The gut microbiome and dysbiosis - good gut health and it's disruptors

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Our awareness of the importance of the microbiome and gastrointestinal health for overall health and wellbeing, is growing rapidly. We need to respond to this information and mitigate damage caused by factors including inappropriate foods, medications, chemicals, stressors, and nutritional inadequacy. Consideration must also be given to genetic selection, dam nutrition, the birth process, early nutrition, and interventions.

What is the gut microbiome?

The gut microbiome is a complex community of trillions of microbes that live in the digestive tract. The microbes include bacteria, fungi, viruses, and protozoa, which may be both helpful and potentially harmful. A healthy individual has a good balance of microbes, coexisting in harmony, predominantly found in the distal small intestine and large intestine.

Increasing knowledge of the microbiome is revealing that it's absolutely fundamental to health. The community of microorganisms have many very important roles involving its host's nutrient metabolism, immunomodulation and protective mechanisms for the host.

Known microbiome roles:

- Provide enzymes to make vitamins - Vit K, B1, B9, B12.
- Produce short chain fatty acids (SCFA) in the large intestine from fermentation of indigestible foods (roughage).
- Protein digestion, absorption, metabolism, and transformation.
- Synthesise essential and nonessential amino acids.
- Regulate the immune system and ability to withstand disease.
- Coat the gut with a protective layer keeping toxins, pathogens, and undigested food particles out of circulation.
- Protect from bacterial translocation.
- Maintenance of structural integrity of the gut mucosal barrier.
- Control inflammation - some inflammation is necessary to fight invaders but too much inflammation is detrimental.
- Biotransformation of bile.
- Drug metabolism.
- Produce various metabolites that influence the health of the intestine and other organs, including kidneys, brain, and heart.

Along with the likelihood of many other jobs that we have yet to identify.

It can be challenging to assess the true population of microbes in an individual's gut (Suchodolski 2022) and we do not yet know the optimal microbiome of dogs and cats (Butowski *et al*. 2022). Most gastrointestinal microbes are strictly anaerobic and may be buried in the crypts of the intestines.

Local laboratory faecal analysis results must be interpreted cautiously. Routine culture is not considered useful with studies showing a failure to distinguish between the diseased and healthy, a lack of agreement between different laboratories and a failure to demonstrate a significant difference in identifying Campylobacter from healthy or diarrhoeic dogs (Werner *et al*. 2021, Orbell 2018). The Dysbiosis Index is currently considered the most accurate tool for assessing the microbiome. (Suchodolski 2022, Sung *et al*. 2023)

What does good gut health look like?

Good gut health involves optimal stomach acidity, a healthy microbial balance and tight intestinal cell junctions.

A complex cascade takes place when a dog or cat ingests food. Food begins to be digested as it is chewed. Important digestion occurs in the stomach, where food mixes with hydrochloric acid and gastric juices. This mixture (acidic chyme) enters the small intestine stimulating the pancreas to secrete digestive enzymes and the gallbladder to secrete bile, to further assist in the process of digestion. Bacterial degradation contributes to the digestion of food in the small intestine, as gut microbes provide digestive enzymes. Once the food is adequately broken down, the smaller, simpler nutrients are absorbed by the membranes of the intestinal mucosa. The remaining food is either further digested and absorbed or moves into the large intestine where it's either fermented and gives rise to metabolites such as short chain fatty acids or passed out as faeces.

In order for this complex process of digestion and nutrient assimilation to work efficiently, the environment of the gastrointestinal tract, including the microbes, must be healthy and functioning well.

More studies are needed to demonstrate the impact of different foods on the microbiome of cats and dogs. We have yet to fully demonstrate the impact of the various aspects of food; including macronutrient and micronutrient composition, synthetic versus whole food nutrients and nutrient cofactors naturally present in whole foods.

Carnivores ingesting their evolutionary diet of prey have naturally strong gastric acidity (Callaway 2024, Beasley *et al*. 2015, Grémillet *et al*. 2012). Meat protein stimulates stomach acidity (Saint-Hilaire *et al*. 1960, Lennard-Jones *et al*. 1968, Lichtenberger 1982, Brooks 1985, DelValle and Yamada 1990) by triggering the production of hydrochloric acid in acid-secreting cells within the stomach. Carnivores need more acidic stomachs in order to lyse the protein in their meat-based diet (Stevens and Hume 1995). Additionally, protein provides the best buffering capacity as food enters the small intestine (Lennard-Jones *et al*. 1968). Carbohydrates do not stimulate strong stomach acidity (DelValle and Yamada 1990). Poorly digestible protein increases colonic putrefaction resulting in products implicated in many inflammatory diseases (Wernimont *et al*. 2020). The palatability of food has also been shown to promote the production of acid within the stomach (Brooks 1985).

These macronutrient influences on the gut are unsurprising given the work of nutritional ecologist, Professor David Raubenheimer, on the established macronutrient preferences for cats and dogs (Raubenheimer *et al*. 2015, Hewson-Hughes *et al*. 2012). For most carnivores, the relevant macronutrient space is two-dimensional; protein and fat are the most important macronutrients, whereas carbohydrate is rare in natural foods and plays a lesser role in nutritional regulation (Raubenheimer *et al*. 2015).

A low gastric pH of around 1-2 is important because digestive enzymes work best in an acidic environment (Heda *et al*. 2023), the acidity initiates peptic hydrolysis of dietary proteins (Marks *et al*. 2018) and liberates vitamin B12 from dietary protein (Marks *et al*. 2018). Stomach acidity modulates the intestinal microbiome by killing microorganisms and preventing bacterial overgrowth (Marks *et al*. 2018). It facilitates the duodenal absorption of inorganic iron (Betesch *et al*. 2015), calcium (Haffner-Luntzer *et al*. 2016) and stimulates pancreatic bicarbonate secretion via secretin release (Chey and Chang 2023). It also suppresses antral gastrin release.

This information supports our observation and deduction that diets high in carbohydrate, high in plant protein and low in meat protein often compromise the optimal digestive process, thus impacting on nutrient assimilation, microbial balance and functions, intestinal permeability and mucosal protection.

Good gastric acidity is important for protection from pathogens from environmental and dietary sources (Callaway 2024, Beasley *et al*. 2015, Smith 2003, Hunt 1988, Cook 1985). It also impacts the action of many medications, such as enhancing the action of pimobendan, fluoroquinolones, antifungals (Zhou *et al.* 2005) and mycophenolate (Gabardi and Olyaei 2012).

What is dysbiosis and what causes it?

Dysbiosis is an imbalance in the gut microbial community that is associated with disease. The imbalance could be due to the gain or loss of community members or changes in the relative numbers of microbes.

The alteration of bacteria in dysbiosis affects the bacteria-derived metabolites, such as short chain fatty acids, amino acids and bile acids (Ziese and Suchodolski 2021, Wu *et al*. 2021). A loss of mucus allows bacteria to attach to epithelial cells, stimulating inflammatory cytokines that disrupt the tight intestinal cell junctions. Loss of brush border transporters leads to dietary malabsorption that can lead to bacterial overgrowth. The resulting inflammation and nutrient malabsorption contribute to dysbiosis.

The resident microbiome is a result of genetics (Rosenberg and Zilber-Rosenberg 2021), dam nutrition (Chu *et al*. 2016) and the birth process, quickly influenced by early nutrition and intervention (Garrigues *et al*. 2022).

Potential microbiome disruptors:

- Antibiotics and other bacteria destroying medications
- Highly processed diets
- Synthetic supplementation
- Biologically inappropriate foods containing a large amount of grains and food additives
- Lifestyle factors causing stress/anxiety
- Ingestion of toxins
- Chemicals
- Overuse of vaccines, insecticides and parasiticides
- Infectious diseases, parasites
- Antinutritional factors
- Obesity

Antibiotics, though sometimes life-saving, kill both good and bad bacteria, disrupting the optimal balance of microbes and depleting the numbers of friendly bacteria that keep the gastrointestinal immune defences strong and resilient. Other medications known to have the same effect are corticosteroids and non-steroidal anti-inflammatory drugs.

As an example, metronidazole has been shown to have negative and persistent effects on the faecal microbiota even weeks to months after cessation of treatment (Pilla *et al.* 2020). Metronidazole may target key intestinal bacteria such as *Clostridium hiranonis*, a beneficial bile-acid converting bacteria important for maintaining a normal microbiome (Chaitman *et al*. 2020).

Although there are many conditions that may contribute to dysbiosis, in any individual patient, the cause and effect links between dysbiosis and gastrointestinal disease may be unclear (Ziese and Suchodolski 2021).

Stomach acidity has a critical influence on the microbiome. Poor stomach acidity allows the inappropriate growth of microbes in the small intestine, resulting in small intestinal bacterial overgrowth (SIBO) (Dukowicz *et al*. 2007). SIBO has been linked with symptoms of reflux.[36] Stomach acidity can be challenged by carbohydrates, ageing, stress/anxiety and medications.

Studies have demonstrated that obese dogs and cats experience larger shifts in the microbiome in response to dietary changes compared to lean dogs and cats, indicating that they have a less stable and resilient microbiome (Li *et al*. 2017, Li and Pan 2020).

What happens downstream from dysbiosis??

"All disease begins in the gut" Hippocrates

"All disease begins in the leaky gut" Fasano (Fasano 2020).

Dysbiosis causes the intestinal mucosa to become inflamed, resulting in the loss of tight intestinal cell junctions, known as increased intestinal permeability or leaky gut. Increased intestinal permeability allows the absorption of inappropriate particles such as toxins, partially digested food and pathogens through the gut wall. These large complex substances are antigenic and allergenic, stimulating the immune system to produce antibodies against them.

Chronic inflammatory diseases have risen dramatically over recent years. A group of proteins that affect gut permeability are implicated in a variety of chronic inflammatory diseases, including autoimmune, infectious, metabolic and neoplastic diseases (Fasano 2020, Fasano 2012, Fasano 2011). The gut microbiome and its metabolites are involved in many metabolic diseases (Wu *et al*. 2021).

Alongside many human studies, dog and cat studies have demonstrated the involvement of dysbiosis in more than gastrointestinal disease (Janeczko *et al*. 2007, Blake *et al*. 2019), including chronic kidney disease (Summers *et al*. 2019), heart disease (Li *et al*. 2021, Seo *et al*. 2020, Li *et al*. 2021), neurological disorders (Jeffery *et al*. 2027), diabetes mellitus (Kieler *et al*. 2019) and obesity (Bermudez Sanchez *et al*. 2020).

Conclusion

We need to optimise the microbiome from the beginning of life, support a healthy microbial balance and minimise the damage. This involves serious consideration of nutrition, breeding, medications, chemicals and the environment of our carnivorous cats and dogs.

Nutritional therapy modifies the microenvironment in the gut. When we destroy and reconstruct food, we may not be as clever as we think we are. We need to meet the optimal, species appropriate nutritional requirements of our carnivores and monitor the individual response to a dietary approach. Nutritional impact considerations beyond protein source, such as carbohydrates and additives, are required.

Some say we are “too clean for our own good” and remind us that bugs are only part of the picture. We need to live in harmony with bugs, not be afraid of them but do everything we can to encourage the right bugs.

The current reality is that many pets are in a dysbiotic state and whilst the secrets of the gut are still plentiful, appropriate foods, nutritional aids and functional medicine can provide excellent therapeutic options.

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