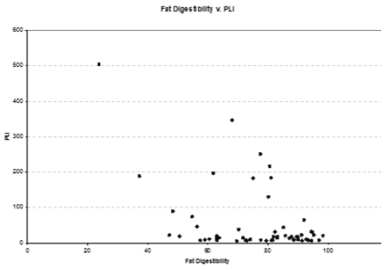
Correlation Fat Digestibility & TLI NT945

- No correlation (P<0.71, r=-0.05) between TLI and fat digestibility

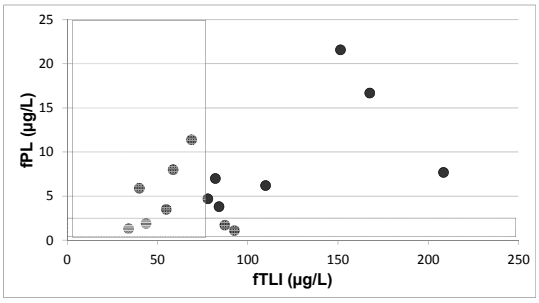


Correlation Fat Digestibility & PLI NT945

- Significant correlation (P<0.04, r=-0.28) between PLI and fat digestibility



Serum fPL and fTLI



fTLI Reference range: 12-82µg/L fPL Reference range: 0.1-3.5µg/L

Small intestinal disease?

- **Is pancreatic function adequate?**
- **Is there dietary sensitivity?**
- **Is there specific GI infection?**
- **Is there malabsorption?**
- **Is there protein-losing enteropathy?**
- **Is there villous atrophy / inflammation?**
- **Is there small intestinal dysbiosis (SIBO)?**

SKINNY OLD CATS: What Changes…What it means…How to feed them?

Identifying cats with reduced digestive capacity

Table 4. Examples of abnormal levels of parameters and percent of cats with low digestibility.

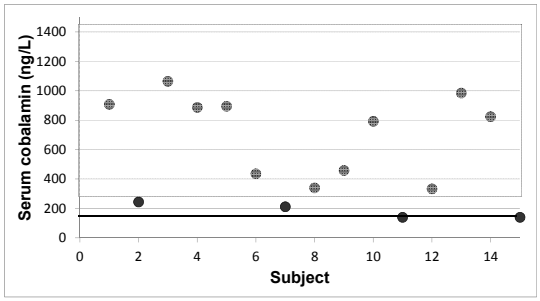
Parameter	Abnormal levels	Percent with low (<80%) fat digestibility	Percent with low protein (<77%) digestibility
Vitamin E	< 5 mg/L	100	80
Vitamin B12	< 100 ng/L	92	67

→ Serum vitamin E and B12 have a strong inverse association with reduced digestive function
→ Easy to perform under clinical conditions vs. digestibility testing

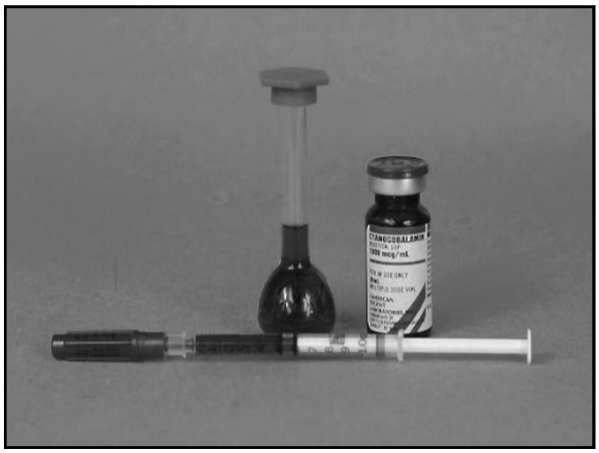
Nestlé Purina PetCare Research

Nestlé

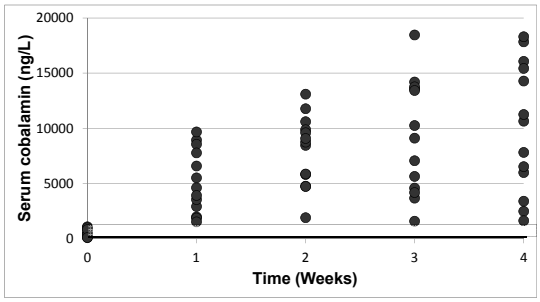
Serum cobalamin



Lower limit of reference range: 290ng/L Lower limit of assay: 150ng/L

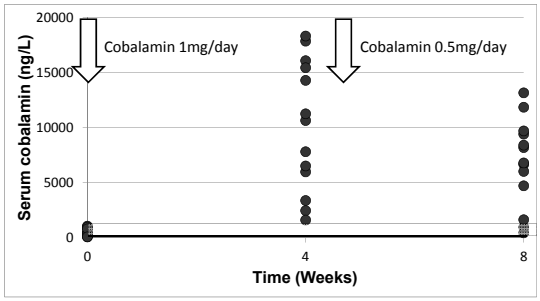


Serum cobalamin after supplementation with 1mg oral cobalamin daily (13 cats)



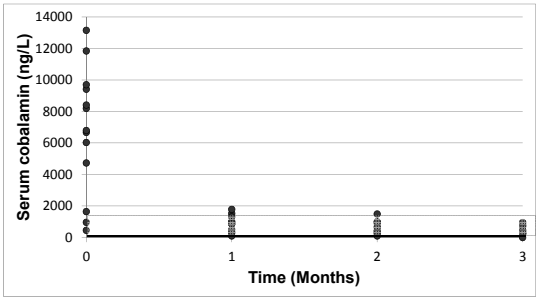
Reference range: 290-1499ng/L Lower limit of assay: 150ng/L

Serum cobalamin after oral supplementation reduced to 0.5mg cobalamin daily (13 cats)



Reference range: 290-1499ng/L Lower limit of assay: 150ng/L

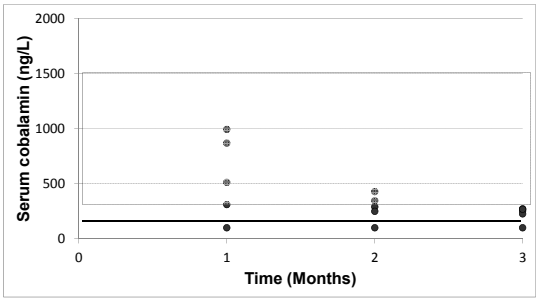
Serum cobalamin after cessation of oral cobalamin supplementation (13 cats)



Lower limit of reference range: 290-1499ng/L

Lower limit of assay: 150ng/L

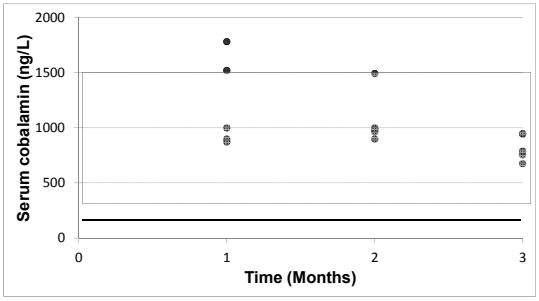
Serum cobalamin after cessation of supplementation (5 cats) – poor responders



Reference range: 290-1499ng/L

Lower limit of assay: 150ng/L

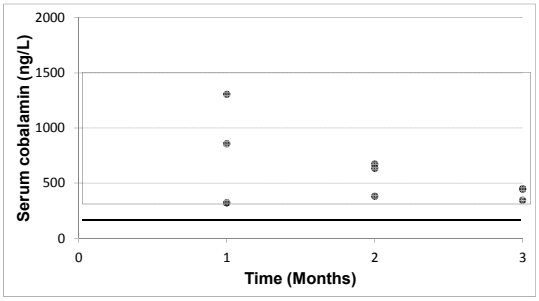
Serum cobalamin after cessation of supplementation (5 cats) – good responders



Reference range: 290-1499ng/L

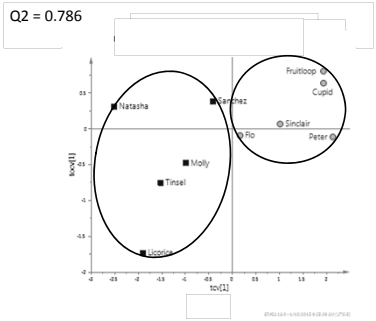
Lower limit of assay: 150ng/L

Serum cobalamin after cessation of supplementation (3 cats) – open responders

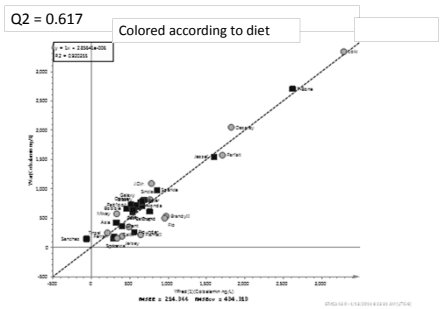


Reference range: 290-1499ng/L Lower limit of assay: 150ng/L

Good (◯) and Poor (□) Cobalamin Responders and Fecal Microbiome



Serum Cobalamin and Fecal Microbiome



Serum cobalamin concentrations correlate with the intestinal microbiome

Summary

- Serum cobalamin increased dramatically within 1 week in every cat following oral supplementation
- Following cessation of supplementation serum cobalamin decreased rapidly in all cats and was subnormal in 5 cats within 3 months
- Differing responses to oral cobalamin are associated with differences in the intestinal microbiome
- Significant correlation between intestinal microbiome and serum cobalamin (across low, normal and high ranges)

Conclusion

- Oral cobalamin supplementation can effectively increase serum concentrations in geriatric ICE cats but needs to be maintained to prevent recurrence of hypocobalaminemia
- Differing serum cobalamin responses are associated with differences in the intestinal microbiome

Small intestinal disease?

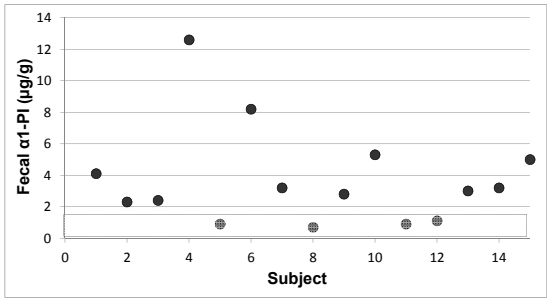
- **Is pancreatic function adequate?**
- **Is there dietary sensitivity?**
- **Is there specific GI infection?**
- **Is there malabsorption?**
- **Is there protein-losing enteropathy?**
- **Is there villous atrophy / inflammation?**
- **Is there small intestinal dysbiosis (SIBO)?**

Fecal α_1-Proteinase Inhibitor

- **Feline assay from GI Lab (Kathrin Burke)**
- **Greater values in cats with IBD of greater histological severity**
- **More sensitive for IBD / GI neoplasia than serum cobalamin (95% vs 56%)**
- **Often no correlation with serum albumin**

Fetz K, Steiner JM, Ruaux CG, Suchodolski JS, Williams DA: Increased α1-proteinase inhibitor concentrations in cats with gastrointestinal disease. J Vet Int Med, 19: 474, 2005.
Burke K *et al.* submitted 2012

Fecal alpha1-Proteinase Inhibitor (α1-PI)



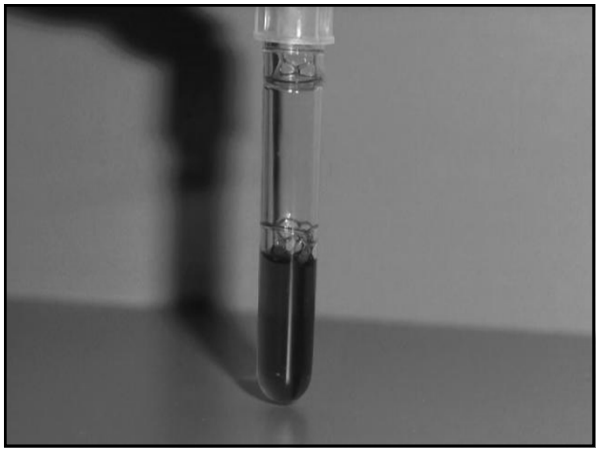
Reference range: ≤ 1.6µg/g

Recent observations

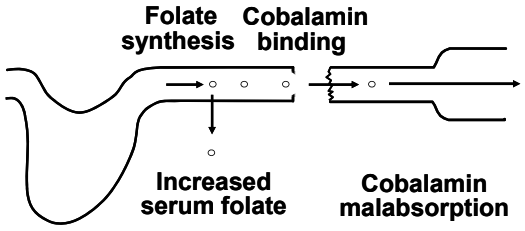
- **Multiple abnormalities in cats >11 years old – especially intestinal, pancreatic, and hepatic, and associated with poor fat and protein digestibility**
- **Hepatic changes generally minimal, and not considered the cause of death**
- **Fecal α_1-PI abnormal in many cats with malabsorption, even when other test results are normal, including serum albumin**
- **Enteric protein loss (PLE) contributes to weight loss**

Small intestinal disease?

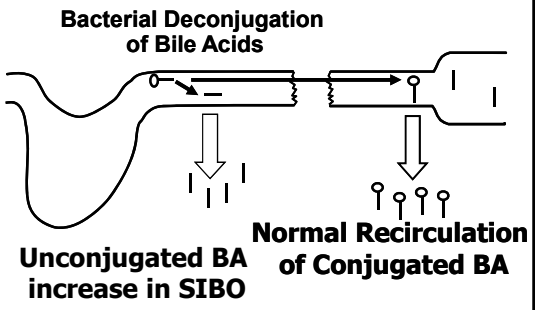
- Is pancreatic function adequate?
- Is there dietary sensitivity?
- Is there specific GI infection?
- Is there malabsorption?
- Is there protein-losing enteropathy?
- Is there small intestinal dysbiosis (SIBO)?
- Is there intestinal histological change



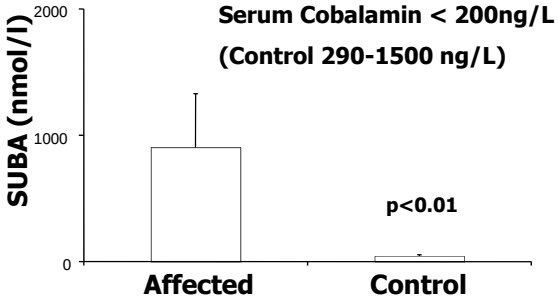
Effects of bacteria on folate and cobalamin



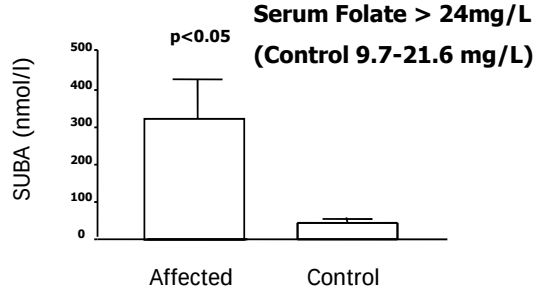
Effects of bacteria on unconjugated bile acids



Unconjugated bile acids in cats with decreased serum cobalamin



Unconjugated bile acids in cats with high serum folate

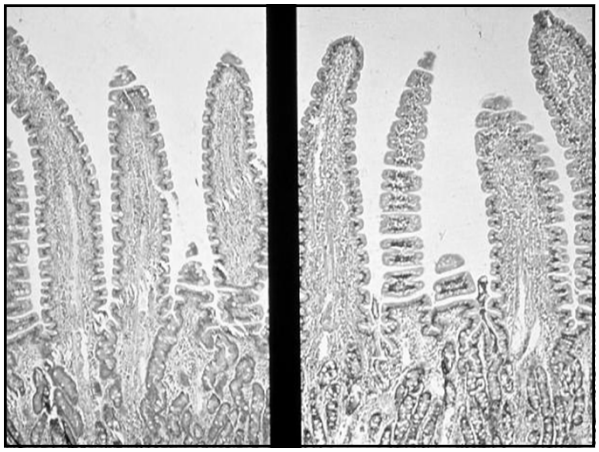


SI Dysbiosis does occur in cats

- Increased serum folate and decreased serum cobalamin in cats with small intestinal disease / IBD
- Increased serum unconjugated bile acids and altered primary to secondary bile acids ratio in cats with small intestinal disease associated with abnormal cobalamin and / or folate
- D-lactic acidosis reported in a cat with EPI and more recently in cats with other GI diseases

Small intestinal disease?

- Is pancreatic function adequate?
- Is there dietary sensitivity?
- Is there specific GI infection?
- Is there malabsorption?
- Is there protein-losing enteropathy?
- Is there small intestinal dysbiosis (SIBO)?
- Is there villous atrophy, inflammation or neoplasia?



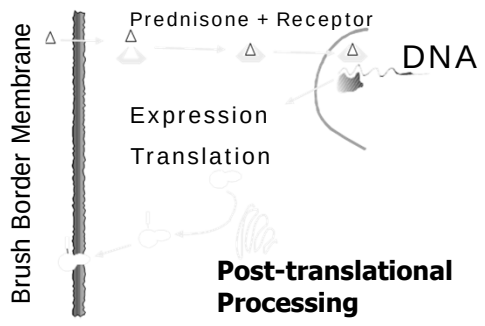
Therapeutic options

- Underlying disease – specific treatment of infectious, obstructive, neoplastic or endocrine diseases identified
- Dietary manipulations:
  - low carbohydrate (cat)
  - highly digestible (low non-fermentable fiber)
  - adequate fermentable fiber
  - MCT oil
  - novel antigen
  - hydrolyzed
- Antibiotics, Prebiotics, Probiotics – SIBO (ARD)
- Vitamin supplements – cobalamin, tocopherol – others?
- Glucocorticoids - prednisolone
- Immunosuppressives:
  - chlorambucil
  - cyclosporine

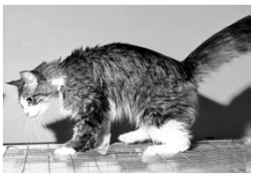
Skinny old cats

- In some cats a presumptive diagnosis of idiopathic enteropathy is the best that can be achieved, and they are managed as if they have histologically confirmed IBD
- dietary change (low-carbohydrate, alternative fiber source, novel antigen, hydrolyzed diet, fatty acid / triglyceride content)
- prebiotic and / or probiotic supplementation
- correction of low serum cobalamin, folate and tocopherol concentrations
- other antioxidants, metronidazole or tylosin
- glucocorticoid therapy (especially if there is PLE?)
- More potent imunosuppressive agents??

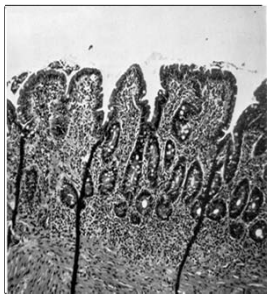
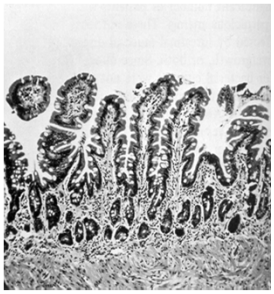
Postulated mechanism of prednisone action



Cobalamin deficient cats

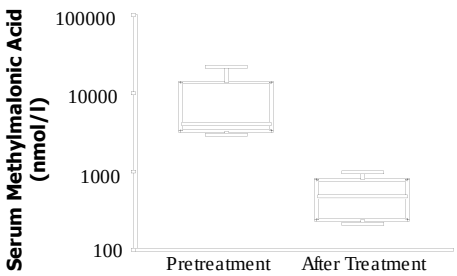


Intestinal mucosal changes in cobalamin deficiency

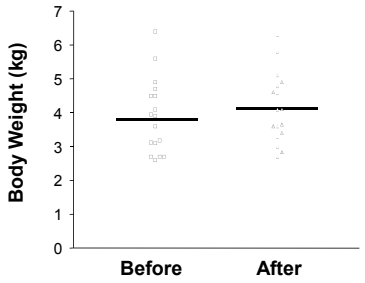



Before Supplementation | After Supplementation

Serum methylmalonic acid - response to cobalamin



Body weight change after parenteral cobalamin supplementation

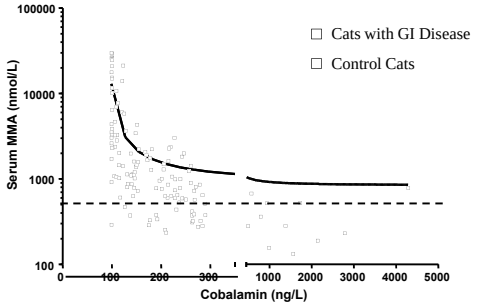


Means (3.8 to 4.1 kg) Significantly Different, p<0.01

10/19 gained weight (up to 1.4kg)

Ruaux CG, Steiner JM, Williams DA. (2005) JVIM

When Should We Start Cobalamin Supplementation?



Conclusion

- In geriatric ICE cats protein losing enteropathy commonly co-exists with nutrient malabsorption
- Therapy needs to be multifactorial and individualized depending in part on the time course of disease

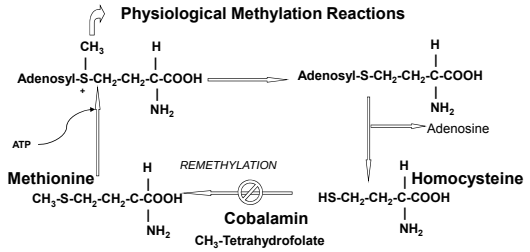
Therapy for SI dysbiosis

- **Metronidazole**
  20mg/kg q12h
- **Tylosin**
  15mg/kg q12h
- **Diet change !!**

Intestinal obstruction

- **Neoplasia**
- **Foreign body**
- **Intussusception**
- **Stricture**
- **Herniation /Incarceration**
- **Diverticulae**
- **Adhesion**
- **Regional Enteritis**
- **Phycomycosis**
- **Pseudo-Obstruction**

Normal metabolism of methionine and homocysteine

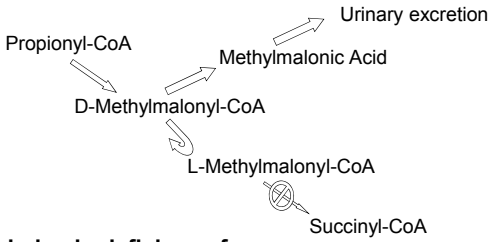


Methionine synthase is a Cobalamin Dependant Enzyme

Cobalamin absorption

- **Feline diets are rich in cobalamin**
- **Dietary deficiency is very unlikely**
- **Deficiency in cats reflects:**
  - **Exocrine pancreatic insufficiency**
  - **Small intestinal disease**
  - **Changes in small intestinal microflora (Dysbiosis - "SIBO")**

Terminal degradation of amino acids

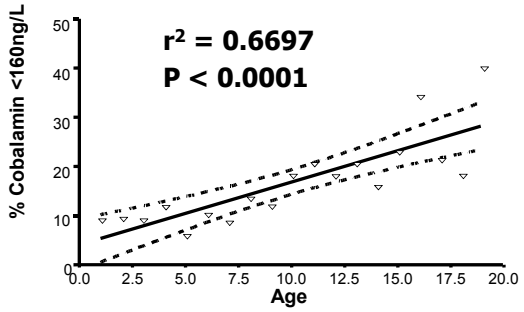


Cobalamin deficiency favours formation of methylmalonic acid

Cobalamin deficiency

- **Subclinical deficiency in humans more common with age:**
  - **-Hyperhomocysteinemia**
  - **-Dementia**
- **Related to increased frequency of gastrointestinal disease in older human beings**
- **Gastrointestinal disease also more common in older cats and dogs**

Results - Cobalamin and age (Serum cobalamin <160ng/L)



Bacterial Overgrowth

- **Deconjugation of bile salts**
- **Hydroxylation of fatty acids**
- **Damage to enterocytes**
- **Competition for nutrients**