VIVALDIS Animal Health

petsmile

The world of happiness

www.vivaldis.co.in | SEP-OCT 2018

Gastroenterology Special

TOP NEWS :

The beneficial side of pets' bacterial microbiome

The GI microbiome as "a highly diverse community of microorganisms, primarily bacteria that inhabit the intestinal tract." There are trillions of bacteria living in intestinal tract, far out numbering the host cells that make up the entire body. At birth, mammals do not have an active bacterial microbiome. However, bacterial colonization of the gut, respiratory tract, and skin starts immediately, beginning with bacteria from the mother's bodily fluids and skin and the newborn's environment. Bacteria in the gut assist in the digestion of nutrients, synthesize vitamins, prevent infection, impact the immune system, and promote the development of several organ systems, including the gastrointestinal tract and brain.

Feb 11, 2018 / Advances in Medicine / Internal Medicine / Preventive Health / Cats / Dogs

Dog Poop Microbiome Predicts Canine Inflammatory Bowel Disease

Tell-tale microbes in fecal samples allow for IBD diagnosis in dogs but not humans

Researchers from California University discovered a pattern of microbes indicative of IBD in dogs. With more than 90 percent accuracy, the team was able to use that information to predict which dogs had IBD and which did not. In this latest study, Knight and team collected faecal samples from 85 healthy dogs and 65 dogs with chronic signs of gastrointestinal disease and inflammatory changes. The 16S rRNA sequencing technique used to quickly identify millions of bacterial species living in a mixed sample, based on the unique genes they harbour. They could distinguish IBD dog faeces from non-IBD with more than 90 percent accuracy.

October 03, 2016 | Heather Buschman, PhD

New viruses associated with canine gastroenteritis

Viral gastroenteritis is a common condition in canine patients with virus particles detectable in up to 60 percent of diarrhoeic faecal samples. Seven novel viruses, along with four main viruses (parvovirus, enteric coronavirus, rotavirus and distemper) are identified which are norovirus, vesivirus and sapovirus from calicivirus family, bocavirus from parvovirus group and a circovirus, a picornovirus and an astrovirus. It is important that veterinary surgeons are aware that five have RNA-based genomes and are capable of mutating at faster rates than DNA-based pathogens.

Sarah Caddy, University of Cambridge, The Veterinary Journal, 232, 57-64

Researchers have made a surprising finding: dogs' gut microbiomes are actually very similar to our own.

In a randomized controlled trial, done on 32 each of beagle and Labrodor retriever variety, it was found that there is almost 63% of overlap between dog's gut microbiomes and that of humans'. The canine patients selected for study were such that half were overweight and half having normal body weight. The researchers collected total 129 samples of dog stool which allowed mapping of 1,247,405 genes in total. There was only 20% and 33% overlap between murine & human microbiome and pigs & human microbiome respectively.

BMC Vet Res. 2016; 12: 49.

Oral chondroitin sulfate and prebiotics for the treatment of canine Inflammatory Bowel Disease: a randomized, controlled clinical trial

Sergi Segarra, Silvia Martínez-Subiela, Marta Cerdà-Cuéllar, Daniel Martínez-Puig, Alberto Muñoz-Prieto, Fernando Rodríguez-Franco, Antonio Rodríguez-Bertos, Karin Allenspach, Alfonso Velasco, and José Cerón

Background

Inflammatory bowel disease (IBD) in dogs is a chronic GI tract disorder of unknown cause although the mucosal immune system, genetic susceptibility, and the enteric microenvironment are considered to be important in its pathogenesis. Treatment protocols for IBD combine diet modification, antibacterials and immunosuppressive therapy, aiming at reducing intestinal inflammation and restoring gut normobiosis. Any long-term treatment protocol for IBD should aim at maintaining patients in clinical remission with minimum associated side effects.

Chondroitin sulfate (CS), a natural glycosaminoglycan present in the extracellular matrix, inhibits NF-κB activity , which is a suggested component of the anti-inflammatory activity of glucocorticoids and cyclosporine A. NF-κB is markedly increased in IBD. Oral CS might therefore reduce intestinal inflammation and benefit dogs with IBD.

Oxidative stress is also believed to play a key role in the pathogenesis of IBD. Paraoxonase-1 (PON1), an antioxidant enzyme used as a biomarker of oxidative stress and inflammation in dogs with IBD given the similarities between human and canine IBD. Decreasing oxidative stress, shown as an increased PON1, could therefore be an effective endpoint for IBD treatment.

Lower bacterial diversity and altered microbial communities have been reported in canine IBD. Orally administered prebiotics promote the growth of beneficial gut microbiota. Short chain fatty acids (SCFA), especially butyrate, which is the preferential source of energy for colonocytes, help maintaining the intestinal mucosal barrier. A reduction in SCFA producing bacteria, especially *Faecalibacterium* spp. and *Fusobacteria*, has been reported in dogs with IBD. Consequently, oral administration of resistant starch could benefit IBD patients by increasing butyrate levels in their gut.

A dietary supplement containing CS and prebiotics (resistant starch, β-glucans and mannanoligosaccharides (MOS)) was developed to target intestinal inflammation, oxidative stress and gut dysbiosis. The purpose of this study was therefore to evaluate the effects of this supplement on clinical disease activity, intestinal histology, gut microbiota, and selected serum biomarkers in dogs with IBD over a time course of 180 days.

Methods

Dogs

Methods: Multicentric randomized double-blind placebo-controlled study.

Inclusion criteria: Client owned dogs with min age of 1yr with persistent GI signs and confirmed IBD of score 4 on Canine IBD activity index (CIBDAI).

Treatment was initiated 15 days after endoscopy. Dogs with biopsy-confirmed IBD were randomized in a 1:1 allocation ratio into one of the 2 treatment groups: placebo and supplement. All dogs were switched to a hydrolyzed diet. Dogs in the placebo group (group A; n=14) received a placebo powder (containing only excipients and flavorings) orally once daily, and dogs in the supplement group (group B; n=13) received an oral daily dose per kg of bodyweight of 215 mg α-glucan butyrogenic resistant starch, 10 mg CS, and 26 mg β-glucans and MOS for 180 days.

Results

During the study period, 35 dogs were assessed for eligibility

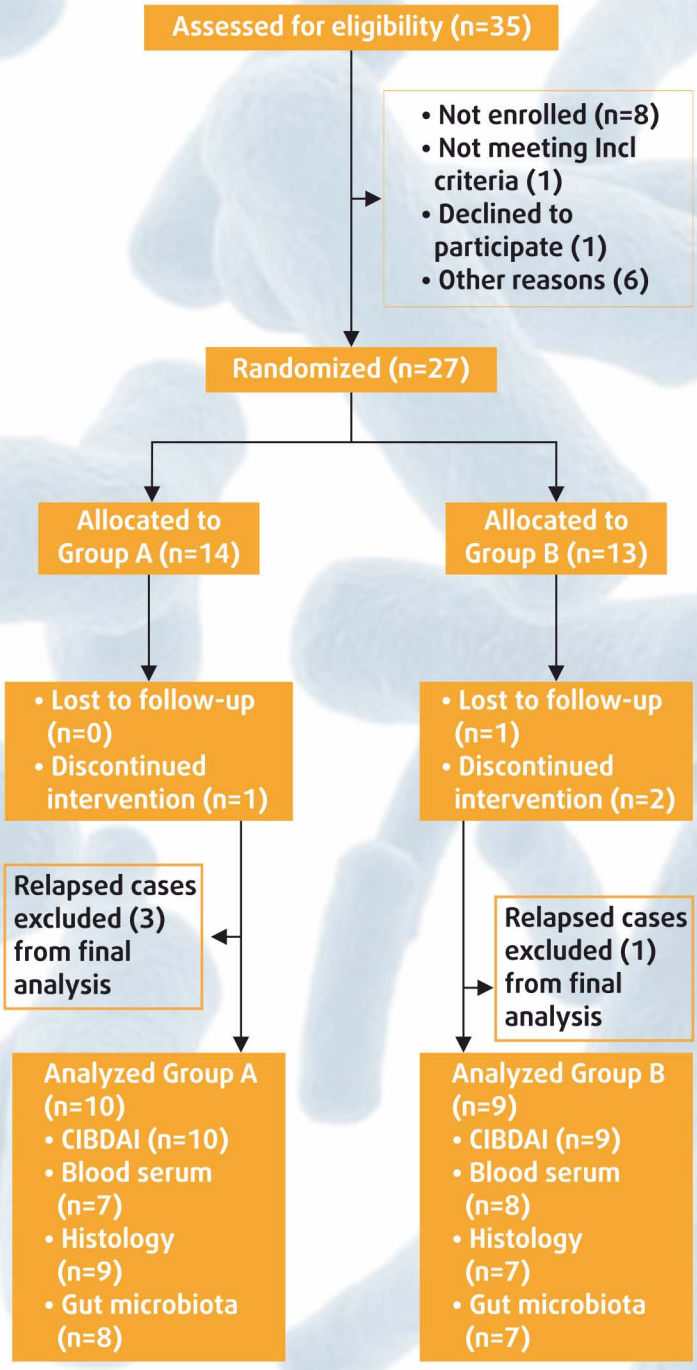

Fig. 1 Flow diagram of IBD dogs. Group A, placebo; group B, supplement

Canine IBD activity index

Fig. 2 shows changes in median CIBDAI scores. At the time of diagnosis, there were no significant differences (p=0.62) between groups placebo = 7 (4.75–8), supplement = 8 (5.5–8)). Compared to baseline median CIBDAI scores, the supplement group showed a 2-fold decrease and a 4-fold decrease after 1 and 60 days of treatment, respectively. In the placebo group, decreases in scores after 30 and 60 days of treatment were 1.75-fold and 3.5-fold, respectively.

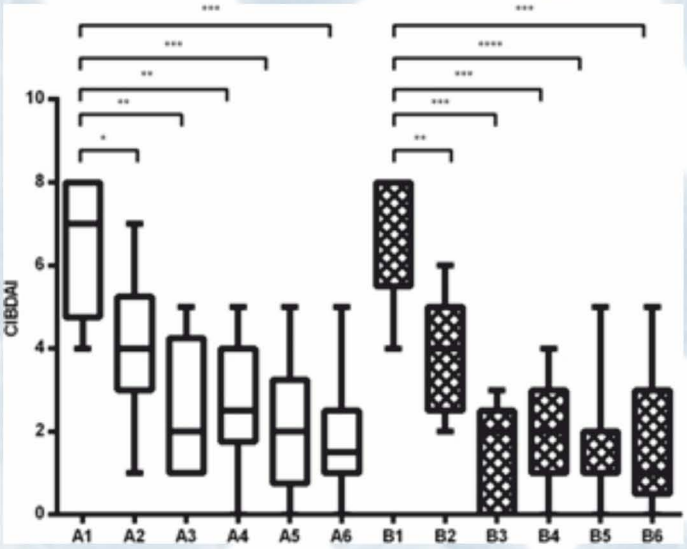

Fig. 2

Serum biomarkers

When groups were compared, the supplement group showed significantly higher cholesterol, and significantly higher PON1 compared to placebo. PON1 remained below the reference range (3–4.3 IU/mL) in all dogs in the placebo group and significantly lower TAC levels. All dogs from supplement group showed TAC levels within range. No significant changes were seen for the other serum biomarkers.

Histologic examinations

Variations in histologic scores are shown in Fig. 3. After treatment, the supplement group showed a significant 1.53-fold decrease in overall histologic score, whereas a non-significant 1.07-fold decrease was observed in the placebo group. With the supplement, a significant decrease was seen in duodenum and colon.

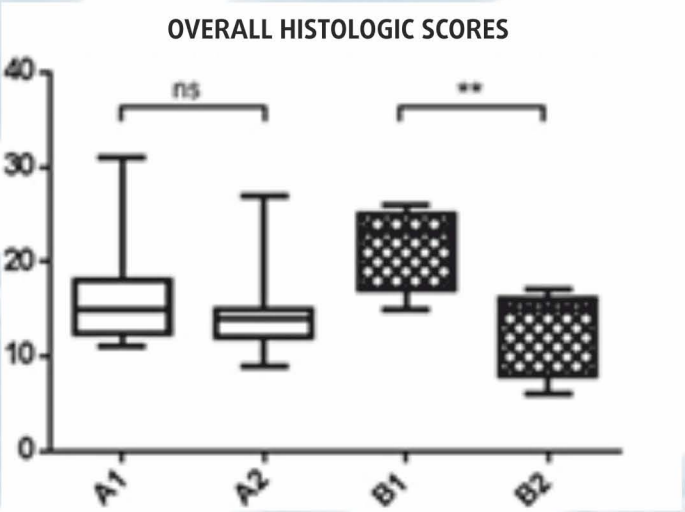

Fig. 3 WSAVA histologic scores

Gut microbiota

The dendrogram formed with the band patterns generated by PCR-RFLP of the fecal samples is shown in Fig. 4. All but two samples were grouped in two main clusters at similarity levels of 62 and 72 %, respectively. Before and after treatment, samples from both the placebo and the supplement groups were not grouped together, but scattered throughout the dendrogram instead. Thus, no differences were observed between the placebo and the supplement groups or between initial and final samples of either group.

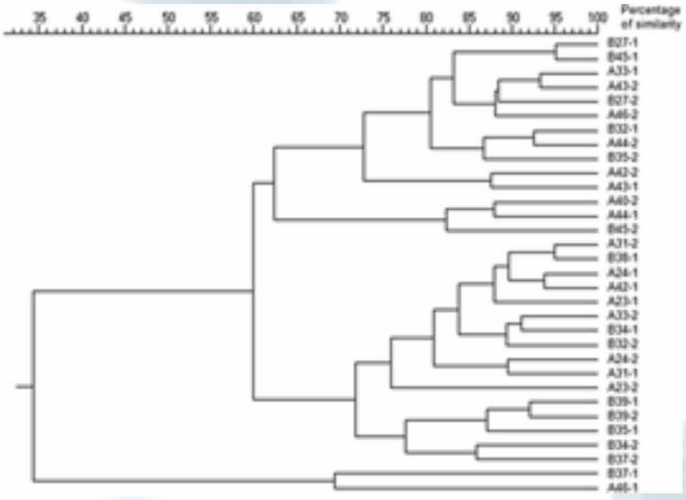

Fig. 4

Conclusions

Our results suggest a beneficial effect of long-term oral administration of a dietary supplement containing CS and prebiotics combined with a hydrolyzed diet in dogs with IBD by increasing serum PON1, TAC and cholesterol in dogs with IBD.

Differential Diagnosis Acute vs. Chronic Diarrhoea

Diagnosis of acute or chronic Diarrhoea is essential in order to apply the correct treatment protocol.

Clinic Presentation

	ACUTE DIARRHOEA	CHRONIC
Development	Fast	Slow
General condition	Decline	Gradual deterioration
Pain on palpation	Yes	None or mild pain
Level of hydration	Dehydration, metabolic acidosis and electrolyte imbalance	Normal or very slight dehydration
Responds to symptomatic treatment	Yes	No

Symptomatic Treatment: Diet + Drug

Diagnosis of chronic diarrhoea

CLINIC DIAGNOSIS (predominance of a group of characteristics)

SMALL INTESTINE	CHARACTERISTICS OF THE FAECES	LARGE INTESTINE
Increased	Volume	Normal or reduced
Light brown, yellow	Colour	Normal
Foul smelling	Small	Normal
No	Presence of mucus/blood	Yes/ fresh
Yes	Steatorrhoea	No
Yes	Presence of undigested food	No
	CHARACTERISTICS OF THE FAECES	
Normal or slightly increased	Frequency	Highly increased
No	Tenesmus	Yes
No	Dyschezia	Yes
No	Urgency	Yes
	OTHER SIGNS	
Yes	Weight loss	Some cases
Increased	Appetite	Normal
Yes	Flatulence	No
Yes	Borborygmus	Normal
Some cases	Halitosis	No
Some cases	Vomiting	No

LABORATORY DIAGNOSIS (discard phases)

1. To rule out inappropriate diet, change to a hypoallergenic diet.
2. Tests to rule out systemic causes when clincal signs and symptoms are compatible: Glucose, Na and K, T4 and TSH, Cushing.
3. To rule out infectious causes, perform a bacteria culture and faecal examination in fresh samples and series of samples.
4. To rule out exocrine pancreatic insufficiency, perform faecal chymotrypsin (or TLI) analysis.
5. To rule out malabsorption syndrome, perform a determination of folates and vitamin B12 in duodenal fluid.
6. To rule out chronic enteritis or tumours, perform gastroscopy and colonoscopy with biopsy.

Chronic or recurring diarrhoea may be the first sign of a malfunctioning digestive tract, but it may also indicate disease in other body systems.

REGULAR TREATMENTS FOR THE MANAGEMENT OF CHRONIC INFLAMMATORY ENTEROPATHIES

Antiinflammatories and immunosuppressives:

NAME	DOSE	SCHEDULE
Córticos (prednisone)	0.5-1 mg/Kg PO minimum (dog)	A/Bid 3-4 weeks to then reduce dose and frequency to the effective minimum.
	1-2 mg/Kg PO (cat)	B/Bid 10 days and reduce 50% dose every 10 days until min maintenance dose (0.5mg/Kg alternate days).
		Treatment can be continued for months/years. Possible side effects: liver and bone marrow toxicity (regular blood testing necessary).
Azathioprine (dogs only)	1-2 mg/Kg PO	OID 4 weeks and reduce dose to reach 50%, to be maintained for several months.
		Slow response possible side effects: liver and bone marrow toxicity (periodic blood control is necessary). Chlorambucil at doses 0.1-0.2 mg/Kg PO Oid (initially) is a good alternative for cats. It is also useful for alimentary lymphoma.
Cyclosporine A	5 mg/Kg PO fasting	OID (some authors recommend 2mg/Kg Bid).
		Combined with Ketoconazole (5-10 mg/Kg PO Oid) allows for dose reduction. pharmacokinetics change and plasma levels must be monitored.
Budesonide		Glucocorticoid with a potent topical anti-inflammatory activity in the intestinal mucosa and very few systemic side effects in dogs. Fifteen times more potent than prednisone.
Salicylates (sulfasalazine, olsalazine and mesalazine)	Sulfasalazine: 10-30 mg /Kg PO (dogs) 10 mg/Kg/12h PO(cats)	Tid, the dose is reduced every 2-3 weeks until clinical signs disappear (dogs).. Sulfasalazine in cats must not be administered for over 14 days
	Olsalazine: 10-20 mg /Kg PO (dogs)	Useful for inflammations in the large bowel.
	Mesalazine: 10-20 mg /Kg PO (dogs) 2 mg/Kg/12h PO(cats)	Possible side effect of sulfasalazine: QCs, necessary to measure tear periodically. Olsalazine is only useful for large dogs due to the impossibility to fractionate the commercial presentation.

REGULAR TREATMENTS FOR THE MANAGEMENT OF CHRONIC INFLAMMATORY ENTEROPATHIES

Antimicrobials:

NAME	DOSE	SCHEDULE
Metronidazole	10 mg/Kg PO	Bid-Tid: Administer for 3-4 weeks and reduce frequency until symptoms are controlled.
		Antiprotozoal, antibiotic and immunosuppressive. Possible side effect: Neurotoxicity.
Doxycyclin	5-10 mg/Kg PO	Tid 3 weeks at least and reduce progressively.
Trimetoprim-sulfa	10-20 mg/Kg PO	Bid 3 weeks at least and reduce progressively.
Tilosina (perros)	Small bowel: 10-20 mg/Kg PO	Tid 3 weeks at least and reduce progressively.
	Large bowel: 40-200 mg/Kg PO	Bid
Enrofloxacin	5-10 mg/Kg PO	Oid
		Useful in chronic histiocyte ulcerative colitis. Do not administer to growing animals or pregnant females or patients with epilepsy or cartilaginous growth disorder.

REGULAR TREATMENTS FOR THE MANAGEMENT OF CHRONIC INFLAMMATORY ENTEROPATHIES

Diet changes:

NAME	DOSE	SCHEDULE
Elimination/exclusion diet	60 days at least in dogs (longer in cats)	Diets based on hydrolysed proteins, with single-origin protein. Hydrolysed can cause diarrhoea. New proteins can cause sensitisation.
High-digestibility diets	Based on outcome of clinical condition	As they are highly digestive, they show fewer substances available for metabolisation by intestinal bacteria. They contain proteins of high biological value, low on fat and fibre. They reduce osmotic pressure in the intestinal lumen and enhance gastric emptying.
Fibre-high diets	Based on outcome of clinical condition	Used in cases where signs of large bowel prevail. Fibre absorbs water and acts increasing faecal consistency and volume.
Adequate diet for fatty acids	Based on outcome of clinical condition	Deviate the metabolism of fatty acids to lypooxigenase, producing less inflammatory metabolites.

REGULAR TREATMENTS IN CHRONIC DIARRHOEA OF UNKNOWN AETIOLOGY OR SYSTEMIC CAUSE

Each condition has its aetiological treatment where **ENTERO-CHRONIC** can be added as support treatment, providing a reduction of bowel inflammation and recovery of the intestinal mucosa.

PO Oid, at least 15 to 15 days (based on the severity of the symptoms) and for up to 6 months depending on the animal's progression.

COMPANION ANIMALS SYMPOSIUM: Microbes and gastrointestinal health of dogs and cats

J. S. Suchodolski

Gastrointestinal Laboratory, Department of Small Animal Clinical Sciences, College of Veterinary Medicine and Biomedical Sciences, Texas A&M University, College Station 77843-4474

Recent molecular studies have revealed complex bacterial, fungal, archaeal, and viral communities in the GI tract of dogs and cats. More than 10 bacterial phyla with Firmicutes, Bacteroidetes, Proteobacteria, Fusobacteria, and Actinobacteria constituting more than 99% of all gut microbiota. Microbes act as a defending barrier against invading pathogens, aid in digestion, provide nutritional support for enterocytes, and play a crucial role in the development of the immune system. Of significance for GI health is their ability to ferment dietary substrates into short-chain fatty acids (acetate, propionate, and butyrate). Microbes can have also a detrimental effect on host health. Specific pathogens (e.g., Salmonella, Campylobacter jejuni, and enterotoxigenic Clostridium perfringens) have been implicated in acute and chronic GI disease. Changes in small intestinal microbiota compositional, leads to changes in intestinal permeability and digestive function, have been suggested in canine small intestinal dysbiosis or antibiotic-responsive diarrhea. Current theories for the development of IBD favor a combination of environmental factors, the intestinal microbiota, and a genetic susceptibility of the host.

J. Anim. Sci. 2011. 89:1520–1530 doi:10.2527/jas.2010-3377

Microbial activity	Products	Representatives
Decarboxylation, deamination of AA	Ammonia	*Clostridium* spp., *Peptostreptococcus* spp., *Peptococcus* spp.
Deconjugation/ dehydroxylation of bile acids	Secondary bile acids	*Clostridium hiranonis, Lactobacillus* spp.
Vitamin synthesis	Vitamin K2, B12, biotin, folate	*Enterococcus* spp., *Pseudomonas* spp., *Sphingomonas* spp., *Lactobacillus* spp.
Carbohydrate fermentation	Lactate, propionate, acetate, butyrate	*Clostridium cluster* XIVa, *Prevotella* spp., *Faecalibacterium* spp., *Bifidobacterium* spp.
AA fermentation	Hydrogen, methane, amines, phenols, NH3, organic acids, hydrogen sulfite	Sulfate-reducing bacteria (SRB), *Desulfovibrio* spp., *Clostridium* spp., *Peptostreptococcus* spp.
Degradation of oxalate	Formate and CO2	*Oxalobacter formigenes*
Inulin and starch degradation	Lactate	*Bifidobacterium* spp.
Metabolism of H2, alcohols, and acetic acid	Methane and CO2	Methanobacteria

INTESTINAL MICROBIOTA OF DOGS AND CATS (Counts)

CULTURE RESULTS		16S rRNA GENE RESULTS		FISH	
Bacterial group	log cfu/g	Bacterial group	Total sequence (%)	Bacterial group	Log^{10} cells/g of feces
SMALL INTESTINE					
Spiral rods	3.0-6.8	Clostridiales	30-50	N/A	
Bacteroides	0-5.5	Enterobacteriales	20-60	N/A	
Lactobicillus Sp.	1.0-5.4	Lactobacillales	5-30	N/A	
Streptococcus Sp.	3.0-5.2	Bacteroidales	0-5	N/A	
Escherichia coli	2.3-5.0	Campylobacterales	0-2	N/A	
Clostridium perfringes	1.0-2.5	Actinomycetales	0-3	N/A	
		Fusobacteriales	0-10	N/A	
		Pasteurellales	2-5	N/A	
		Spirochaetes	0-12	*N/A*	
LARGE INTESTINE					
Bacteroides	7.3-10.2	Aeromonadales	0.2-0.5	*Bacteroides sp.*	9.1
Bifidobacterium sp.	8.0-10.0	Bacteroidales	0.5-35	*Bifidobacterium sp.*	8.3-9.3
Clostridium perfringes	5.5-8.0	*Bifidobacterium sp.*	N/A	C. Cluster IX	8.3
Clostridia sp	7.3-9.5	Coriobacteriales	1-2.5	C. Cluster XI	8.03
Escherichia coli	6.4-8.6	Clostridiales	10-78	*C. histolyticum group*	7.9-8.0
Lactobacillus Sp.	5.5-9.0	Enterobacteriales	0.1-2	*Desulfovibrio*	7.3
Prevotella	7.0-8.5	Erysipelotrichales	0-8	*Escherichia coli*	6.9
Ruminococcus	7.0-8.0	Fusobacteriales	0.3-25	*Eubacterium*	9.2
Staphylococcus Sp.	5.2-5.3	Lactobacillales	1-5	*Lactobicillus*	8.6-9.4
Streptococcus Sp.	8.8-9.1				

Table 3: Microbial changes in cats and dogs with gastrointestinal disease

Disease	Microbial changes in diseased animals	Reference
Dogs: Sampling from Duodenum: Tissue type: Biopsies		
IBD	Increase in Proteobacteria; decrease in Clostridia	*Suchodolski et al.*, 2010
IBD	Increase in Proteobacteria; decrease in Faecalibacterium,	
	Ruminococcus, and Dorea spp.	*Jergens et al.*, 2010
	within the Clostridium clusters IV and XIVa	
Chronic enteropathies (SRD, FRD, ARD)	reduction in biodiversity	*Craven et al.*, 2009
Dogs: Sampling from Duodenum: Tissue type: Mucosal/Luminal brushings		
IBD	Increase in Enterobacteriaceae (*E. Coli*)	
	Reduction in biodiversity	*Xenoulis et al.*, 2008
Chronic enteropathies (FRD, ARD)	Increase in Lactobacillales (Streptococcus and Abiotrophia)	*Allenspach et al.*, 2010
Dogs: Sampling from Feces: Tissue type: Fecal Samples		
Chronic diarrhoea	Increase in bacteroides	*Jia et al.*, 2010
Diarrhoea	Increase in Cl. perfringes, E. fecalis, E. faecium	*Bell et al.*, 2008
Dogs: Sampling from Colon: tissue Type: Biopsies		
Granulomatous colitis of boxer dogs	Intracellular translocation of adherent and invasive E. coli	*Simpson et al.*, 2006
Cats: Sampling from Small Intestine: Tissue type: Biopsies		
IBD	Increase in Enterobacteriaceae	*Janeczko et al.*, 2008
Cats: Sampling from Feces: Tissue type: Fecal samples		
Small & large bowel IBD	Decreased total bacteria, Bifidobacterium spp. and	
	Bacteroides spp.; increase in Desulfovibrio spp.	*Inness et al.*, 2007