

비엔동물전문의료센터 내과 세  
미나

# Chronic enteropathies and Gut Microbiota in Dogs and Cats

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의사



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- 01** : Chronic enteropathy and  
Inflammatory bowel disease
- 02** : Gut microbiota
- 03** : Probiotics and BASOD
- 04** : Fecal microbiota  
transplantation

# Case Presentation

Signalment) Poodle, 7Y, SF

## Chief complaint)

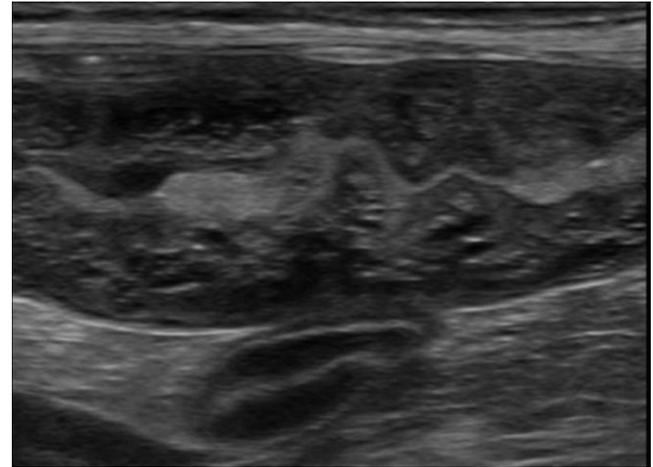
- 2주 전부터 간헐적 구토와 설사
- 지역병원에서 위장관 증상에 대한 대증처치 진행 시 개선 없음
- 최근 3일 간 물만 마셔도 구토할 정도로 증상 악화
- 설사도 지속됨

## Objective)

- P/E: BCS 4/9, No dehydration
- B/A: CBC, Serum chemistry, Electrolyte all WNL
- Fecal exam: 구균 70% 가량으로 dysbiosis 확인됨
- Abdominal US: 소장분절 전반의 벽 비후, 주변 림프절 종대 동반
- US- guided FNA : 세포 탈락 수 적어 유의미한 소견 x

P)

진단 위해 full-thickness biopsy 진행

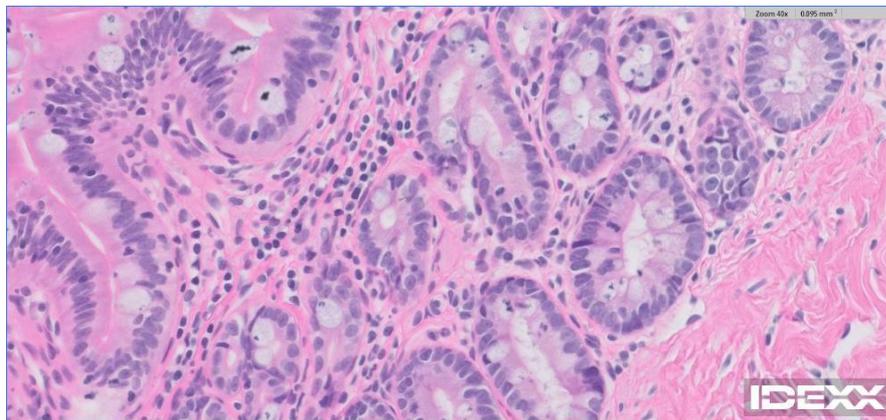


# Case Presentation

## Assessment) IBD (Inflammatory bowel disease)

### Treatment)

- Hydrolyzed diet (Hypoallergenic, Z/D...)
- Antibiotics (Metronidazole, tylosin...)
- Corticosteroids
- Other immunosuppressants (Cyclosporin, MMF, azathioprine, chlorambucil...)
- Other supportive care (fluid therapy, appetite stimulants, liver protenctants..)



# Chronic Enteropathy and Inflammatory Bowel Disease

► J Vet Intern Med. 2018 Dec 6;33(1):11–22. doi: [10.1111/jvim.15345](https://doi.org/10.1111/jvim.15345) 

**Narrative review of therapies for chronic enteropathies in dogs and cats**

[Kelly Makielski](#)<sup>1</sup>, [Jonah Cullen](#)<sup>2</sup>, [Annette O'Connor](#)<sup>2</sup>, [Albert E Jergens](#)<sup>1,✉</sup>

**Chronic enteropathy is the preferred term for chronic, relapsing, or intermittent gastrointestinal disturbances (anorexia, vomiting, diarrhea, weight loss) lasting more than three weeks, when extra-intestinal disease, neoplasia, and active infection are ruled out.**

**Chronic enteropathy includes**

- food-responsive enteropathies
- antibiotic-responsive enteropathies
- immunosuppressant-responsive enteropathy

**A prevailing hypothesis is that most forms of CE involve a complex interplay among host genetics, the intestinal microenvironment (primarily bacteria and dietary constituents), and the immune system**

**Some patients with chronic enteropathy respond favorably to probiotics, fecal transplants, and/or antibiotics, suggesting that an imbalance in the gastrointestinal microflora may be contributing to clinical signs**

# Chronic Enteropathy and Inflammatory Bowel Disease

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## Diet as primary and adjuvant treatment

- : Highly digestible, gluten-free diets with a novel protein sources or hypoallergenic, hydrolyzed diets
- : Elimination diet(eg, selected novel protein, cereal grains), Hydrolyzed diet were effective for clinical remission
- : High fat vs low fat diet showed no difference in treatment response (Laflamme et al, 2011)

## Antimicrobials as primary and adjuvant treatment

- : Tylosin (15 mg/kg BID) and metronidazole (5-10 mg/kg BID) for about 4-6 weeks
- : Tylosin is thought to be immunomodulatory by supporting the development of enterococci with probiotic effect
- : Metronidazole affects anaerobic bacteria and protozoa, and is supposed to have immunomodulatory effects by inhibiting cell mediated immunity and leukocyte--endothelial cell adhesion
- : Ulcerative colitis in Boxers, E coli play major role in the pathogenesis, and the use of enrofloxacin are often successful

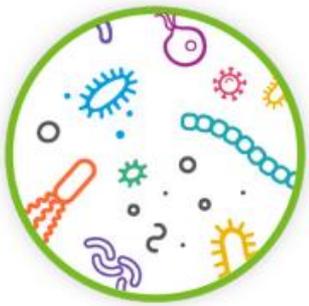
## Immunosuppressants

- : Prednisone/prednisolone has been used as single agent or in combination with other medications
- : Starting the treatment with an immunosuppressive dosage (2 mg/kg per day) until clinical improvement and then gradual reduction of the corticoid dose over several weeks to months
- : Some patients need lifelong glucocorticoid treatment / Others can be gradually taken off the medication and stay clear of clinical signs without further immunosuppression

# Gut microbiota

**There are trillions of bacteria, viruses, fungi, and other microorganisms along the intestinal tract**

- Break down food
- Activate immune system
- Produce hormones
- Compete with other microbiomes
- Make vitamins



***“Feed good food, feed good microorganisms”***

**Research shows that high-protein, high-fiber, and low-carbohydrate diets are ideal for both cats and dogs.**



# Gut microbiota



## Proteins

- Protein is essential for cats and dogs
- As protein is digested, it is broken down into important molecules that are critical for beneficial gut bacteria to perform their functions
- Not only are the building blocks of protein an important source of energy for gut bacteria, but they are also important for improving the diversity of the gut community



## Fiber

- Dietary fiber is important for maintaining a healthy stool consistency and frequency of bowel movements
- It also feeds beneficial gut bacteria
- When bacteria break down fiber in a process called fermentation, they produce important molecules that are critical for healthy immune system function and for combating inflammation
- Diets high in fiber are associated with lower rates of cancer and several other long-term health conditions



## Carbohydrates

- Long-term feeding of higher-carbohydrate diets and treats can result in poor gut health
- Too many carbohydrates can cause an overgrowth of a group of bacteria called Firmicutes
- The body needs some Firmicutes to keep the microbiome healthy, but too many of these bacteria can spread excess inflammation throughout the body

# Gut microbiota



## Dietary fiber

: Carbohydrate macronutrient that resists enzymatic digestion in the mammalian small intestine

: In a more encompassing term, includes more of the soluble or gel-forming polysaccharides

Sources: cellulose, hemicellulose, pectins, gums, lignin...

### \* Fructooligosaccharides(FOS)

: Some fibers are termed prebiotics, which “feed” beneficial bacteria

: FOS are complex carbohydrates that are fermented by colonic microbes to produce SCFAs

: Adding FOS to the diet seems to increase the normal colonic beneficial flora

: One study found FOS had no effect on bacterial numbers or species in the duodenum, but did alter the fecal microbiota in healthy cats by increasing lactobacilla and Bacterioides species and decreasing Escherichia coli and Clostridia species. (*Freiche V et al, 2011*)

# Gut microbiota

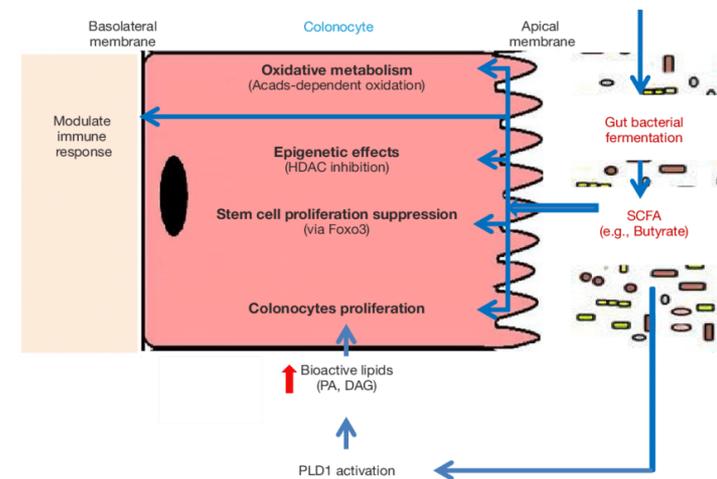
## Dietary fiber, effects on the intestine

- When fiber is fermented by colonic bacteria, SCFAs are formed.
  - : The SCFAs, especially butyrate, provide more than 70 per cent of the energy for colonocytes, which is important for cell renewal and repair.
  - : Butyrate also appears to directly inhibit tumor formation in the large intestine

- Increased SCFA also increases colonic ammonia absorption by decreasing the pH and trapping the ammonium ions.
  - : The decreased pH also discourages the growth of some pathogenic bacteria, such as *Clostridium perfringens*, *Salmonella* and pathogenic *Escherichia coli*.

- A study in dogs with chronic idiopathic large intestinal diarrhea showed a good to excellent response to the addition of psyllium in 96 per cent of the dogs (*Leib M S, 2000*)

- Fiber producing viscous gels, such as psyllium, will increase the faecal water and faecal bulk, and the SCFA produced may stimulate colonic smooth muscle contractions.
- However, these may worsen constipation in an animal with colonic dysmotility.
- In two studies in cats with constipation, 82 per cent to 93 per cent showed improvement on a psyllium-enriched diet.
- However, diets with increased fiber should not be used in cats with severe obstipation



# Gut microbiota

## Diet's Influence on the Gut Microbiome

Macronutrients can promote the growth or reduction of populations of different bacterial groups.

*Megamonas*

Increase with Fiber

*Clostridium*

Decrease with Fiber & Carbohydrate, Increase with Protein

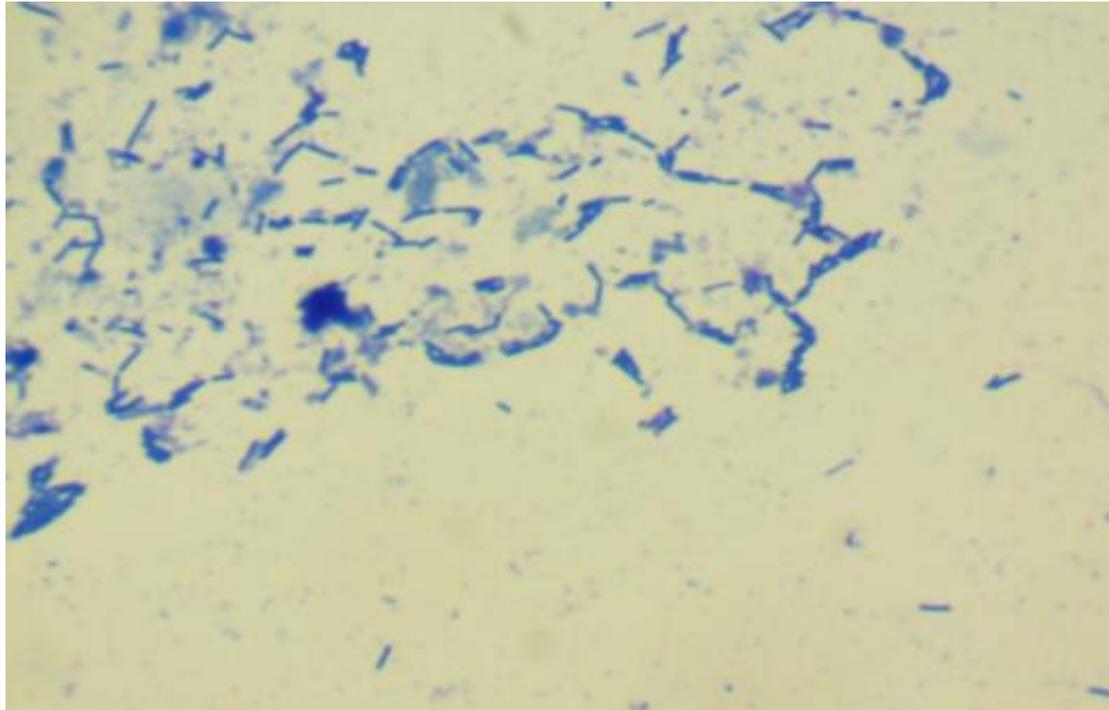
*Ruminococcus*

Decrease with Carbohydrate, Increase with Fiber

*Fusobacterium*

Decrease with Fiber, Increase with Protein

# Gut microbiota

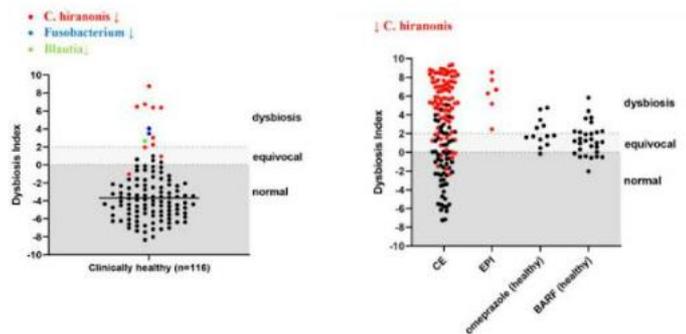


**Clostridial enteritis**

# Gut microbiota

## Clostridium

✓ C.hiranonis 감소 -> 2차 BA의 감소 -> Intestinal Dysbiosis



Primary bile acid change into 2nd bile acid by C. hiranosis,

2nd bile acid works local and systemic inflammatory character

- There are over 150 different kinds (species) in the Clostridium group
- Clostridium hiranonis, (also called Peptacetobacter) which assists in bile acid metabolism.
- Most of Clostridium perfringens strains are nonpathogenic and produce beneficial compounds like butyrate.
- Only certain strains may contribute to intestinal disease through the production of specific toxins.

# Gut microbiota

**Intestinal dysbiosis : Imbalance among the types of microorganisms in the GI tract**

- Overgrowth of potential pathogens
- Decrease in commensal organisms
- Decreased overall abundance of organisms

Dysbiosis : no single gold standard for assessing the GI microbiota and dysbiosis

## **Conclusion**

**: One or two population of bacteria dominant >> bacterial overgrowth**

**: Nucleated cells should not be seen**

**: More than 3-5 /hpf suggests a clostridial overgrowth**

**: Presence of rare campylobacter spp. organisms is a significant finding, especially in the patient with diarrhea**

# Gut microbiota

## **The impact of medication**

- Most antibiotics aren't selective in which bacteria they target, they can be very disruptive to gut bacterial communities and can kill off entire groups of beneficial bacteria.
- Bacteria that survive the antibiotic treatment can spread resistance genes in the host and the environment, contributing to the global decrease in the effectiveness of antibiotics.
- As the gut bacterial community recovers after the course of antibiotics, the bacteria that were present originally often do not grow back in the same proportions as they were before.

## **During the treatment**

- : Give the antibiotics exactly as the guideline directs you to
- : Monitor for symptoms of reaction to antibiotics

## **After the treatment**

- : Increase prebiotic fiber in your pet's diet to help rebuild populations of beneficial bacteria
- : Be vigilant about diet and exercise routines in the months

# Gut microbiota



**Bentonite** (a montmorillonite clay), which is superior to Kaolin in absorption

**Pre/Probiotics** to balance intestinal flora

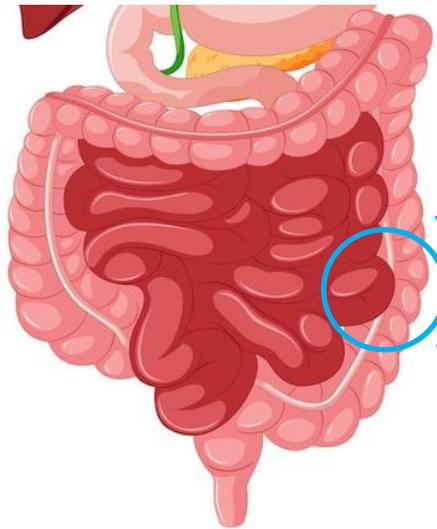
**Glutamine** supports intestinal cell regeneration

## Ingredients:

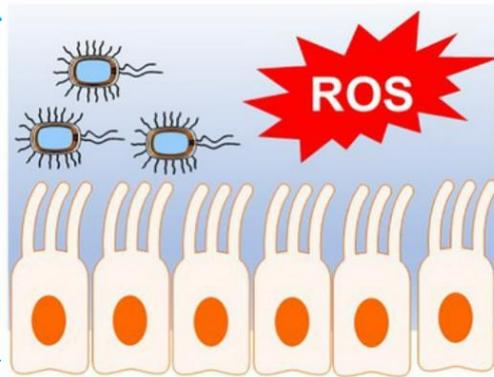
Psyllium Seed Peels, Sugar Beet Fiber, Wheat Bran Thickness, Inulin, Beta Glucans, Mannan Oligosaccharides (MOS), Kiwi Powder, Aroma, Oleic High Sunflower Oil, Sodium Chloride



# Probiotics and BASOD

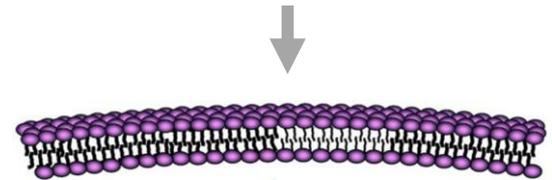
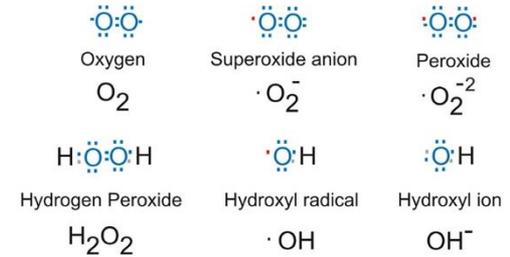


[https://kr.freepik.com/free-vector/gastrointestinal-tract-anatomy-for-education\\_24093235.htm#query=gastrointestinal&position=0&from\\_view=keyword](https://kr.freepik.com/free-vector/gastrointestinal-tract-anatomy-for-education_24093235.htm#query=gastrointestinal&position=0&from_view=keyword)



<https://www.frontiersin.org/articles/10.3389/fcell.2021.665591/full>

<https://www.biotek.com/resources/white-papers/an-introduction-to-reactive-oxygen-species-measurement-of-ros-in-cells/>



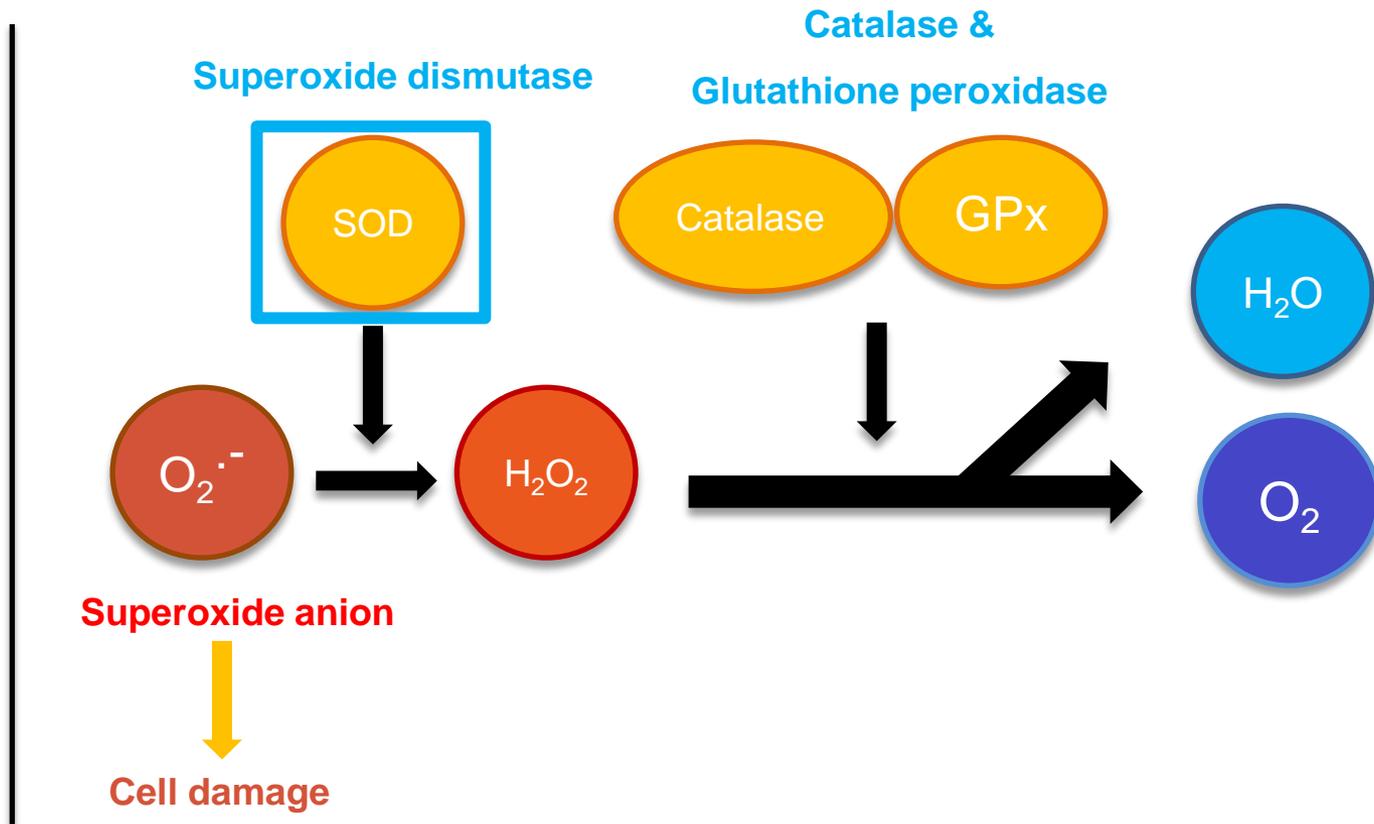
## Lipid derived electrophiles

- Acerolin
- 4—hydroxynonenal
- Malondialdehyde
- Epoxyketoctadecenoic acid

## Chronic and degenerative diseases

# BASOD

## Superoxide dismutase (SOD)



# BASOD



*Bacillus amyloliquefaciens*



SOD over-expressed natural strain  
**SOD1** production and Transfer

**BASOD**<sup>TM</sup>



- ✓ **Spore forming bacteria**
  - Resistant to heat, stomach acid, digestive enzymes, etc
- ✓ **Therapeutic effect**
  - Regulation of inflammatory cells and inflammatory cytokines in the intrinsic layer of intestinal mucosa
  - Easily settle in intestinal mucosa cells to produce antioxidant enzymes and substances

# BASOD, Clinical Trials

The logo for BASOD, featuring the word "BASOD" in a bold, sans-serif font. The letters "BA" are blue, "SO" are green, and "D" is blue. A small "TM" trademark symbol is positioned to the upper right of the "D".

1 tablet per 5kg, Per oral  
For 12 weeks, Once daily



Control group

2 Dogs

Treatment group

3 Dogs, 6 Cats

# BASOD, Clinical Trials

## Control

2 Dogs

Diet (Hypoallergenic foods)

Antibiotics (2 weeks)

Corticosteroids

+/- Immunosuppressives

## Treatment

3 Dogs, 6 Cats

Diet (Hypoallergenic foods)

**BASOD**<sup>™</sup>

# BASOD, Clinical Trials

## ❖ First Outcome

Clinical signs improvement (CCEAI, FCEAI)

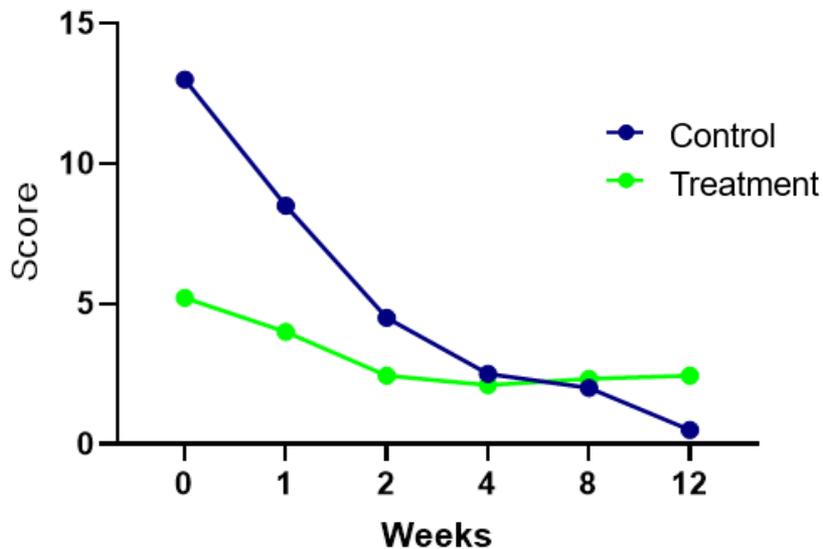


Figure 1. Changes in clinical symptoms in control and test groups in suspected IBD patients (average scores of CCEAI and FCEAI)

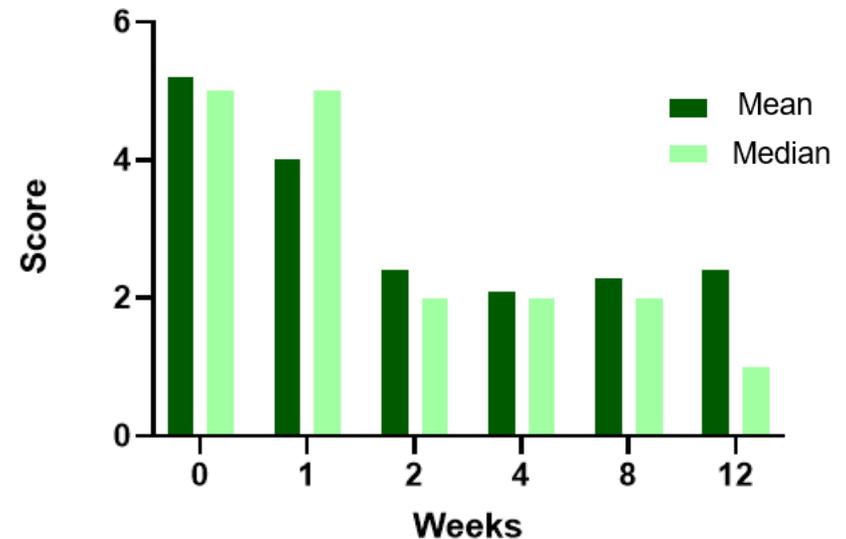


Figure 2. Changes in clinical symptoms according to administration of test drugs in suspected IBD patients (test group)

# BASOD, Clinical Trials

## ❖ First Outcome

Clinical sign improvement (CCEAI, FCEAI)

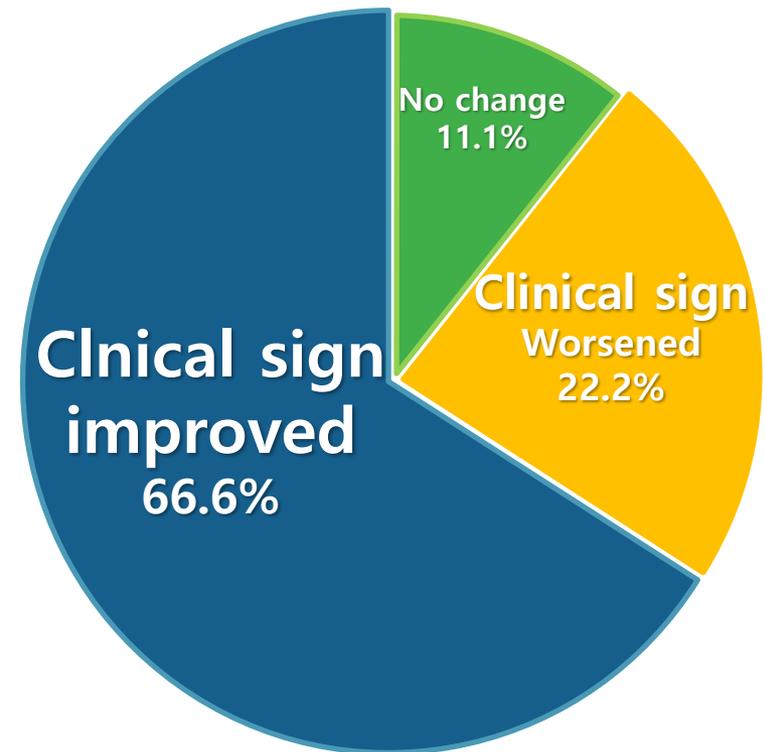
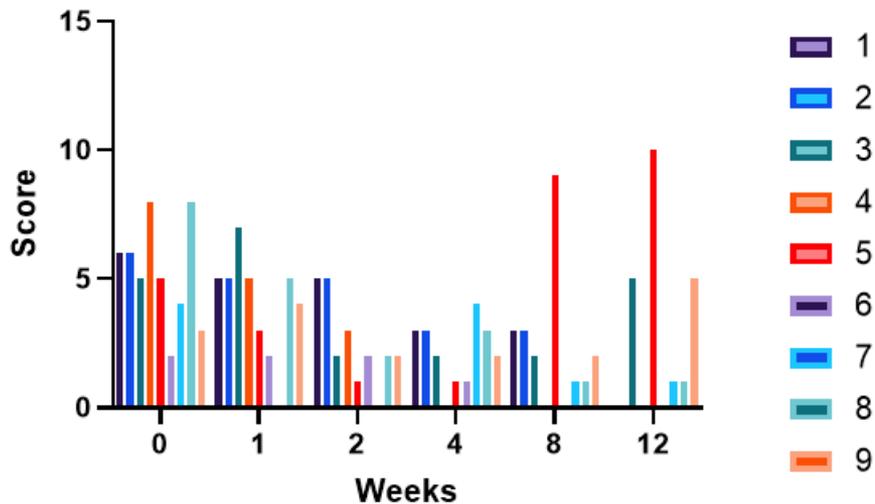


Figure 3. Changes in clinical symptoms according to administration of test drugs in suspected IBD patients (treatment group, individual patient score)

# BASOD, Clinical Trials

## ❖ Adverse reactions



Subjective evaluation



Physical examination

**No significant adverse reactions were observed**

# Clinical Relevance & Limitations

## ❖ Conclusion

**IBD**

Clinical sign



Overall improvement (66.6%)

Adverse reactions



Not observed

**BASOD can be used as supportive therapy or alternative treatment in dogs and cats with IBD**

# Fecal Microbiota Transplantation

## FMT

- Transfer of feces from a healthy donor into the gut of a diseased recipient with the goal of modulating the recipient's intestinal microbiome
- The procedure can be done via enema, colonoscopy, duodenoscopy, nasogastric/nasojejunal tube, or by ingesting oral capsules.

### **The gut microbiota (bacteria, archaea, fungi and protozoa) and Health of hosts**

- Development and support of the immune system
- Production of metabolites with nutritional value or signaling function
- Maintenance of homeostasis (eg, maintenance of the intestinal barrier)
- Resistance to colonization with pathogenic bacteria

### **The beneficial effects of FMT**

- An increase in richness in the microbiome and a shift of recipient microbial profiles toward those of the healthy donor
- Create less favorable conditions for the growth of C difficile, for instance by providing bacteriocins and reestablishing the prominence of secondary bile acids over primary bile acids in the feces
- Restoring the integrity of the intestinal barrier through secretions of mucin to support the mucous layer separating the epithelial cells from the gut lumen
- A significant shift toward butyrate-producing species of bacteria following FMT may induce regulatory T cells and promote interleukin-10 production, ultimately resulting in favorable modulation of the mucosal immune response and decreased inflammation

# Fecal Microbiota Transplantation

## 1. Infection

1) Parvovirus infection (Pereira et al, 2018, non-randomized clinical trial)

- 33 received standard treatment, 33 received FMT in addition. FMT administered within 6-12 h of admission and q48 h thereafter by enema
- Clinical effect: No difference in mortality rate, quicker resolution of diarrhea, and shorter hospital stay in dogs receiving FMT

2) *C. perfringens* infections unresponsive to metronidazole and AMC (Murphy et al, 2014, Case report)

- 8 dogs receiving between 1 and 3 FMT by enema
- Clinical effect: Immediate resolution of diarrhea after FMT in all dogs
- 6/8 dogs had negative fecal PCR for *C. perfringens* toxin after FMT

## 2. IBD

1) IBD refractory to conventional treatment (Bottero et al, 2017, Case report)

- 16 adult dogs with severe refractory IBD of >1yr duration. Oral group received FMT q48-72h by Endoscopy+Oral (9) or Oral (7)
- Overall, mean chronic canine enteropathy clinical activity index seemed to decrease in most dogs following FMT
- Heterogenous clinical presentation and concurrent treatments complicate evaluation

2) IBD refractory to antibiotic and immune-suppressive treatment over time (Niina et al, 2019, Case report)

- One 10-year-old toy poodle, Received 9 FMT by enema over 6 months
- Improved Clinical IBD Activity Index and fecal consistency during the treatment period
- Increase in Fusobacteria, Frimicutes and Bacteroidetes, decrease in Proteobacteria

# Fecal Microbiota Transplantation

## 3. Diarrhea

1) Various chronic GI diseases associated with diarrhea and vomiting (Gerbec, 2016, Case report)

- 3 dogs receiving 1 single FMT by endoscopy
- Owners reported clinical improvement for 1-2 month followed by relapse in 2 dogs, no changes in 1 dog
- Improvement of the fecal dysbiosis index in 2 of 3 dogs

2) Acute hemorrhagic diarrhea syndrome (Burchell et al, 2019, Randomized clinical trial)

- 4 dogs received a single FMT and 4 dogs received saline by endoscopy
  - No difference in clinical score between FMT and saline
  - Diversity index improved in FMT dogs at discharge but not 30 d later.
- 3) Uncomplicated acute diarrhea of <14 d duration (Chaitman et al, 2020, Clinical trial)
- 11 dogs received a single FMT, 7 dogs received metronidazole(MTZ) 15 mg/kg q12 h for 7 days, 14 healthy control dogs
  - Lower(better) fecal score at days 7 and 28 for both treatments, FMT fecal score lower than MTZ at day 28
  - Fecal dysbiosis index better with FMT than MTZ at days 7 and 28. FMT dogs tended to cluster with healthy dogs at day 28 unlike MTZ dogs

# Fecal Microbiota Transplantation

## Preparation and administration of the fecal solution

1. Use feces within 6-12 h of defecation.
2. Mix 1 volume feces with 4 volumes of 0.9% NaCl (20% solution)
3. Blend on high until the stool is liquefied and no large pieces are seen
4. Filter solid material using gauze or other method.
5. If freezing, add glycerol (10 mL per 100 mL final solution) and store at -80°C

### Box 1

#### Recommended selection criteria for canine fecal donors

##### History and physical examination

- Preferably between the ages of 1 and 10 years
- Preferably no travel history outside the local area
- No health issues in the last 6 or 12 months
- No history of chronic GI diseases, allergies, and immune-mediated diseases
- Has not received any antibiotics in the last 12 months
- Regularly vaccinated according to existing guidelines
- Fed a balanced diet
- Not overweight or underweight (9-point body condition score between 4 and 6)
- Normal fecal consistency
- Deemed healthy on physical examination

##### Laboratory screening

- Normal CBC and serum biochemistry
- Consider evaluation of basal cortisol, thyroxine
- Negative for parasite ovas on fecal floatation, consider empirical deworming with a broad-spectrum anthelmintic drug
- Negative for *Giardia* oocysts on fecal floatation and ELISA fecal test, see above for empirical deworming
- Consider testing for fecal pathogens such as *Salmonella* spp., *Campylobacter* spp., etc.

##### Fecal microbiome evaluation

- Fecal dysbiosis index<sup>31</sup> less than 0

Abbreviations: CBC, complete blood count, ELISA, enzyme-linked immunosorbent assay.

# Fecal Microbiota Transplantation

- In human medicine, a recent systematic review identified FMT via colonoscopy and oral capsules as superior to FMT via nasogastric tube and enema for the treatment of CDI
- However, a randomized clinical trial showed high efficacy of FMT administered as enema without colonic lavage
  
- Human FMT recipients are requested to remain on their back for approximately 30 minutes after completion of the procedure in order to limit the urge to defecate.
  
- Complications of FMT in human patients seem to be generally limited to abdominal discomfort, bloating, cramping, diarrhea/constipation, nausea/vomiting, and low- grade fever
- However, rarely more serious infectious complications have been reported such as highgrade fever and bacteremia with multidrug resistant (MDR) bacteria, and death was described recently in 2 patients

# Fecal Microbiota Transplantation



- DoggyBiome and KittyBiome are fecal microbiota transplant (FMT) in a capsule
  - Convenient capsules are an alternative to surgical FMT, which is equally effective but more invasive and less convenient
  - It is superior to probiotics and prescription diets because it contains a complete, healthy, and well-functioning community of gut microorganisms
  - Helpful for chronic digestive issues and skin conditions, including diarrhea, vomiting, constipation, itchy skin, and atopic dermatitis.
- \* Give capsules whole, by mouth, for at least 30 days. Do not open or crush capsules.
- \* If the patient is particularly sensitive to new supplements, start by giving just 1 capsule and waiting 3-4 days before giving the next one. Then, gradually move towards more frequent dosing.
- \*If the patient is currently stable, give 1 capsule daily for the first 3 days, then progress to more frequent dosing according to this dosing chart.

비엔동물전문의료센터 내과 세  
미나

**Thank you**  
**Any questions or comments?**

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