



Innovative Pet Lab

Canine and Feline Guide

1.	Inflammation & Immunity	<ul style="list-style-type: none">• Calprotectin• Secretory IgA
2.	Leaky Gut (Intestinal Permeability)	<ul style="list-style-type: none">• Zonulin• Antigliadin IgA
3.	Digestion & Detox	<ul style="list-style-type: none">• Pancreatic Elastase• Beta-glucuronidase

Why is this test important?

Identifying the status of gut health is key to a pet's overall health. In addition to the gut-immune connection, research has identified the gut-brain connection, gut-skin connection, gut-heart connection, gut-liver connections, and more.

What does this test involve?

- Collect a fresh stool sample
- Fill the included collection tube
- Utilizing provided materials, place sample in mail

Inflammation & Immunity

Available For:
Cats & Dogs

Analytes:
Calprotectin & Secretory IgA

Why is this Test Important?

Inflammation and immune reactions are cornerstones of health and a vital first assessment. GI inflammation and impaired immune reactions can manifest in a variety of symptoms. While some symptoms are easy to correlate directly to the digestive tract, others may be less obvious such as asking conditions. Chronic intestinal inflammation is associated with increased risk of immune related diseases and impair digestion and absorption, leading to nutrient insufficiencies. The test can connect symptoms and root cause.

Calprotectin

Calprotectin is a marker of gastrointestinal inflammation in the gut lining. Specifically, it is an accumulation of white blood cells known as neutrophils which release calprotectin. The level of inflammation is directly correlated with the level of calprotectin, making it a useful marker to quantify the extent of intestinal inflammation. Calprotectin has been shown to be a useful non-invasive biomarker for identifying level of inflammation and following treatment.

Inflammation is known to cause redness and swelling that can be seen when it's outside the body. There are also immune reactions internally that cannot be seen, which can cause damage to cells and impair function. Many conditions that are common in pets are often related to intestinal inflammation.

Knowing the level of inflammation can help identify if there is inflammation, its severity, and better target treatments. This can provide guidance for natural treatments when the inflammation is mild and stronger treatments when there is more inflammation.

Borderline high levels may be responsive to change in diet such as a change in protein or an anti-inflammatory diet, targeted supplements, probiotics, probiotics, or other treatments. It may also help avoid more serious prescription medication.

Pets should be retested in 3-6 months after making changes to monitor treatment effectiveness. Conditions such as obesity or diabetes can also be associated with higher levels.

A high calprotectin level $>100 \mu\text{g/g}$ in dogs and $>125 \mu\text{g/g}$ in cats may identify a more serious condition such as Inflammatory Bowel Disease (IBD). Oftentimes changes in diet and supplements may help to reduce high levels and retesting can help to monitor treatments. Concern is given to dogs who have high levels and significant

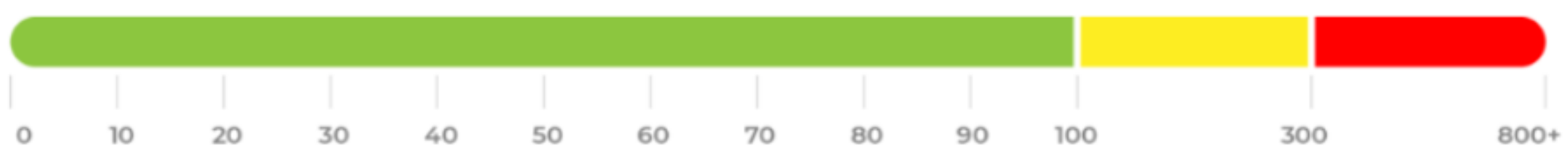
symptoms such as pain, persistent diarrhea, mood disorders, change in sleep habits, or skin cond.

Conventional veterinary care has not developed specific guidelines for treatment of IBD. It generally includes some combination of dietary and drug treatments, with the optimal protocol yet to be defined.

Calprotectin

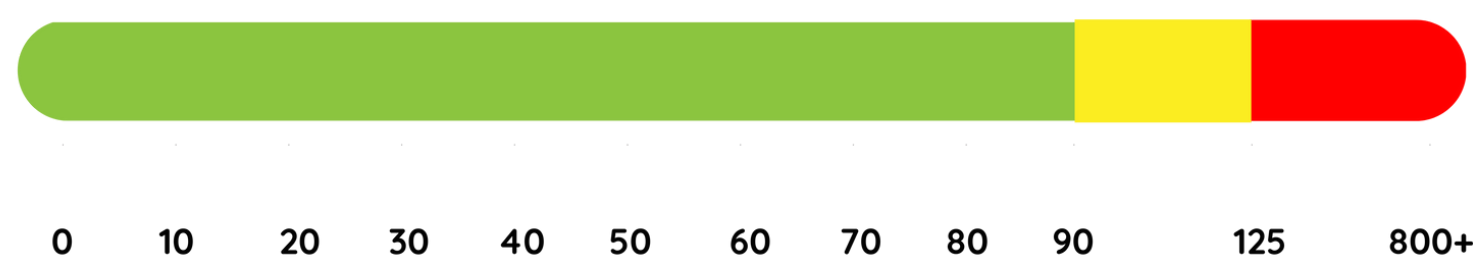
Dogs:

- Normal: $<10 \mu\text{g/g}$ - No intestinal inflammation was noted
- Borderline: $10-100 \mu\text{g/g}$ - May benefit from testing again in 3-6 months
- High: $>100 \mu\text{g/g}$ - Inflammation has been noted. If associated with symptoms seek further veterinary evaluation. Retest in 3 months



Cats:

- Normal: $<90 \mu\text{g/g}$ - No intestinal inflammation was noted
- Borderline: $90-125 \mu\text{g/g}$ - May benefit from testing again in 3-6 months
- High: $>125 \mu\text{g/g}$ - Inflammation has been noted. If associated with symptoms seek further veterinary evaluation. Retest in 3 months



Results

If Results Are Normal:

- Continue with current diet and lifestyle, retest in one year

If Results Are High Consider:

- **Changing pet food**
 - A human grade or small-batch food
 - **Dogs:** Farmer's Dog, Wild Earth, Chi Dog Foods (Fire, Water or Earth Diets), Square Pet Ideal Digestion, Evermore Pet Food, Ziwi Dog Food, or Barkful for dogs
 - **Cats:** Ziwi cat food, Fresh Pet cat food, or Just Food For Cats human-grade cat food, Wellness CORE Digestive cat food
 - Considering changing the type of protein
 - Hydrolyzed protein may help to reduce inflammation
- **Anti-inflammatory supplemental support from real foods or supplements**
 - Real polyphenol rich, anti-inflammatory foods such as, blueberries, alfalfa, apples (no seeds), carrots, pumpkin, red pepper) can be added as food toppers
 - Targeted anti-inflammatory supplements:
 - Omega-3 fatty acid (such as Nordic Naturals Pet Cod Liver Oil, Standard Process VF Omega-3, or Fera Pet Organics Fish Oil), turmeric, cat's claw root extract, mushrooms (such as Fera Pet Organics or RealMushrooms Mushroom Immune Pet Chews),
 - Combination immune support products (such as Standard Process Canine Immune System Support)
 - A combination of cirsium japonicum and aralia elata are natural herbs with potent canine antioxidative effect
- **Adding probiotics may help support healthy gut bacteria which helps support normal GI inflammatory response**
 - Look for probiotics with a variety of healthy gut bacteria, referred to as multi-strain, spore-forming probiotics or *Saccharomyces boulardi*.
 - For dogs consider Visbiome Pet Probiotic, Fera Pet Organics Probiotics, or RX Vitamin's NutriGest
 - For cats consider Complete cat probiotics or Nutrathrive for cats
 - Consider testing gut bacteria to see if it is a contributing factor
- **Reducing stress, evaluate circadian rhythms and set schedules for eating, sleeping and exercise.**
- **Avoid toxins such as air pollutants, pesticides sprays in the house or on lawns.**
- **Retest in 3 months**

Article: Verification of the fCAL turbo immunoturbidimetric assay for measurement of the fecal calprotectin concentration in dogs and cats. Enderle LL, Köller G, Heilmann RM. J Vet Diagn Invest. 2022 Sep;34(5):813-824. PMID: 35879875

- Fecal calprotectin was found to be linear, precise, reproducible, and sufficiently accurate when measuring in dogs and cats.
- Fecal calprotectin levels were higher in cats with acute or chronic gastrointestinal diseases, compared to healthy controls and cats with conditions not localized to the gastrointestinal tract.

Article: Biomarkers of gastrointestinal functionality in dogs: A systematic review and meta-analysis. Felix, A.P. Animal Feed Science and Technology, 2022 January: vol 283, 115183

- Dogs with GI diseases also had higher fecal calprotectin levels ($P < 0.05$)
- A total of 27 studies with 815 healthy dogs and 786 dogs with GI diseases were included in the meta-analysis. Compared to healthy dogs, those with GI diseases presented with impaired gut bacteria, probiotics may help to improve:
 - Lower α -diversity (healthy guts have higher diversity, meaning lots of different kinds of bacteria in the gut)
 - Lower abundances of good bacteria (such as Faecalibacterium, Turicibacter, Blautia, Fusobacterium, and Clostridium hiranonis), and higher abundance of bad bacteria (such as Escherichia coli).
 - A higher dysbiosis index (dysbiosis is when dysregulation of gut bacteria, and is associated with disease)

Article: Analytical validation of an enzyme-linked immunosorbent assay for the quantification of S100A12 in the serum and feces of cats. Bridges CS, et.al. Vet Clin Pathol. 2019 Dec;48(4):754-761. PMID: 31820477

- Measuring fecal calprotectin in serum and feces is a marker of inflammation, such as seen with chronic gastrointestinal inflammation in people, dogs and cats.

Article: Intestinal S100/Calgranulin Expression in Cats with Chronic Inflammatory Enteropathy and Intestinal Lymphoma. Riggers DS, et.al. Animals (Basel). 2022 Aug 11;12(16):2044. PMID: 36009635

- Calprotectin plays a role in the pathogenesis of feline chronic enteropathies (FCE), including chronic inflammatory enteropathies (CIE) and intestinal lymphoma (IL). Cats with FCE had slightly higher gastrointestinal mucosal calprotectin cell counts than controls.
- Calprotectin positively correlated with histologic findings in feline CIE, and with severity of inflammatory lesions in the gut (n=20).
- Serum cobalamin was positively correlated with calprotectin.

Article: Serologic and fecal markers to predict response to induction therapy in dogs with idiopathic inflammatory bowel disease. Otoni CC, et,al. J Vet Intern Med. 2018 May;32(3):999-1008. PMID: 29624721

- Evaluate relationship between disease severity and serum and fecal biomarkers in dogs (n=29) with idiopathic IBD before and after treatment.
- Research indicated that measurement of fecal calprotectin was a useful biomarker for noninvasive evaluation of intestinal inflammation. Dogs with severe signs of gastrointestinal disease more often have abnormal fecal calprotectin than dogs with less severe disease.
- Despite clinical remission, many dogs have ongoing histopathologic inflammation with low clinical activity scores, which could underestimate disease activity.
- Fecal calprotectin is among the most used and reliable fecal markers for IBD in humans. Concentrations of fecal calprotectin in humans with IBD have been correlated to disease activity, endoscopic findings, and the degree of histologic inflammation.
- The fecal cCP concentration in healthy control dogs was low, and was extremely elevated in dogs with IBD, though lowered to normal after treatment.
- Canine IBD activity index (CIBDAI) scores before treatment showed a significant correlation with fecal cCP concentrations before treatment.

Article: Biomarkers of gastrointestinal functionality in animal nutrition and health. Pietro, C. Animal Feed Science and Technology. 2019 April. Vol 250. 9-31.

- Diet composition also plays a key role in immunonutrition.
 - Dietary antioxidant supplementation to modulate redox balance.
 - Inflammation occurs in the gastrointestinal tract, it can result in a decrease in digestive efficiency and reduced absorption, partly by disrupting the structure and function of the intestinal mucosa. Both iron and zinc may be significantly impacted.
- Fecal calprotectin is a marker of neutrophil activity. It correlates well with the severity of inflammation, assessed by both endoscopic and histological scoring systems.

Article: Preanalytical validation of an in-house radioimmunoassay for measuring calprotectin in feline specimens. Heilmann RM. et. al. Vet Clin Pathol. 2018 Mar;47(1):100-107.

- Fecal calprotectin is analytically sensitive, linear, reproducible, accurate, and sufficiently precise for use with feline feces.

Article: Association of fecal calprotectin concentrations with disease severity, response to treatment, and other biomarkers in dogs with chronic inflammatory enteropathies. Heilmann RM, et. el. J Vet Intern Med. 2018 Mar;32(2):679-692.

- Dogs (n=127) were assigned a canine chronic enteropathy clinical activity index (CCECAI) score, and histologic lesions severity was assessed. Fecal calprotectin, fecal S100A12, and serum C-reactive protein (CRP) were measured.
- Fecal calprotectin could be a useful surrogate marker of disease severity in dogs with CIE (chronic inflammatory enteropathy).
- Fecal calprotectin correlated with CCECAI ($\rho = 0.27$, $P = .0065$). Based on the response to treatment, canine non-infectious CIE are classified as food-responsive enteropathy (FRE), antibiotic-responsive enteropathy (ARE), or steroid-/immunosuppressant-responsive (or -refractory) enteropathy (SRE/IRE).
- Dogs with SRE/IRE (steroid-/immunosuppressant-responsive or -refractory) had higher fecal calprotectin (median: 2.0 $\mu\text{g/g}$) than FRE/ARE (food-or antibiotic-responsive) dogs.
 - Within the SRE/IRE group, dogs with PR/NR (PR - partial response, or NR - no response), had higher fecal calprotectin than dogs with CR (complete remission).
 - An elevated fecal calprotectin separated both groups with an 80% sensitivity and 75% specificity.

Secretory IgA

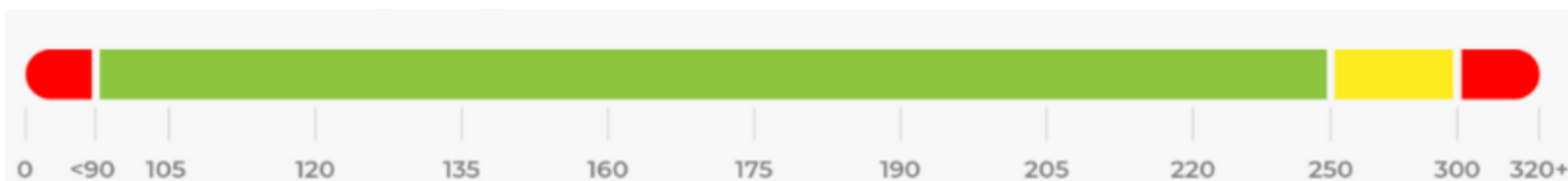
Secretory IgA is the first line of immune defense at the gut lining. It is an indicator of intestinal immune protection, and a marker of intestinal maturity in young animals. Low levels of secretory IgA may identify an inability to have a full immune response and high levels can identify a reaction to something, such as inflammation, parasites, vaccines, pathogens, food sensitivities or allergies. High levels return to normal once the reactive item is addressed.

Low levels of secretory IgA have been associated with autoimmune conditions, allergies, skin conditions and may be impacted by low levels of good gut bacteria. The small intestines are a major site of IgA producing cells. Research is ongoing as to why overactive immune reactions are associated with decreased IgA. Though much focus has been on the gut microbiome. Research studies found secretory IgA from duodenal biopsies and fecal samples to be similar.

Secretory IgA

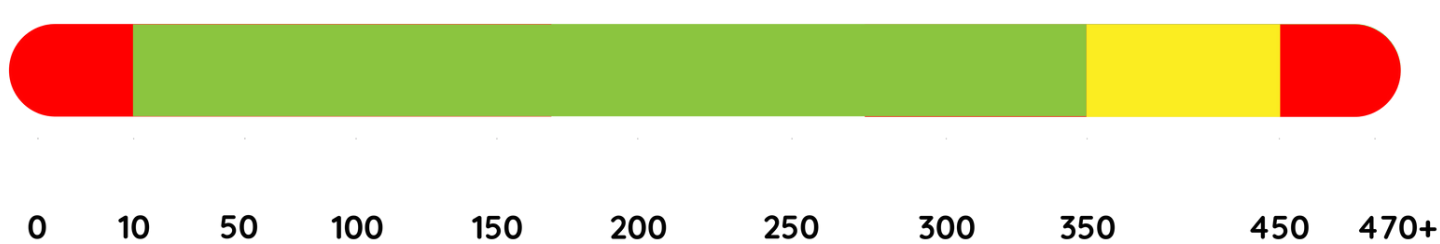
Dogs:

- Normal: 10-300 ug/g - No excess or impaired immune response
- Low: < 10 ug/g - May have an impaired response, support and retest in 3-6 months
- Borderline: 301-350 ug/g - Continue to monitor, consider treatment options and retest in 3-6 months
- High >350 ug/g - Identifies a significant reaction, provide support and retest in 3 months



Cats:

- Normal: 10-350 ug/g - No excess or impaired immune response
- Low: < 10 ug/g - May have an impaired response, support and retest in 3-6 months
- Borderline: 351-450 ug/g - Continue to monitor, consider treatment options and retest in 3-6 months
- High >450 ug/g - Identifies a significant reaction, provide support and retest in 3 months



Results

If Results Are Normal:

- Continue with current diet and lifestyle, retest in one year

If Results Are High:

- Elevated results may be a normal response to parasites, pathogens or food reactions, as well as increased mucosal inflammation.
- Consider a change in diet such as Chi Dog Water Diet or human grade pet food

If Results Are Low:

- Provide overall support of a healthy lifestyle including exercise, reducing stress and treatment of gut inflammation. Some research suggests adding time in nature and with other pets to lower overall stress levels
- Build good gut bacteria which is related to secretory IgA levels. Look for probiotics with a variety of healthy gut bacteria, referred to as multi-strain (ex. Visbiome Pet), spore-forming probiotics or *Saccharomyces boulardii*
 - Support with probiotics, as increases in normal gut flora may help to crowd out opportunistic bacteria in the gut. Research has noted that prebiotics and probiotics in dogs showed an improvement of intestinal IgA excretion
 - Consider a *Saccharomyces boulardii* supplement. In research, it is known to increase secretory IgA and has shown GI improvement in dogs with enteropathies. *Saccharomyces boulardii* induced greater production of secretory IgA than did *Escherichia coli*, *B. animalis* and *L. casei*
 - *Lactobacillus kefir* has shown to be safe for dogs, and has been shown to increase IgA secretions
 - An increase in the total fecal IgA concentration was observed in the 7 dogs after treatment with *Lactobacillus murinus* strain LbP2, at 5×10^9 CFU.
- Consider gut lining support such as glutamine, aloe, slippery elm, etc.

Research

- **Article: Canine IgA and IgA deficiency: Implications for immunization against respiratory pathogens.** Ellis JA. Can Vet J. 2019 Dec;60(12):1305.
 - Immunoglobulin A (IgA) is widely recognized as the important antibody involved in protective responses on mucosal surfaces, where it effectuating immune exclusion of foreign material.
 - Selective IgA deficiency is the most common immunodeficiency in dogs and has consequences for mucosal immunity.
 - Low IgA has been associated with canine atopic dermatitis (CAD), as well as recurrent respiratory and gastrointestinal infections.
 - Higher IgA has been associated with increased inflammation.
 - IgA deficiency may be underappreciated in dogs, and similar to humans some ~50% with low levels may not have symptoms.
- **Article: Altered fecal microbiota, IgA, and fermentative end-products in adult dogs fed prebiotics and a nonviable Lactobacillus acidophilus.** Panasevich MR. et. al. J Anim Sci. 2021 Dec 1;99(12):skab347.J Anim Sci. 2021 Dec 1;99(12):skab347
 - Fecal IgA increased with prebiotic blend (beet pulp, FOS, MOS, inulin, and kelp)
- **Article: Consumption of identically formulated foods extruded under low and high shear force reveals that microbiome redox ratios accompany canine immunoglobulin A production.** Jackson MI. et. al. J Anim Physiol Anim Nutr (Berl). 2020 Sep;104(5):1551-1567.
 - Increased IgA was associated with higher levels of short chain fatty acid (colonocyte fuel) with resistant starch intake.

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Leaky Gut

Available For:
Cats & Dogs

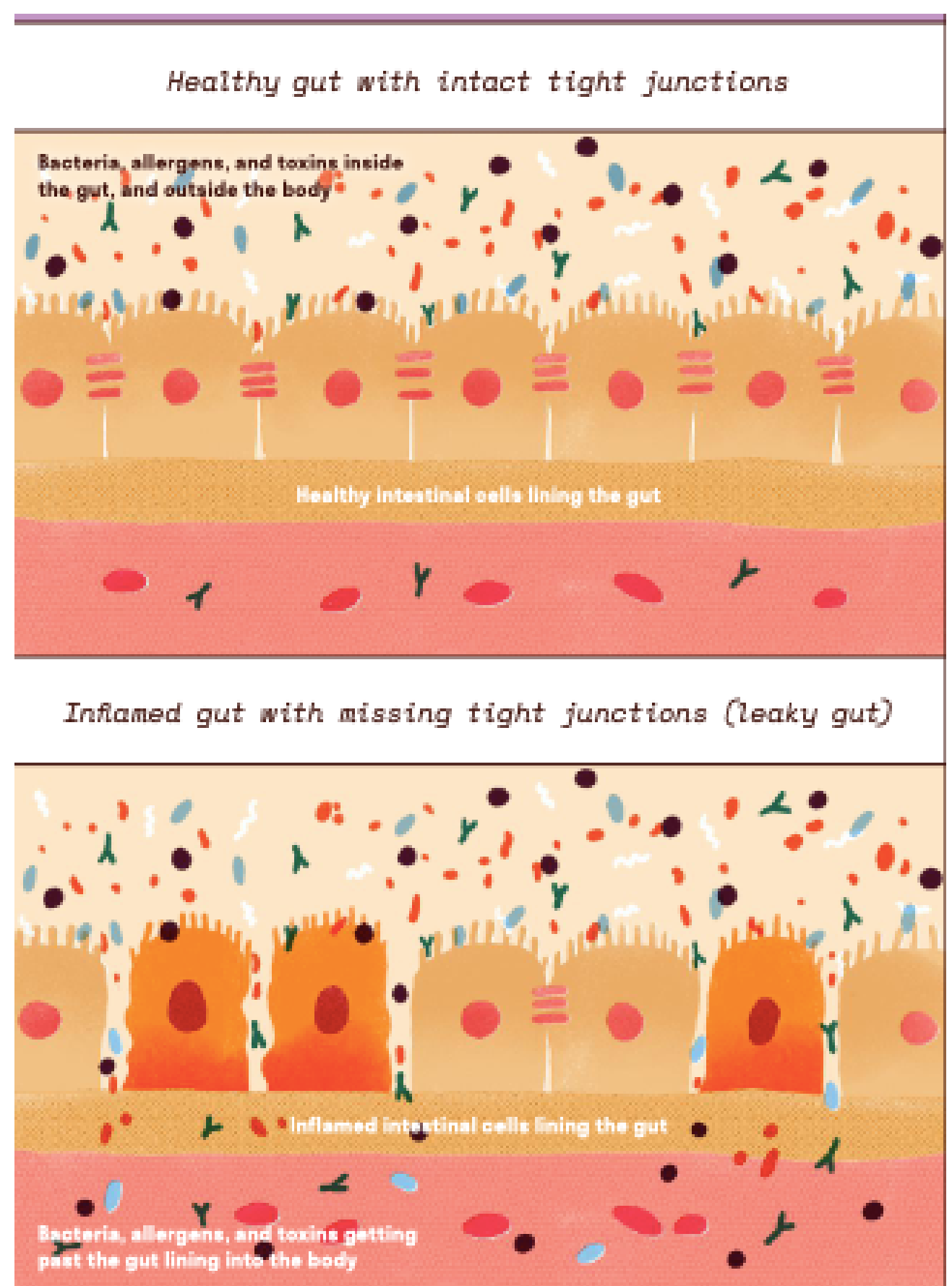
Analytes:
Zonulin & Antigliadin IgA

Why is this Test Important?

Leaky gut describes an increase in the permeability of the intestinal cells. Increased intestinal permeability allows substances (such as bacteria, food allergens, toxins, and more) that would normally not pass through the intestines to cross the intestinal walls leading to an immune reaction. Issues with intestinal permeability have been related to overall gut health, which has been noted to have varied symptoms including weight issues, gas, soft stools, inflammatory conditions, skin reactions, fatigue, and more. A leaky gut has been identified as a link between gut function and systemic illness.

Zonulin

Zonulin is a protein that increases permeability in the epithelial layer of the small intestine. It modulates intercellular tight junctions. Tight junctions help hold intestinal cells together. A leaky gut can happen gradually over time and is linked to several disease states. Though there is not currently a test to officially diagnose intestinal permeability, Zonulin can help identify the level of intestinal permeability.



Zonulin identifies intestinal permeability which has been associated with inflammation, an imbalance of healthy gut bacteria, autoimmune conditions, and may be a risk factor for food allergies and food sensitivities, and is known to react to gluten.

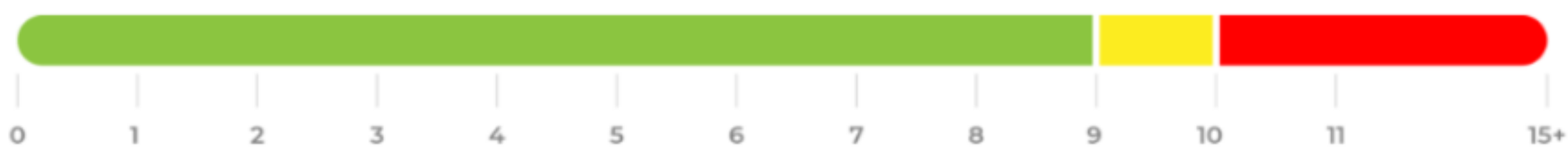
Possible Symptoms of Leaky Gut:

- Digestive issues such as diarrhea, bloating, constipation, weight loss, changes in appetite, gas and fatigue
- Skin issues such as dry skin, hair loss, redness, rashes and scratching
- Chewing, licking, or gnawing paws and paw pads
- Pets can also have no symptoms in early stages

Zonulin

Dogs:

- Normal: <6.6 ug/g
- Borderline: 6.5-11 ug/g - Retest again in 3-6 months
- High: >11 ug/g - Associated with Leaky Gut, treat and retest in 3 months



Cats:

- Normal: <2.0 ug/g
- Borderline: 2.0-6.0 ug/g - Retest again in 3-6 months
- High: >6.0 ug/g - Associated with Leaky Gut, treat and retest in 3 months



Results

If Results Are Normal:

- Continue with current diet and lifestyle, retest in one year

If Results Are High:

- Probiotics have been shown to improve good gut bacteria and may improve Zonulin levels. Consider multi-strain probiotics, spore-forming probiotics or *Saccharomyces boulardii*, such as Visbiome Pet Probiotic, Fera Pet Organics Probiotics, or RX Vitamin's Rx Biotics or NutriGest
- Research has found benefits with changing dietary protein sources or utilizing hydrolyzed protein foods. Adverse food reactions are common in pets with GI conditions such as leaky gut

If Results Are High (continued):

- Evaluate inflammation levels, as reducing inflammation may decrease Zonulin
- Check overall health as obesity and type 2 diabetes may lead to increased inflammation
- Some herbal formulas may provide support for gut mucosal cells, such as licorice root, aloe vera, glutamine, slippery elm
- Reduce stress and evaluate circadian rhythms of eating, sleeping and exercise
- Set and maintain a regular schedule. Avoid lawn and house pesticides, glyphosates, mycotoxins, NSAIDS, and gluten
- In humans, cigarette smoke has been associated with increased intestinal permeability. Check second hand smoke for pets
- Retest in 3 months to see if pet has responded to changes

- **Article:** Fecal Bile Acids and Microbial Amino Acid Metabolites in Serum are Correlated with Fecal Zonulin in Dogs with Exocrine Pancreatic Insufficiency ECVIM Online Congress 2021 <https://www.vin.com/apputil/content/defaultadv1.aspx?pld=27507&catId=170815&id=10362481&ind=54&obTypeID=17>
 - Zonulin is a biomarker for intestinal barrier integrity and increased fecal zonulin is associated with increased intestinal permeability.
 - Fecal zonulin was higher in dogs with exocrine pancreatic insufficiency (EPI) compared with healthy controls.
 - Mucosal barrier dysfunction could contribute to the persistence of clinical signs in dogs with EPI.
- **Article:** Clinicopathological and Fecal Proteome Evaluations in 16 Dogs Presenting Chronic Diarrhea Associated with Lymphangiectasia. Rossi G. et. al. Vet Sci. 2021 Oct. 8(10), 242.
 - Researchers found significantly increased levels of zonulin in dogs with intestinal lymphangiectasia compared to healthy controls dogs, in both serum and feces, suggesting that it may be increased due to mucosal damage.
 - Increased fecal zonulin was related to the histopathological lesion of intestinal biopsies and villus/lactal dilation, indicating a direct involvement of the gut lining, also known as “leaky gut”
 - Canine intestinal lymphangiectasia (IL) is a condition characterized by variably severe gastrointestinal signs.
 - Serum CRP, bacterial LPS, cCK18, and zonulin, and fecal zonulin were higher in intestinal lymphangiectasia dogs. Zonulin (in both serum and feces) is a promising marker for canine intestinal lymphangiectasia.
- **Article:** Randomized, controlled trial evaluating the effect of multi-strain probiotic on the mucosal microbiota in canine idiopathic inflammatory bowel disease Gut Microbes. White R. et. al. 2017 Sep 3:8(5):451-466.
 - Dogs with IBD fed probiotics had increased tight junction expression suggesting that probiotics may have beneficial effects on mucosal homeostasis. Probiotic therapy was associated with upregulated ($P < 0.05$) expression of TJPs E-cadherin, occludin, and zonulin versus standard therapy. The probiotic used was Visbiome™.

Antigliadin IgA

Antigliadin IgA is an antibody to gliadins, a component of gluten. In some types of chronic enteropathy, gliadins can cross the intestinal epithelial barrier due to increased permeability, resulting in Antigliadin IgA production.

Antigliadin IgA

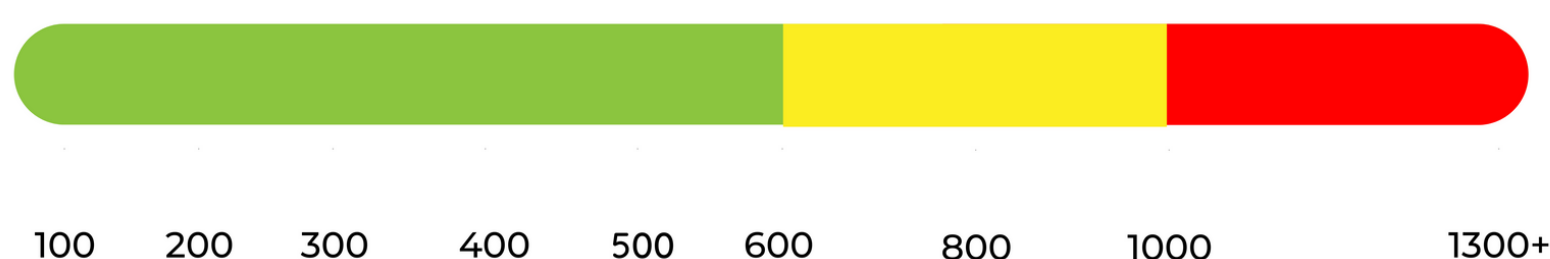
Dogs:

- Normal: <750 µg/g
- Borderline: 750-900 µg/g - Indicates moderate reaction
- High: >900 µg/g - Highly reactive to gluten



Cats:

- Normal: <600 µg/g
- Borderline: 600-1000 µg/g - Indicates moderate reaction
- High: >1000 µg/g - Highly reactive to gluten



Results

If Results Are Normal:

- Continue with current diet and lifestyle, retest in one year

If Results Are High:

- Try a gluten free dog food and note a change in symptoms
- Wheat, rye and barley all contain gluten
- Research recommends that test diets be fed for at least 10 weeks
- Monitor for intestinal permeability and increased Zonulin levels
- Retest in 3 months

- **Article:** Diagnostics New Diagnostic Test for Dogs with Chronic Gastrointestinal Signs. https://files.brief.vet/2021-06/Antech_IBD_C.pdf
 - A gliadin-free diet should be considered in cases of elevated Antigliadin IgA, even if results are not consistent with chronic enteropathy/inflammatory bowel disease.
 - Research has noted that dogs with chronic gastrointestinal disease had increased antigliadin antibodies. It was identified in 54% of dogs with extraintestinal chronic diarrhea and in 75% of dogs with chronic enteropathy (CE)/inflammatory bowel disease (IBD), compared to just 6% of healthy dogs.
- **Article:** Response to letter regarding “Utility of the combined use of 3 serologic markers in the diagnosis and monitoring of chronic enteropathies in dogs” Estruch JJ., et. al. *J Vet Intern Med.* 2021 Nov-Dec; 35(6): 2570–2571.
 - Research suggests an association between repetitive inflammatory stimulation by gliadin peptides (gluten) and subsequent intestinal lymphoma in dogs, via ELISA testing.

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Digestion & Detox

Available For:
Dogs

Analytes:
Pancreatic Elastase 1 &
Beta-glucuronidase

Why is this Test Important?

Properly digesting food and absorbing adequate amounts of essential nutrients is an important part of overall gut health. Chronic irritation to the gut lining can lead to maldigestion and malabsorption of nutrients. Deficiencies result in a wide array of health issues. Increased levels of beta-glucuronidase can identify gut dysbiosis and increase the impact of toxins and hormones.

Pancreatic Elastase 1

Pancreatic elastase 1 is a digestive enzyme. Low levels can identify impaired pancreatic function. A dog's digestion depends on enzymes secreted by the pancreas to digest food. Dogs who don't secrete enough digestive enzymes may not fully digest food or absorb enough nutrients from food or supplements and could have a condition known as Exocrine Pancreatic Insufficiency (EPI).

The symptoms of poor digestion are varied but can include diarrhea, weight loss, gas, or other symptoms related to nutrient deficiencies. Some dogs have no symptoms. The main treatment for low pancreatic elastase 1 is supplementing with digestive enzymes and vitamin B12. If low follow-up testing is recommended. Low pancreatic elastase in dogs can be more serious in dogs than people.

Pancreatic Elastase 1



Dogs:

- Normal: $>30 \mu\text{g/g}$ - Can be used to exclude pancreatic insufficiency
- Borderline: $10\text{-}30 \mu\text{g/g}$ - Retest in 3-6 months
- Low: $<10 \mu\text{g/g}$ - Indicates digestive issues and recommend further testing
 - A serum trypsin-like immunoreactivity (TLI) is likely a follow up test in dogs with extremely low fecal Elastase 1 and significant symptoms

Results

If Results Are Normal:

- Continue with current diet and lifestyle, retest in one year

If Results Are Low:

- Consider further testing if pancreatic elastase 1 levels are low and significant symptoms such as weight loss and diarrhea are present. Low pancreatic elastase 1 can be related to autoimmune conditions, and some healthy dogs may have low levels. Digestive enzymes may be recommended
- Consider switching to a digestive care dog food that is lower in fat (<12% fat in dry dog food, <16% in wet dog food, <20% fat in raw food diet), with easy to digest carbohydrates, and adequate protein. Such as Square Pet Low Fat Digestive Support Food, Annameat Lean Reduced Fat dog food, Wellness Core Reduced Fat dog food
- Support GI health with prebiotics, omega-3 fatty acids (Nordic Naturals Pet Cod Liver Oil, Standard Process VF Omega-3, Fera Pet Organic Fish Oil) and the addition of antioxidants/polyphenol.
 - Provide additional fiber, such as 1-2 tablespoons of canned pumpkin a day, or other high fiber foods such as greens or carrots
- Consider supplementing with a basic vitamin and mineral supplement

Research

- **Article:** Effect of intestinal inflammation on fecal elastase concentration in dogs. February 2005 Veterinary Clinical Pathology 34(1):49-51. <https://pubmed.ncbi.nlm.nih.gov/15732018/>
 - A single fecal elastase 1 concentration >20 µg/g can be used to exclude EPI in dogs with chronic diarrhea. A value of <20 µg/g in association with typical clinical signs of EPI is suggestive of severe pancreatic dysfunction. Research has reported the sensitivity of fecal elastase for clinical exocrine pancreatic insufficiency from 95-96% whereas specificity varies from 85 to 92%. This test is not sufficiently sensitive to diagnose subclinical EPI and partial PAA.

- **Article:** An immunoassay for canine pancreatic elastase 1 as an indicator for exocrine pancreatic insufficiency in dogs. Spillmann T, et al, J Vet Diagn Invest. 2001 Nov;13(6):468-74.
 - The test does not detect human, bovine or porcine pancreatic elastase 1. Pancreatic function can be monitored without interrupting an enzyme replacement therapy.
- **Article:** Merck Veterinary Manual: Exocrine Pancreatic Insufficiency in Cats and Dogs. <https://www.merckvetmanual.com/digestive-system/the-exocrine-pancreas/exocrine-pancreatic-insufficiency-in-dogs-and-cats>
 - Exocrine Pancreatic Insufficiency is caused by decreased production of digestive enzymes, with the most common signs polyphagia, weight loss and large amounts of loose stool. Fecal elastase has been validated in dogs, though diagnosis with serum trypsin-like immunoreactivity is often preferred, and is treated with supplementation.

Beta-glucuronidase

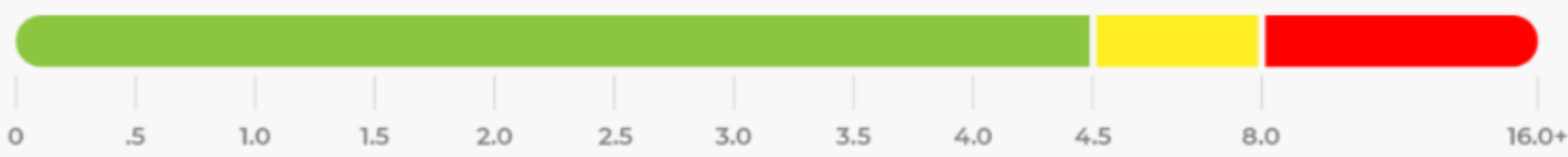
Beta-glucuronidase is an enzyme both people and dogs make that catalyzes the breakdown of complex carbohydrates. Gut microbial β -glucuronidase is involved in the disposition of many endogenous and exogenous compounds. It is also made by gut bacteria. High levels can be due to an imbalance of healthy gut bacteria, which is called dysbiosis.

Additionally, high levels of beta-glucuronidase is known to free toxins that have previously gone through detoxification. Specifically, beta-glucuronidase pulls glucuronide off of toxins and hormones that have gone through glucuronidation. Once the glucuronide molecule is pulled off the toxin or hormone is free to cause damage.

Glucuronidation is a detoxification process that makes toxins more water soluble to bind and excrete them to be eliminated through urine or feces. Toxic substances are less toxic after glucuronidation. Thus, increased levels of beta-glucuronidase are associated with increased levels of free toxins and hormones which can lead to negative health effects.

Consistently elevated beta-glucuronidase has been associated with intestinal disease. The fecal test cannot identify Mucopolysaccharidosis Type VII (Beta-glucuronidase deficiency) a rare genetic disease.

Beta-glucuronidase



Dogs:

- Normal: < 4 µg/g
- Borderline: 4-6 µg/g - Retest in 3-6 months
- High: >6 µg/g - Indicative of issues with gut bacteria or increased levels of toxins. Provide treatment and retest in 3 months

Results

If Results Are Normal:

- Continue with current diet and lifestyle, retest in one year

If Results High

- Elevated levels may be seen in dogs with an imbalance of gut bacteria
 - Consider probiotics to support healthy gut bacteria. Look for probiotics with a variety of healthy gut bacteria, referred to as multi-strain, spore-forming probiotics or *Saccharomyces boulardii*, such as Visbiome Pet Probiotic, Fera Pet Organics Probiotics, or RX Vitamin's NutriGest
 - Consider a higher quality small batch dog food such as Chi Dog Earth Diet
- Reduce exposure to toxins such as household and lawn toxins.
 - Supports detoxification mechanisms, such as glutathione support

Research

- **Article:** Res Vet Sci. 2002 Jun;72(3):223-7.
 - Fecal Beta-glucuronidase was decreased in dogs feed a dry dog food that increased gut bacteria, in comparing dry and wet commercial pet foods. High levels have been associated with liberation and it is released within the bowel.

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