Diagnostic Approach to Diarrhea

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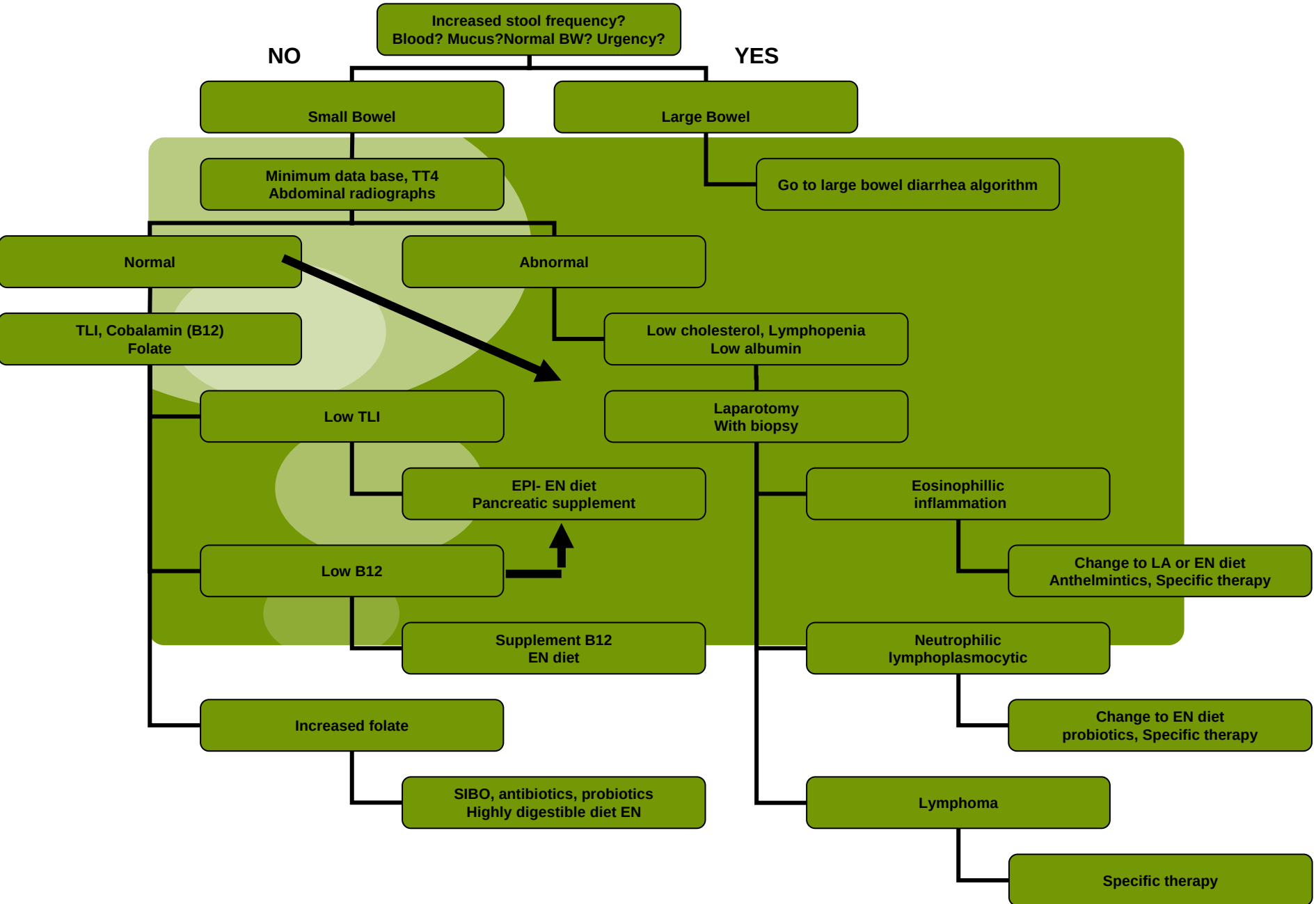
Diarrhea. . .

- is the passage of feces containing excess water, resulting in an increase in the fluidity, volume and/or frequency of defecations.
- can be categorized functionally as osmotic, hypersecretory, hyperpermeability or disordered motility
- can also be categorized based on duration (acute vs chronic) and by location (small intestine vs large intestine)

Diarrhea

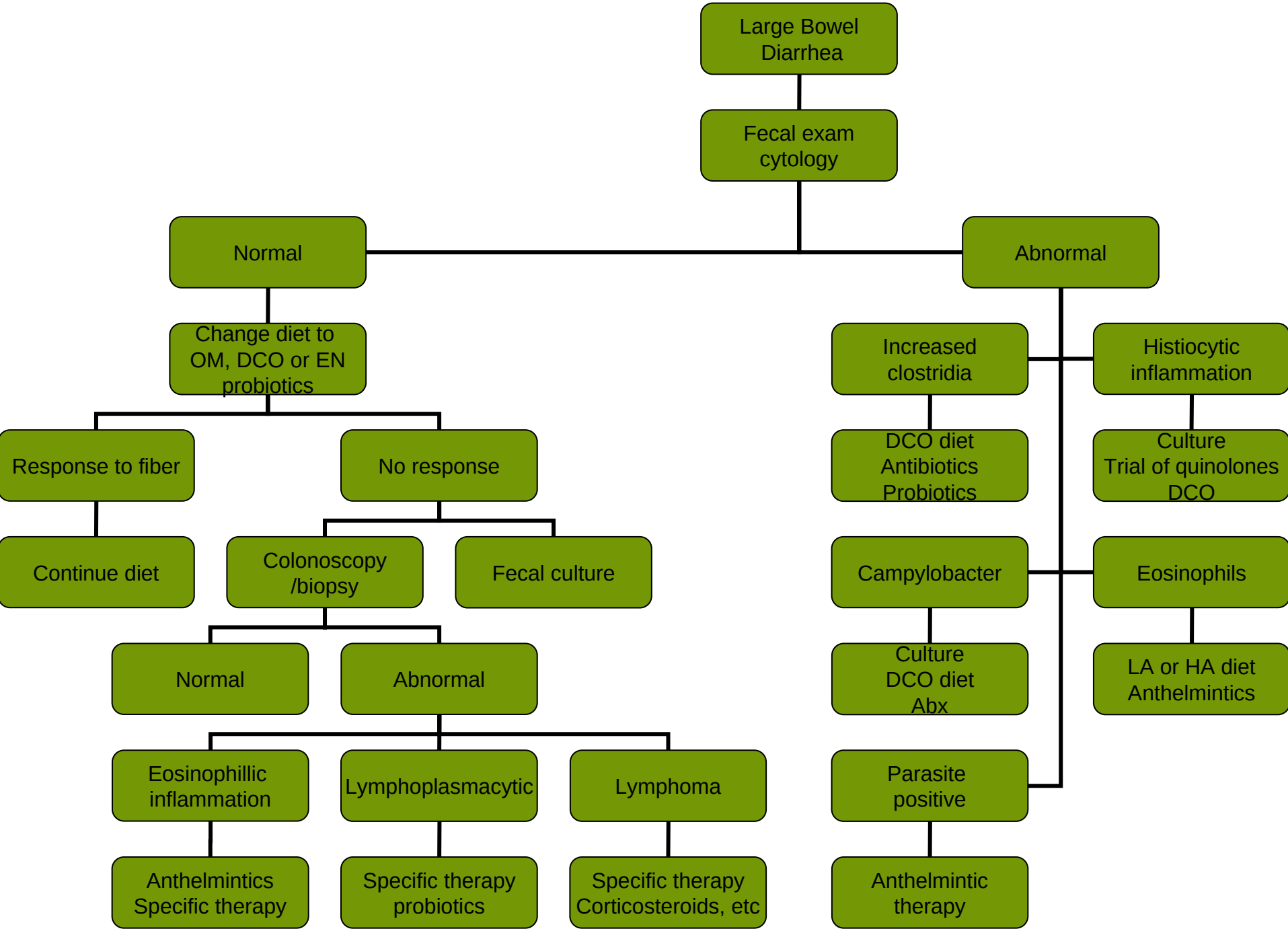

Increased stool frequency?
Blood? Mucus?Normal BW? Urgency?
NO
YES
Small Bowel
Large Bowel
Minimum data base, TT4
Abdominal radiographs
Go to large bowel diarrhea algorithm
Normal
Abnormal
TLI, Cobalamin (B12)
Folate
Low cholesterol, Lymphopenia
Low albumin
Low TLI
Laparotomy
With biopsy
EPI- EN diet
Pancreatic supplement
Eosinophillic
inflammation
Low B12
Change to LA or EN diet
Anthelmintics, Specific therapy
Supplement B12
EN diet
Neutrophilic
lymphoplasmocytic
Increased folate
Change to EN diet
probiotics, Specific therapy
SIBO, antibiotics, probiotics
Highly digestible diet EN
Lymphoma
Specific therapy

Large vs Small Intestinal Diarrhea

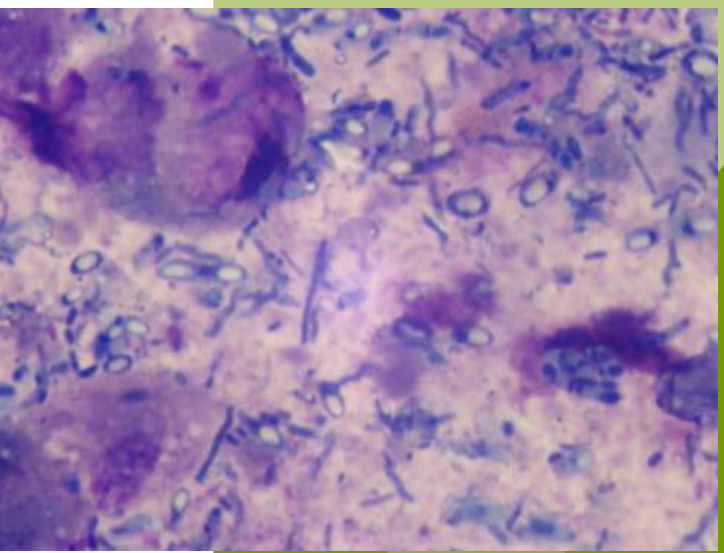
Signs	Small	Large
Tenesmus	Rare	Common
Frequency	2-3x normal	> 3x normal
Urgency	Uncommon	Common
Volume	Increased	Small, but multiple
Mucus	Rare	Common
Fresh blood	Uncommon*	Common
Weight loss	Common	rare

Fabio: 3 yr old MI Standard Poodle

- Show dog
- Repeated bouts of diarrhea preceding show days
- Characteristics of diarrhea
  - Mucus
  - Small amount of fresh blood
  - Increased frequency
  - Small volume
- One episode of vomiting


Large Bowel Diarrhea
Fecal exam cytology
Normal
Abnormal
Change diet to OM, DCO or EN probiotics
Response to fiber
No response
Continue diet
Colonoscopy /biopsy
Fecal culture
Normal
Abnormal
Eosinophillic inflammation
Lymphoplasmacytic
Lymphoma
Anthelmintics Specific therapy
Specific therapy probiotics
Specific therapy Corticosteroids, etc
Increased clostridia
Histiocytic inflammation
DCO diet Antibiotics Probiotics
Culture Trial of quinolones DCO
Campylobacter
Eosinophils
Culture DCO diet Abx
LA or HA diet Anthelmintics
Parasite positive
Anthelmintic therapy

Fabio: Fecal



- Large numbers of clostridial spores
- No WBC, eosinophils, histiocytes

Fabio Dietary Therapy

- Probiotics
- Antibiotics
  - 5 day course of metronidazole
- Change to DCO or LA with added fiber
  - Prebiotics as in DCO : Pea fiber
  - LA with Psyllium
- Fortiflora

Dietary fiber: for LBD

- Soluble fiber
  - Water soluble
  - Viscous
  - Fermentable
  - Slow GI transit

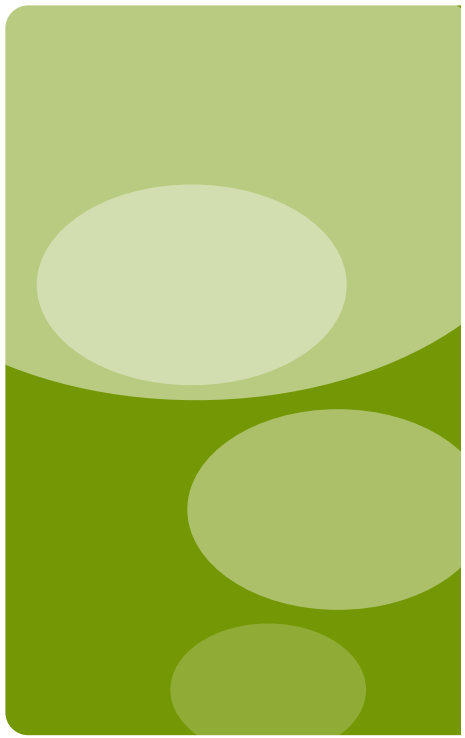
Excess = watery stools

Insoluble fiber

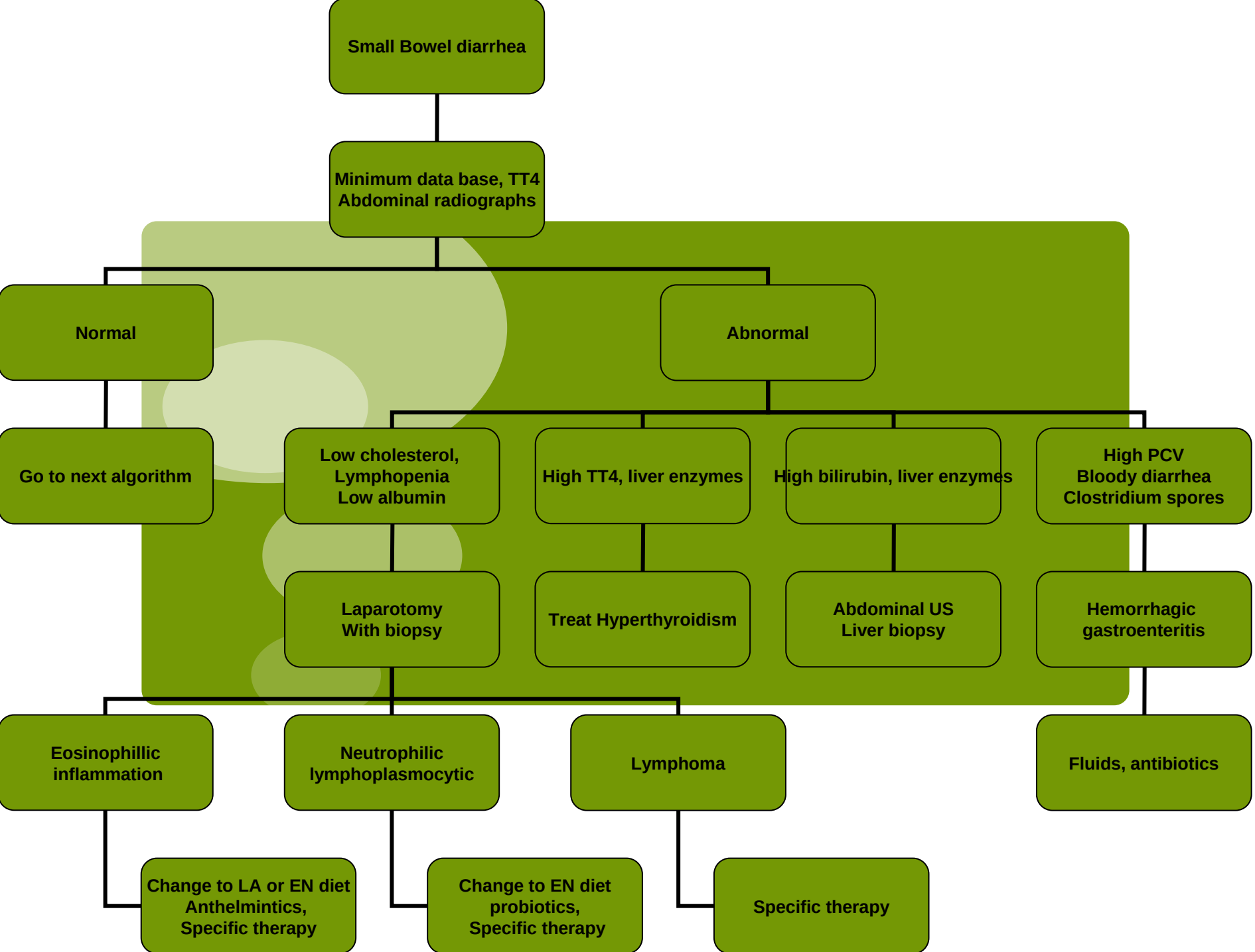
- Not water soluble
- Adsorbs water
- Fecal bulk
- Less fermentable

Excess = large stool volume

Use of Fiber to Manage Diarrhea



- Experimentally - minimizes clinical signs and/or bacterial counts from Clostridium & other infections
- Clostridial diarrhea / Fiber-responsive diarrhea
  - Prebiotics such as Psyllium added to diet at 1 – 2 Tbsp/ 25kg bwt
  - Commercial diets with increased fiber—DCO


Small Bowel diarrhea
Minimum data base, TT4
Abdominal radiographs
Normal
Abnormal
Go to next algorithm
Low cholesterol,
Lymphopenia
Low albumin
High TT4, liver enzymes
High bilirubin, liver enzymes
High PCV
Bloody diarrhea
Clostridium spores
Laparotomy
With biopsy
Treat Hyperthyroidism
Abdominal US
Liver biopsy
Hemorrhagic
gastroenteritis
Eosinophillic
inflammation
Neutrophilic
lymphoplasmocytic
Lymphoma
Fluids, antibiotics
Change to LA or EN diet
Anthelmintics,
Specific therapy
Change to EN diet
probiotics,
Specific therapy
Specific therapy

“Weeble Sherman”

12 yr old MC DSH, red tabby

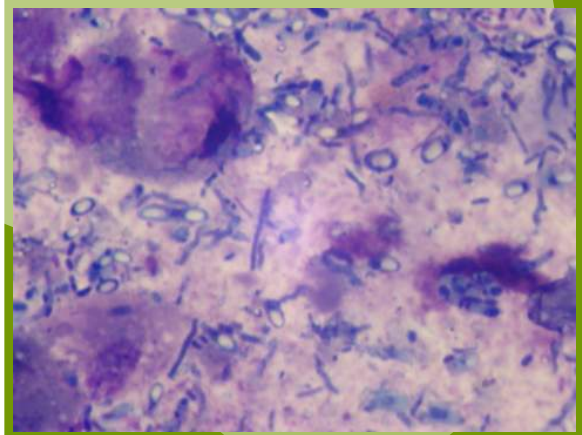
1 year history of diarrhea, weight loss

Used to weigh 20 lbs 1 yr ago

Current Rx: 2.5 prednisone, Viokase

Diet: Iams chicken dry food

Diagnostics



Fecal smear:

- increased clostridium,
- negative for giardia and parasites

Increased TLI,low cobalamin, high folate

Ultrasound

- Increased echogenicity of pancreas
- Enlarged mesenteric nodes
- Thickened bowel loops

What diet is appropriate for Weeble?

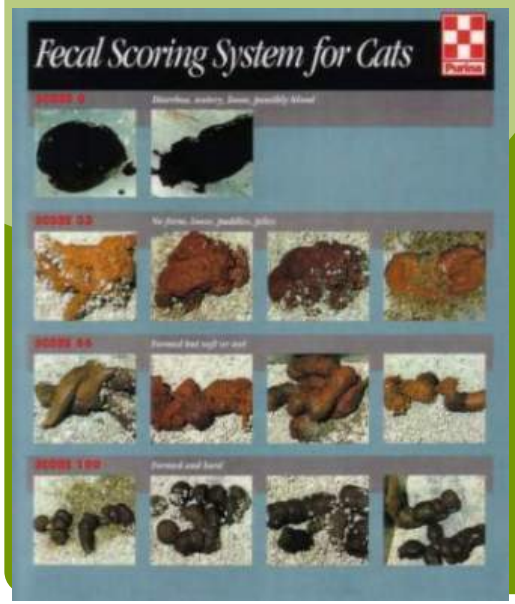
- High fiber, low fat diet
- Low carbohydrate, moderate fat diet
- Low fat diet
- Limited antigen diet
- Low carbohydrate diet

Carbohydrate digestion

- Cats lack salivary amylase İntestinal sucrase, lactase, maltase. Some cats lack lactase
- Absorption at villus tip as monosaccharides
  - Villus stunting or atrophy can cause CHO maldigestion or malabsorption
  - Non-absorbed monosaccharides can cause osmotic diarrhea

Carbohydrate malabsorption is common in feline IBD (Ugarte, J Nutri 2004)

Feline Diarrhea - Carbohydrates

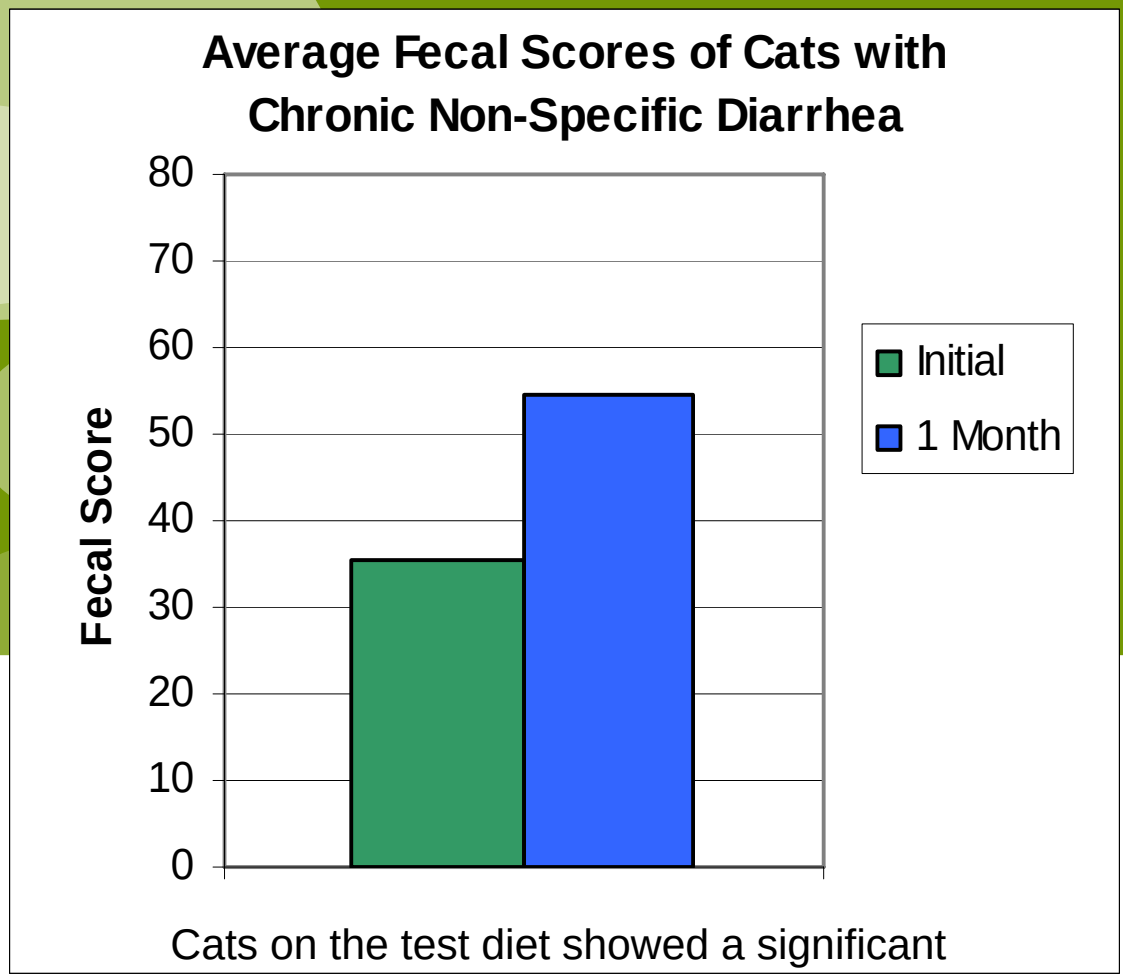


Observations of diabetic cats fed high protein, low CHO diets suggested benefit in diarrhea

Clinical trial compared highly digestible diets with 15% vs 32% CHO

Cats monitored for change in fecal frequency and fecal score If not sufficiently improved, switched to alternate diet

Clinical Trial – Chronic Diarrhea



Cats on the test diet showed a significant improvement in fecal scores (internal data)

Do cats with diarrhea need a low fat diet?

- 55 client-owned cats with chronic diarrhea
- Cats fed low (10%) or high fat (23%)

Significant improvement in fecal score:

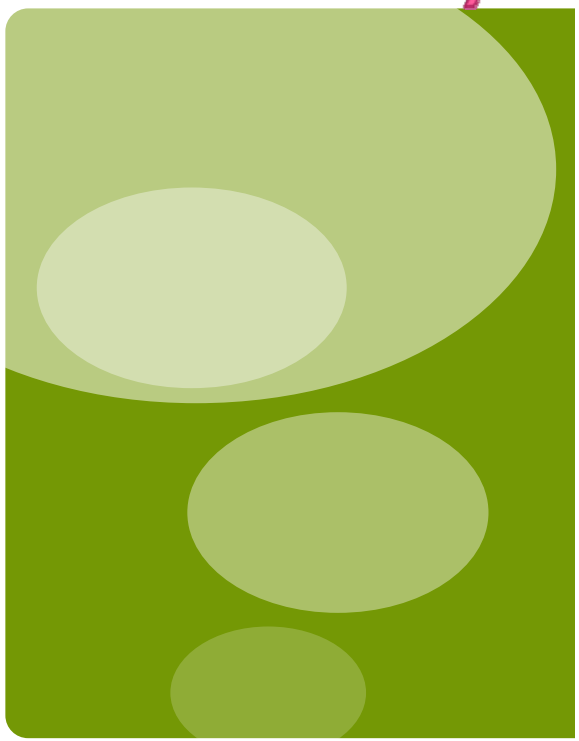
> 75% of cats improved >25 points

> 75% of cats improved to >66

> 25% of cats improved to 100

No differences between diets

Feline Diarrhea– Diet Summary



Most cats with chronic diarrhea respond to dietary change to a highly digestible diet.

Options to try:

- Low Carbohydrate diet (DM, EN)
- Expect response within 2 weeks
- High protein, soluble fiber for LBD if fecal score is mid-range--OM
- For feline diarrhea, dietary fat does not appear to be an issue.

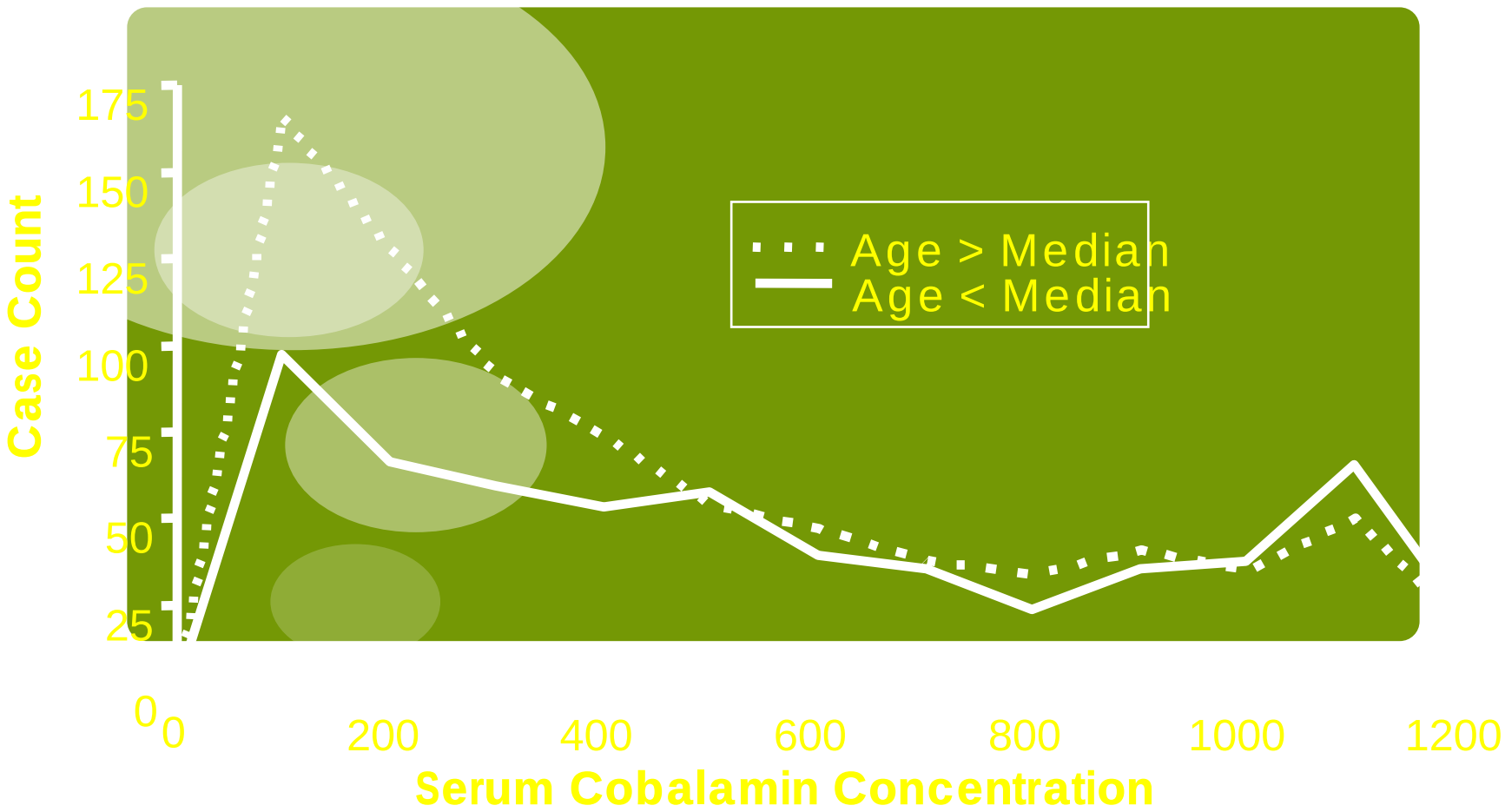
What other treatments should be instituted for Weeble?

- Probiotics, antibiotics
- Probiotics, corticosteroids, B12
- Cobalamin injections
- Cobalamin and probiotics

Vitamin Deficiencies in cats with DM and gastrointestinal disease

- **B-vitamin deficiency**
- **In particular cobalamin (B12)**
- **Co-factor in enzymes involved in transmethylation, DNA synthesis, and cellular turnover**
  - **Deficiency leads to enteropathy with villous atrophy & fat malabsorption**

Older cats more likely to be B12 Deficient



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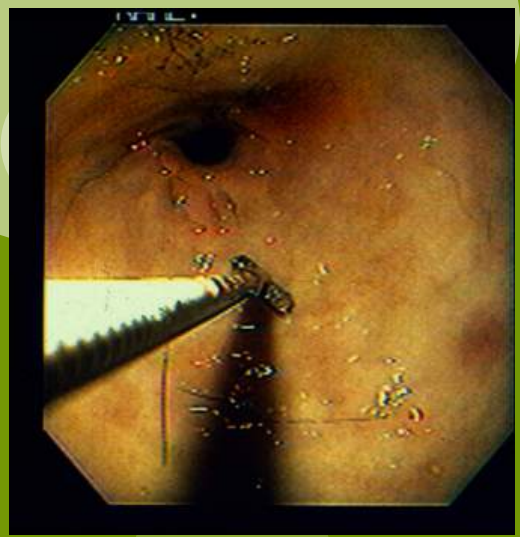
Cobalamin deficiency: Treatment

Body Weight (Species)	Dose/ injection
Cats & Dogs <5kg	250 μg
Dogs 5 – 15 kg	500 μg
Dogs > 15 kg	1000 μg

- **Supplementation* must be parenteral**
  - **1 dose/wk x 6 wks**
  - **1 dose/ Q 2 wks x 6 wks**
  - **1 dose/month**

GI consultation



Suspect IBD or lymphoma

Rec: Biopsy of intestine after d/c pred

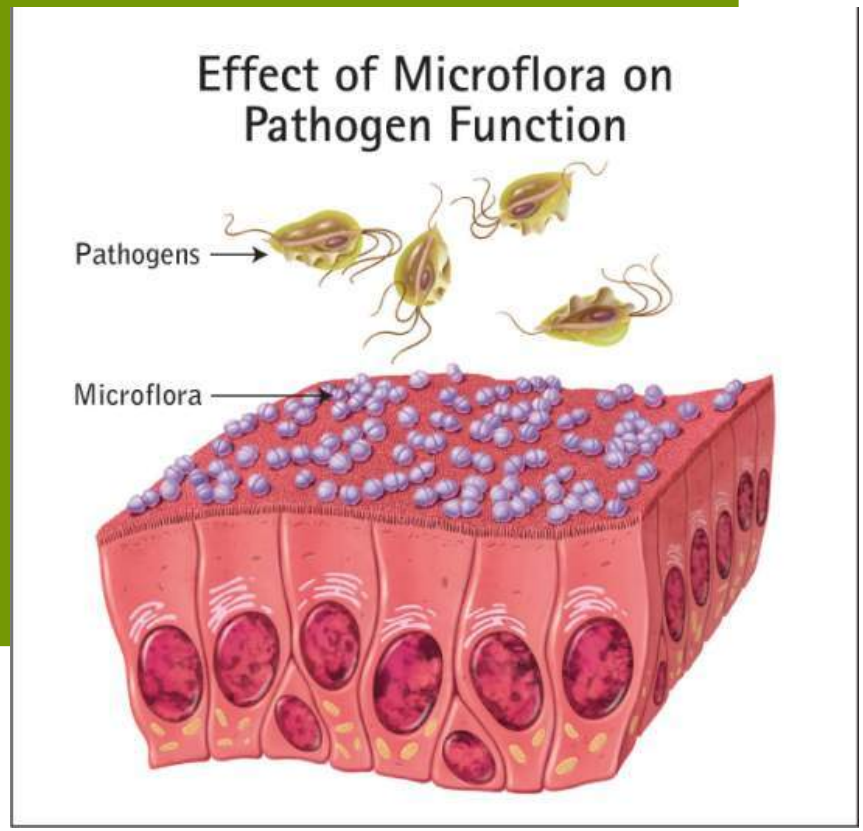
Biopsy by endoscopy:
Lymphocytic/plasmacytic enteritis

Rx: Medrol 4 mg q 24 hrs, continue low carbohydrate diet, cobalamin, and tylan

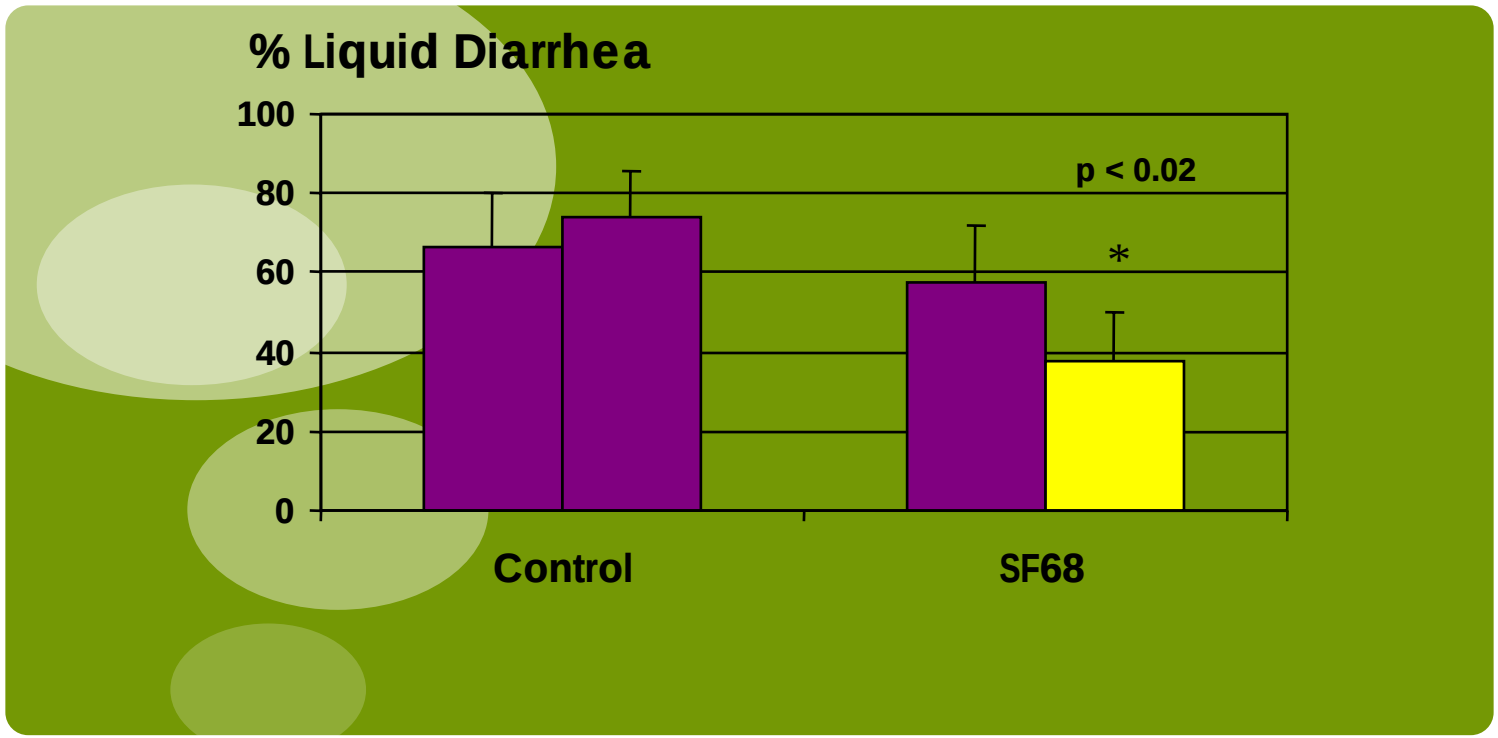
Fortiflora

What Makes a Good Probiotic?

- Safe, and Non-Pathogenic
- Survive in the GI tract to form Normal Flora
- Adhere to Intestinal cells
- Direct Effect on Pathogen Growth
- Block Attachment of Pathogens



Fortiflora improves fecal quality in cats with intractable diarrhea



Trial Design:

- Cats with long term intractable diarrhea
- Fed SF68 for three weeks
- % liquid diarrhea was determined

– Fecal quality improved in 7/8 cats fed SF68

Conclusions

– **SF68 improved fecal quality in cats with long term intractable diarrhea**

12 mo blood work/AUS

Increased ALT, AST, BUN (64), sl increased Cr (2.9)

CBC: WNL

U/A: culture neg, AUS: normal pancreas, hyperechoic, mottled liver, nephromegaly

22 month ck up

Doing well on 4 mg medrol q 24 hr, Fortiflora and tylan powder

Stool is firmer, mild weight gain

CBC/panel: High BUN, low TLI, microcytic anemia progressing

Add Viokase to treatment for presumed EPI (low TLI), iron supplementation

2.5 years later: Final visit

CC: shifting leg lameness, ascites, swelling of both front legs

Radiographs of front legs: periosteal reaction radius bilateral

AUS: Large abdominal mass: LSA on aspirate

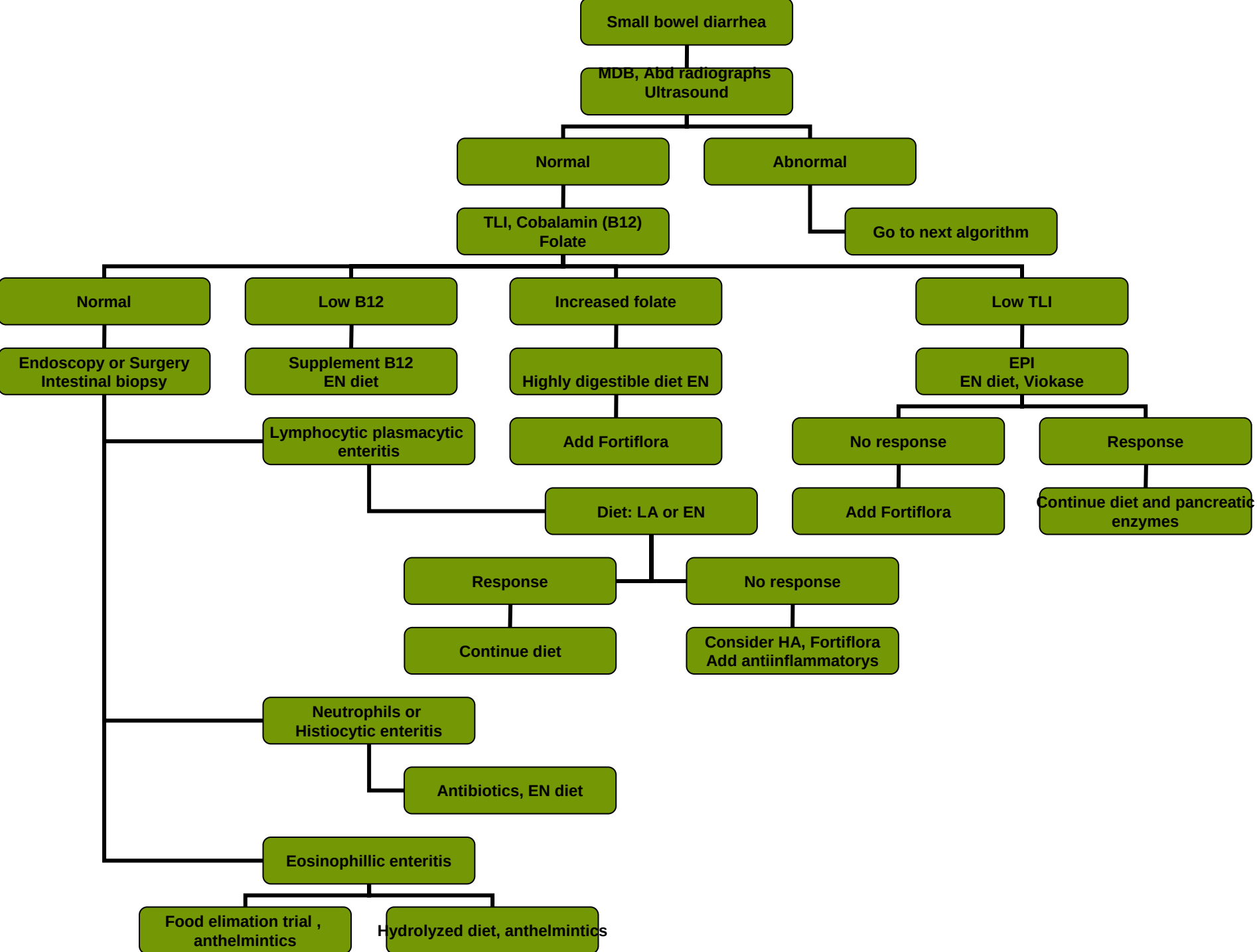
Owners elect euthanasia

Summary: Feline IBD and DM

- Low carbohydrate diet, moderate fat diet
- Medical management usually necessary
  - Probiotics
  - Prednisilone 1-2 mg/kg daily PO x 2 – 4 weeks, tapered
  - Antibiotics if needed
  - (vitamin B12) supplementation

Wunjo: 5 yr old MC Malamute

- 1 year history of itchy skin, particularly in perianal area, feet
- Currently on antibiotics, antifungals and limited antigen diet (lamb and rice)
- Presents for chronic small bowel diarrhea with bouts of LBD. Periods of inappetence and weight loss
- RDVM: Normal MDB, normal ultrasound except intestinal thickening, TLI, B12 and folate normal.


Small bowel diarrhea
MDB, Abd radiographs
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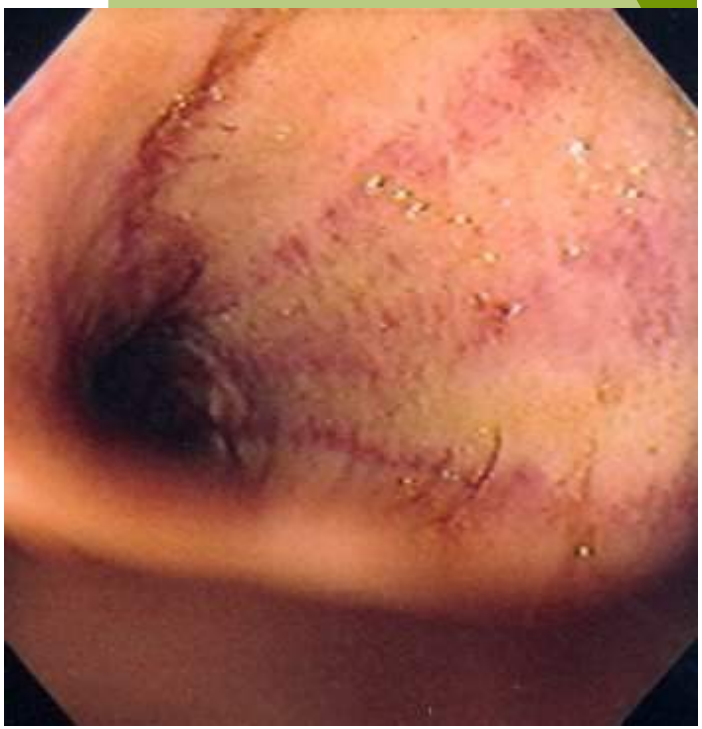
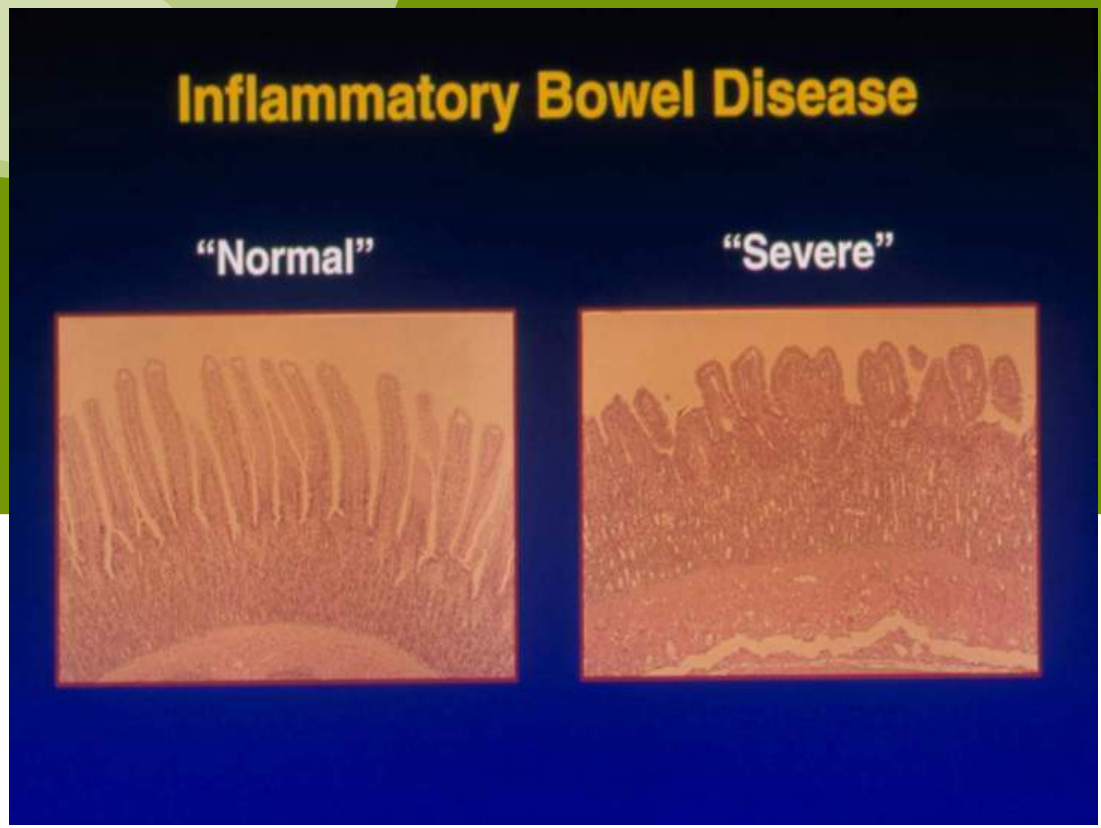
Normal
Abnormal
TLI, Cobalamin (B12)
Folate
Go to next algorithm
Normal
Low B12
Increased folate
Low TLI
Endoscopy or Surgery
Intestinal biopsy
Supplement B12
EN diet
Highly digestible diet EN
EPI
EN diet, Viokase
Lymphocytic plasmacytic
enteritis
Add Fortiflora
No response
Response
Diet: LA or EN
Add Fortiflora
Continue diet and pancreatic
enzymes
Response
No response
Continue diet
Consider HA, Fortiflora
Add antiinflammatorys
Neutrophils or
Histiocytic enteritis
Antibiotics, EN diet
Eosinophillic enteritis
Food elimation trial ,
anthelmintics
Hydrolyzed diet, anthelmintics

Wunjo:



- Normal MDB, TLI, ultrasound, fecal etc.
- Endoscopic evaluation and biopsy
  - Gastric---mild eosinophillic inflammation, no Helicobacter
  - Duodenum: Moderate to severe lymphocytic plasmacytic enteritis
  - Colon: Eosinophillic inflammation

Biopsy: Malamute with Food allergic gastroenteritis and IBD



Inflammatory Bowel Disease (IBD)

Diagnosis by elimination of all other potential causes, including food allergy,

AND

Presence of moderate to severe inflammatory changes on biopsy

Clinical signs range from intermittent diarrhea +/- vomiting to intractable diarrhea, inappetance and weight loss.

Food allergy or IBD?

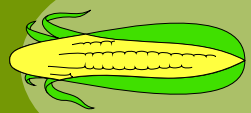
- Several studies show many dogs/cats with apparent IBD respond to novel or hypoallergenic diet
  - Food allergen
  - GI microflora
  - Other??

  Omega-3 fatty acids may be of benefit

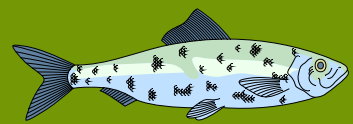
8. Source of omega 3 fatty acids

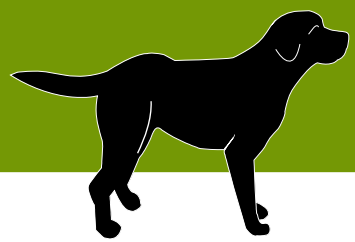
- From fish oil
- Provide an anti-inflammatory effect

Chicken fat
Vegetable fat



Fish oils
Linseed





Omega-6FAs

Omega-3FAs

MORE inflammation

LESS inflammation

Omega-3 EPA and IBD in dogs

Recent study of 57 pet dogs fed “novel” protein diet with EPA (Purina LA)

- Dogs referred for refractory chronic diarrhea
- 63% (36) responded to diet < 2 weeks

(Allenspach 2005)

Wunjo: Treatment

- Because of lack of response to limited antigen diets in the past, HA diet was recommended

  Ancillary therapy added:
  - One course of Panacur to rule out parasitic infections (eosinophillic inflammation in colon)
  - Probiotics: Fortiflora
  - Steroids if needed

- Complete remission on HA and probiotic therapy after Panacur

Clinical signs of food allergy

Food allergies can mimic other diseases

- **Dermatological symptoms (pruritus/itching)**
  - Non-seasonal
  - No sex predisposition
  - More frequent before 1 year old but can occur in dogs of any age
- **Gastrointestinal symptoms (vomiting & diarrhoea)**

97% show dermatological symptoms only

10-15% show GI with or without dermatological symptoms

Clinical signs of food allergy

Review of 116 canine cases

Affected areas =

Ears: 57 % **Feet/limbs: 50 %**

Ventrum: 38 % **Dorso-lumbar: 24 %**

Photographs courtesy of Dr Ross Bond

Food allergy diagnosis

- **No simple, rapid test**
  - **Blood and skin tests very unreliable and NOT recommended**
- **Food elimination diet trials**
  - **6-12 week elimination diet**
    - **Home cooked or commercial diets**
    - **Novel protein (e.g. PVD DRM) or hydrolysed (modified) protein diets (e.g. PVD HA)**
  - **Challenge and provocation diet trials**
    - **Reintroduce original diet once positive response been seen and clinical signs should recur**

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Two Nutritional Strategies:

Dietary management of food allergy

1. Novel protein diet

e.g. PVD DRM

WHY ?

- Avoid potential antigenic proteins
- Feed diet containing only novel proteins that are not recognised by the body

RISKS !

- Potential for cross reaction?
- Animal may develop hypersensitivity to the new protein(s)
- Not truly hypoallergenic



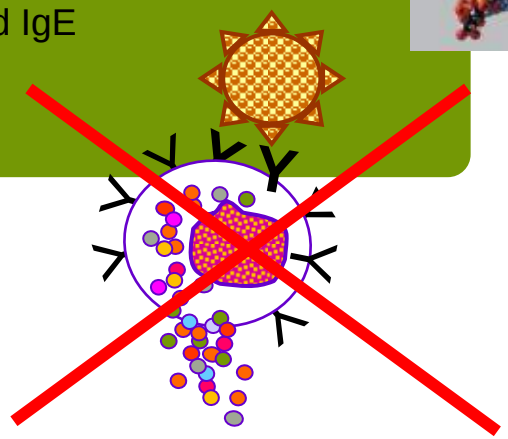

2. Modified protein diet

e.g. PVD HA

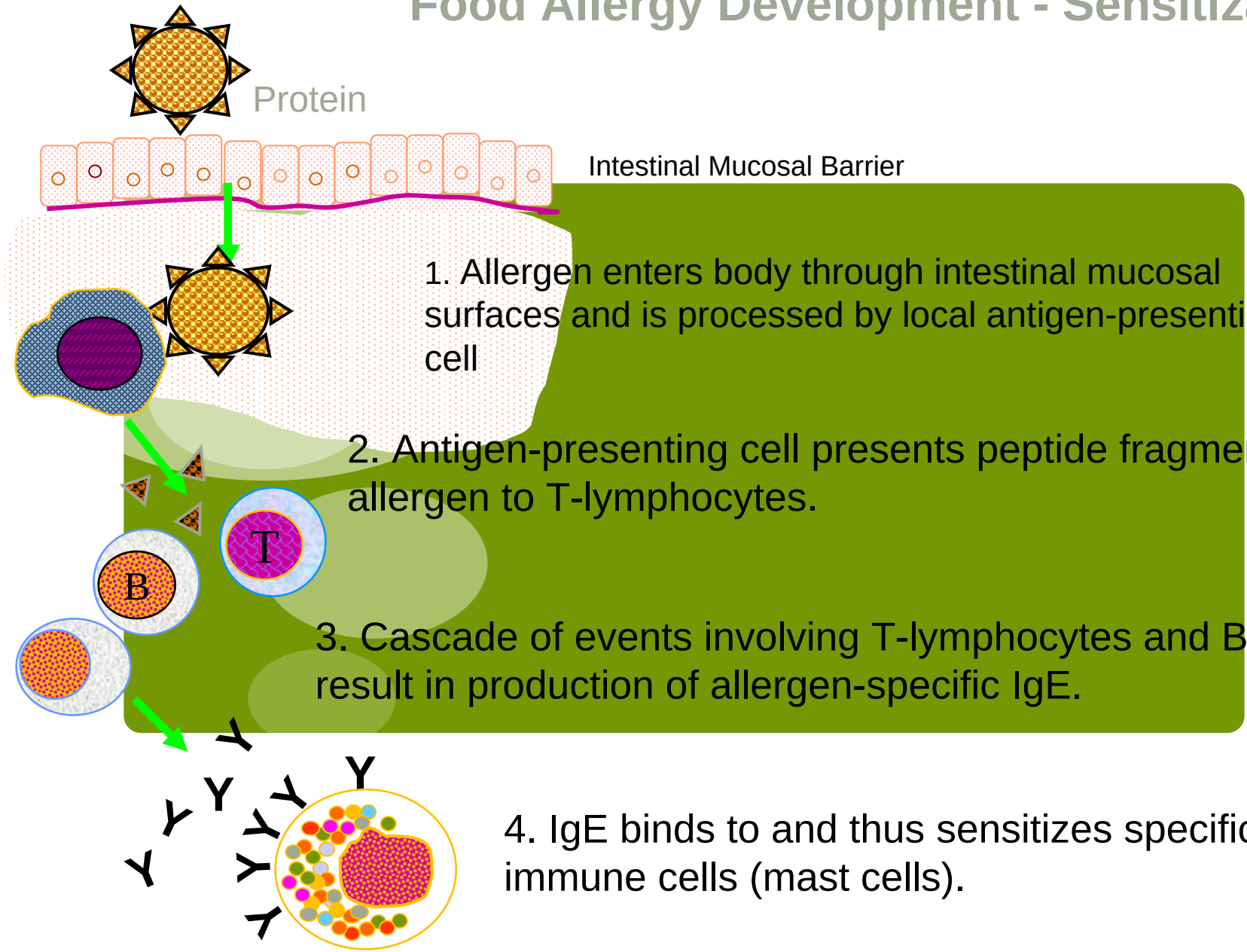
WHY ?

- Modification (reduction) of protein size by process called hydrolysis
  - ✓ Protein fragment too small to cause allergic reaction
  - ✓ Increases digestibility
  - ✓ Reduces likelihood of cross-linking of cell-bound IgE

NO RISK !

Food Allergy Development - Sensitization



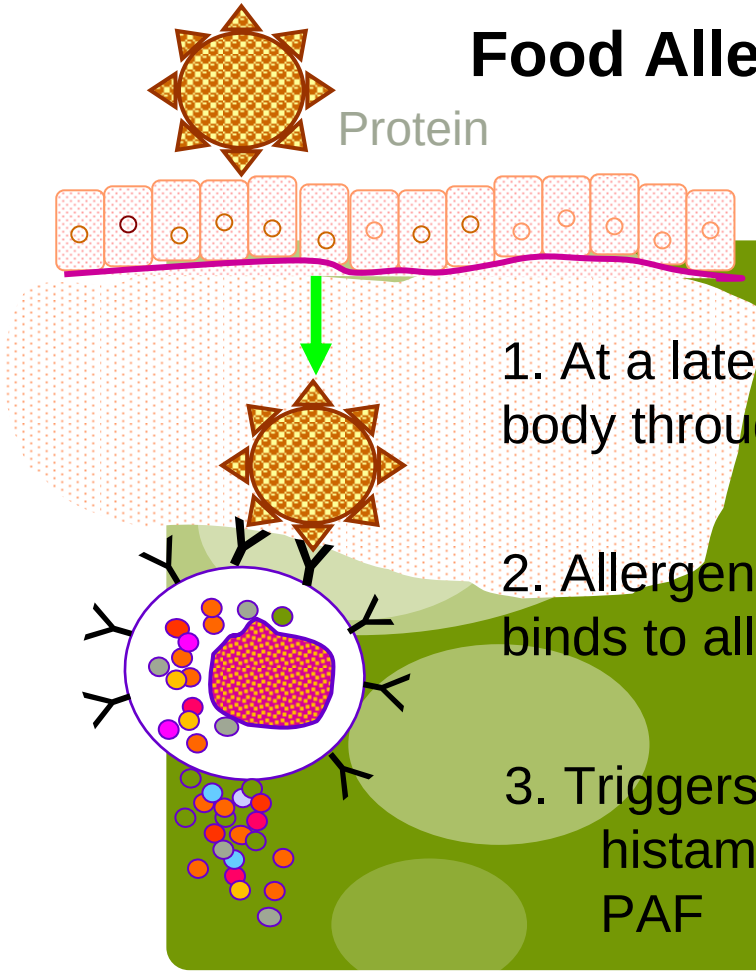
1. Allergen enters body through intestinal mucosal surfaces and is processed by local antigen-presenting cell

2. Antigen-presenting cell presents peptide fragments of allergen to T-lymphocytes.

3. Cascade of events involving T-lymphocytes and B-cells result in production of allergen-specific IgE.

4. IgE binds to and thus sensitizes specific immune cells (mast cells).

Food Allergy – Response to Allergen



1. At a later time, same allergen enters the body through mucosal surface

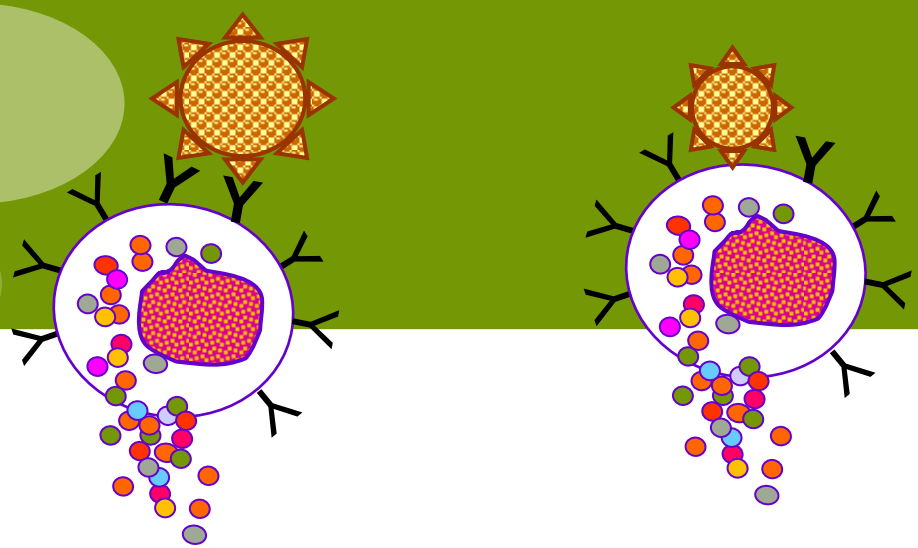
2. Allergen recognized by IgE on mast cell surface and binds to allergen.

3. Triggers release of granules containing
   histamines leukotrienes ECF-A
   PAF

4. Result: inflammation, pruritis and gastrointestinal disturbances

How do size and structure influence antigenicity?

- Antigen must be large enough to 'bridge' two IgE antibodies bound on mast cells to stimulate degranulation.



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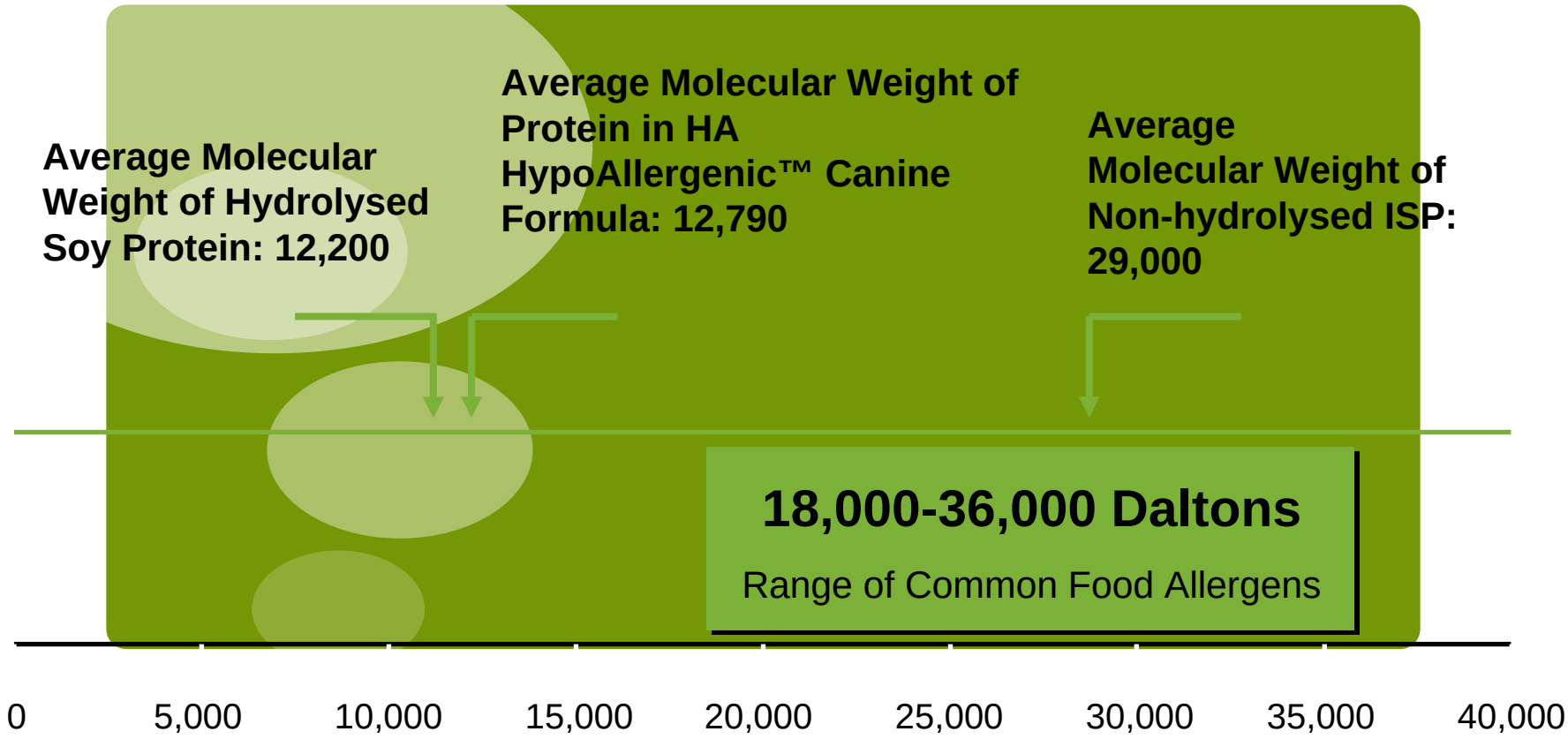
Why are hydrolyzed proteins hypoallergenic?

- Modification of protein size and structure can alter physiochemical properties
  - Decreases protease resistance (digestibility)
  - Reduce number of epitopes per molecule
  - Disrupt 3° presentation of epitopes
  - Reduce cross-linking of cell-bound IgE
- However modification can result in “new antigens”

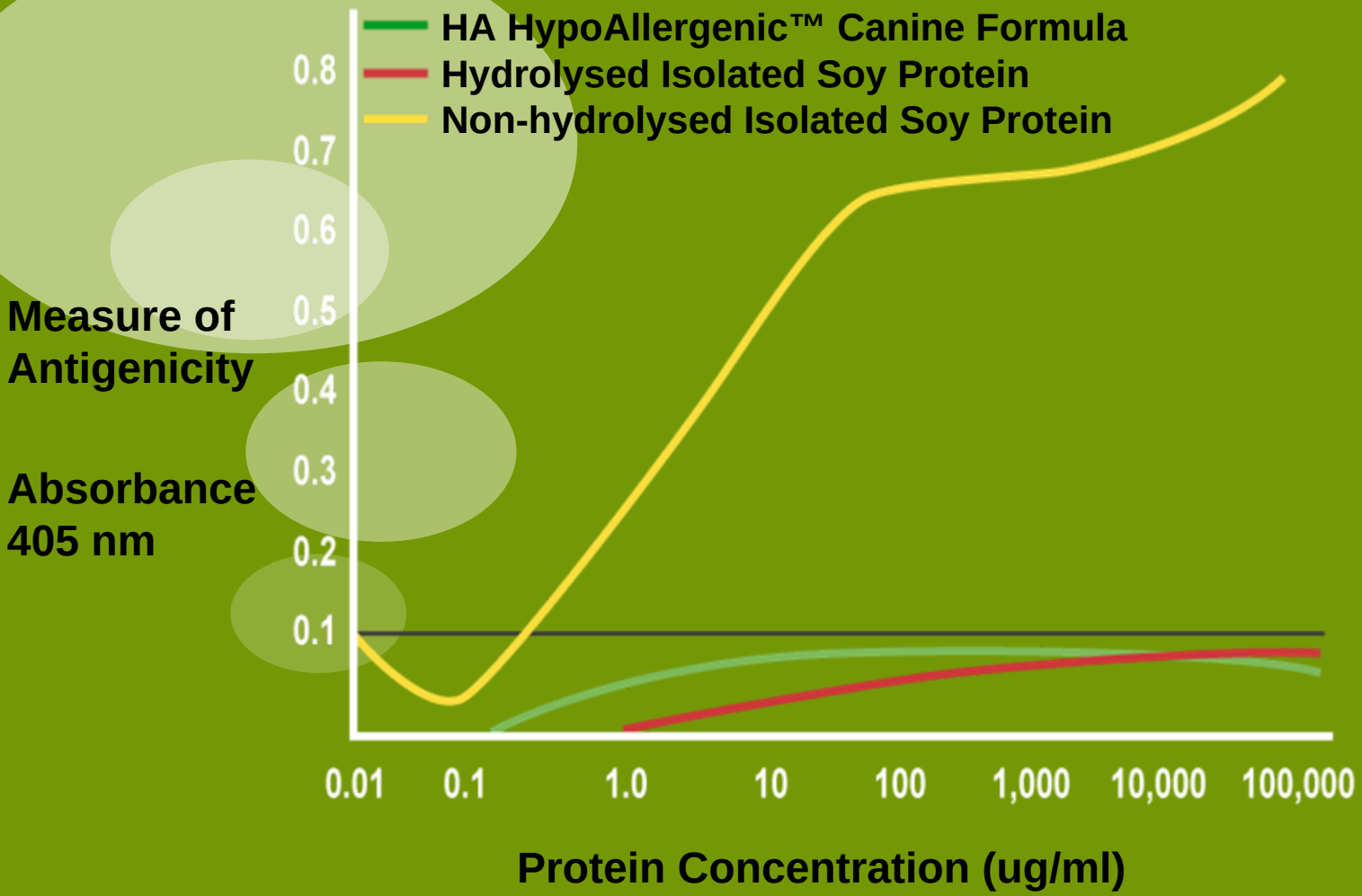
HA -

- Hydrolysed soya protein with a low molecular weight (less likely to cause an immune response)
- Single protein and carbohydrate source to reduce antigenicity of the diet
- High levels of omega 3s to help reduce inflammation
- Source of easy to digest Medium Chain Triglycerides
- Highly digestible to reduce intestinal workload
- Suitable for puppies as well as adult dogs
- Highly palatable
  - Diet useless if the animal won't eat it

Average molecular weight



Antigenicity



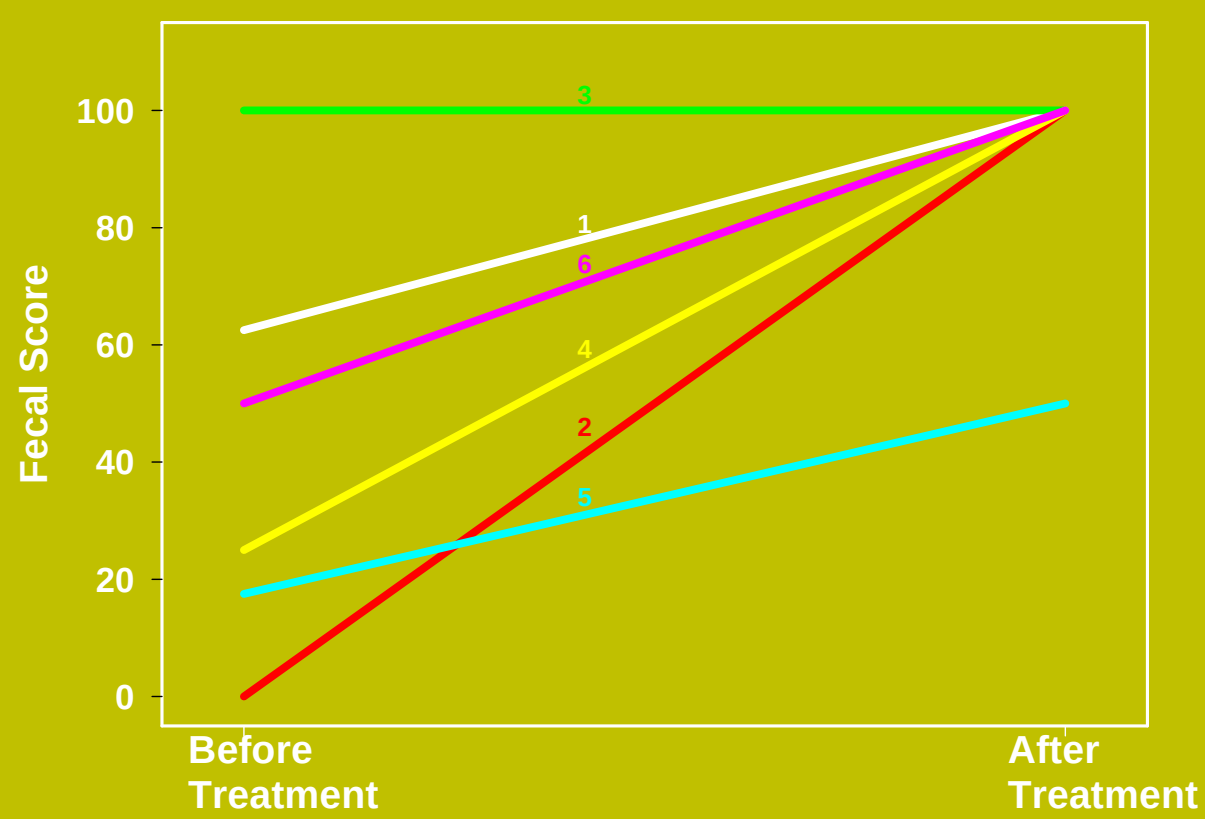
Hydrolyzed Protein Diet in IBD

Patient criteria:

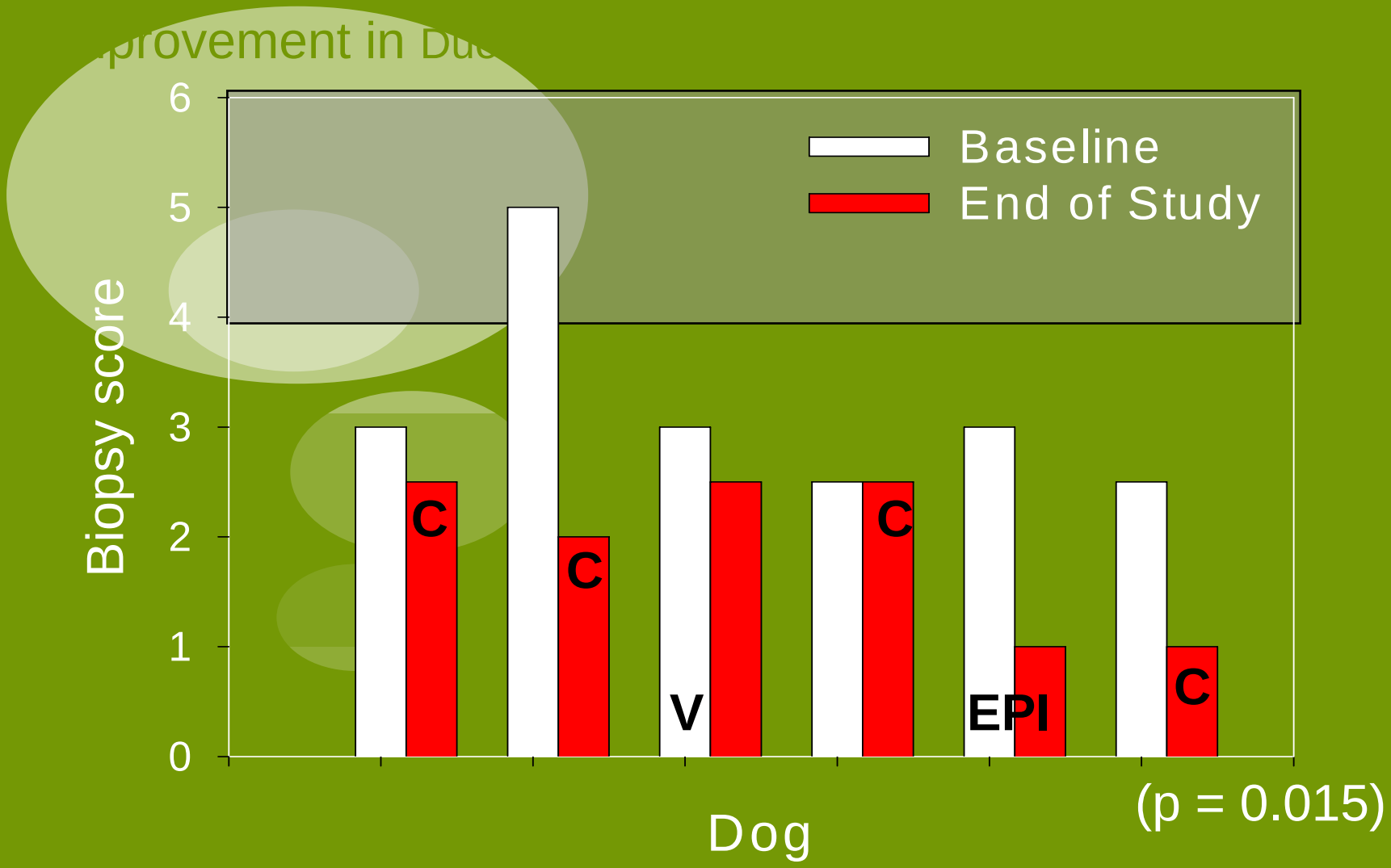
- **Chronic vomiting and/or diarrhea > 3 mo**
- **Non-responsive to prior treatment with limited antigen diet**
- **Fecal float/smears negative for parasites**
- **Histologic evidence gastric/duodenal inflam**
- **Treatment:**
- **2 to 4 weeks of therapy with ONLY a hydrolyzed soy protein diet**
- **8 additional weeks on diet plus appropriate therapy as needed for control of clinical signs**

(Marks 2002)

Hypoallergenic Diet in IBD: Fecal Scores



Fecal scores: (0=very watery: 100=very dry, firm stool)


Baseline
End of Study
Biopsy score
6
5
4
3
2
1
0
C
C
V
C
EPI
C
Dog
(p = 0.015)

Common Causes of Fat Malabsorption Diarrhea

- Inflammatory small bowel disease
- Intestinal lymphosarcoma
- Food allergy / gluten sensitivity
- Lymphangiectasia
- Exocrine pancreatic insufficiency
- Small intestinal bacterial overgrowth
- Pancreatitis
- Severe cholestasis
- Villus atrophy

Fat Digestion: LCT vs MCT

	LCT	MCT
Digestion		
Hydrolysis by gastric lipases	Slow	Fast
Hydrolysis by pancreatic lipases	Fast	Very Fast
Luminal transport		
Water solubility of FFA	Low	High
Requires bile acid micellarization	Yes	No
Absorption		
Paracellular absorption	None	Some
Re-esterification and chylomicron formation	Yes	Limited
Primary transport route from gut	Lymphatic	Portal

MCTs

PROs

- Easily digested – without bile salts or pancreatic lipase
- Easily absorbed – primarily portal blood
- Easily oxidized – ready source of energy

CONs

- Some entry into lymphatics
- Not a source of essential fatty acids
- May not aid absorption of fat-soluble vitamins
- MCT oil is unpalatable

Summary: Approach to Diarrhea

- Characterize diarrhea as Acute vs Chronic and small bowel vs large bowel diarrhea

  Use MDB, ultrasound and intestinal panels (TLI, B12 and folate) to rule out extra-intestinal causes of diarrhea

  Use endoscopy or full-thickness surgical biopsies to narrow down histologic diagnosis

  Use Dietary therapy as elimination diet (HA) or LA while awaiting biopsy results or prior to biopsy

- Specific therapy as indicated.l