# Journal of Integrative Veterinary Therapies

Gastrointestinal - GIT - Edition



# Journal of Integrative Veterinary Therapies

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college of integrative veterinary therapies

# JIVT: An Introduction

The Journal of Integrative Veterinary Therapies (JIVT) is published twice a year by the College of Integrative Veterinary Therapies (CIVT). It contains papers on all aspects of integrative veterinary medicine, including Chinese and Western herbal medicine, natural nutrition, environmental medicine, philosophy, history, clinical cases and commentary.

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# Approaching disease globally by addressing "leaky gut syndrome"



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## Introduction

Over the last 20 years, researchers have found how increased gut permeability has been playing a part in the development of disease. "Leaky gut syndrome" is characterized as an increase in the permeability of the intestinal mucosa, which may allow bacteria, bacterial toxins, toxic digestive metabolites and small molecules to leak into the bloodstream (Obrenovich, 2018). In complementary/ alternative medicine circles, "leaky gut syndrome" has been widely discussed for decades (Obrenovich, 2018). The simplistic term "leaky gut" reflects intestinal permeability, a function that was extensively studied in these diseases and reported in the scientific literature from 1970-1990 (Camilleri, 2019). The permeability of the epithelial lining may be compromised in pathologic conditions allowing the passage of toxins, antigens, and bacteria in the lumen to enter the blood stream creating a "leaky gut" (Mu et al, 2017).

# **Pathophysiology**

The microbiota gastrointestinal barrier, together with transport proteins, acts at the interface of blood permeability barriers to help regulate trafficking of macromolecules between the digestive environment and the host (Obrenovich, 2018). The intestinal barrier

includes the mucus layer preventing bacterial adhesion, tight junctions and junctional complexes, the lamina propria innate, and acquired immunity cells which secrete Ig and cytokines. The type of molecules that pass the intestinal barrier depends on the type of lesions present (Camilleri, 2019). How diet, lifestyle, antibiotics, and other factors shape the microbiota-gut, and its integrity, constitutes a rapidly growing area of research interest. In humans, gluten and gluten sensitivity are considered triggers for this syndrome in individuals genetically predisposed to celiac disease (Obrenovich, 2018).

# Conundrum of which came first, "leaky gut" or the chronic disease state

"Leaky gut syndrome" affects more than just those with celiac disease. Alterations in gut microbiota, inflammatory responses by the body and external conditions perpetuating these imbalances are at the root of most conditions treated by veterinarians. As 2020 has shown us, we cannot continue to act and think the way we used to, and we must evolve to think globally, not just for our planet, but our own microcosm, the body. The same goes for treating "leaky gut syndrome". Although gut is in the title, "leaky gut syndrome's" global body effects need to be taken into consideration when forming a diagnostic and treatment plan. In human

patients, systemic inflammation resulting from "leaky gut" may be associated with celiac disease, depression and psychiatric comorbidities (Obrenovich et al. 2007). There is a neurophysiological component of "leaky gut", now known as "leaky brain" as well as other "leaky" organ syndromes (Obrenovich, 2018). The contributing role of the microbiota to inflammation, gastrointestinal and bloodbrain-barrier integrity has been established through the interactions between intestinal bacteria and the host immune system as well as through microbial metabolites (Suchodolski, 2016). There are vast numbers of papers that link "leaky gut" with altered microbiota in disease models in experimental animals, from allergy to nonalcoholic steatohepatitis to depression and amyotrophic lateral sclerosis (Zhu et al, 2013; Camilleri, 2019). A preliminary study looked at plasma levels of gut permeability markers in patients with a recent suicide attempt and subjects with no history of suicide attempt and related these markers to symptom severity and inflammation (Ohlsson et al, 2019). There was a significant correlation with higher intestinal fatty acid binding protein levels in the serum of subjects with recent suicide attempts (Lamprecht et al, 2012; Ohlsson et al, 2019). For our veterinary patients with behaviour issues, an imbalance in the microbiome is known to play a role in their behaviour (Mondo et al, 2020; Kirchoff

et al, 2019).

At the heart of it is the microbiome. The intestinal microbiota plays a large role in maintaining the overall health of the host's gastrointestinal tract. Its functions include defending against non-resident intestinal pathogens, aiding in the development of a healthy epithelium and immune system, and providing nutrients for the host via fermentative and metabolic activities (Blake & Suchodolski, 2016). The mutually beneficial relationship between the host and its resident gut microbiota, bacterial products and metabolites from commensal micro-organisms are essential for the host and overall health. There exists a co-metabolism between the microbiota and host system, and it is these microbes which have the ability to control integral segments of our neurobiology including the brain and digestive system (Obrenovich et al, 2007). The microbiota-gut is an integral component of the gut-brain neuroendocrine metabolic axis and any disruption that can occur, such as antibiotic use and during disease, could upset homeostasis and share an inflammatory component (Obrenovich et al, 2007). There is the 'which came first' question for the association of dysbiosis and disease state. One hypothesis argues that increased endogenous production of ethanol by gut bacteria (e.g., E. coli) caused by small intestinal bacterial overgrowth results in increased intestinal permeability, bacterial translocation and hepatic inflammation due to the translocated bacteria or their products (Zhu et al, 2013). An alternative hypothesis is that the liver disease causes a systemic inflammatory response that leads to increased intestinal permeability, with bacterial translocation and further hepatic damage (Luther et al, 2015). Either way, the intestinal permeability needs to be addressed.

One must consider the contributions of "leaky gut" and bacterial translocation



to inflammation and multiple diseases. Reversing gut leakiness is an attractive therapeutic strategy. Growing evidence shows that the gut microbiota is important in supporting the epithelial barrier and therefore plays a key role in the regulation of environmental factors that enter the body. Prebiotics, probiotics, as well as postbiotics can be used to reduce intestinal permeability (Lamprecht et al, 2012; Cuevas-Gonzalez et al, 2020). Diverse probiotic, postbiotic and parabiotic species have been uncovered that possess the properties to protect the intestinal barrier through targeting different components of the mucosal barrier system (Mu et al, 2017; Cuevas-Gonzalez et al, 2020). Several recent reports have shown that probiotics can reverse the "leaky gut" by enhancing the production of tight junction proteins (Mu et al, 2017).

Looking at "leaky gut" from a holistic stance is more than modulating the microbiome through the use of probiotics and prebiotics. Often times the phrase "weed, seed and feed" is used when it comes to treating "leaky gut". This process consists of weeding out pathogenic microbes and foods that are not tolerated by the host, feeding the "good" microbiota that are already present, then seeding in new beneficial microbes to establish residency, and finally feeding nutrients to support the organs of elimination and detoxification including the liver and intestine to support barrier structure and function. Addressing the intestinal barrier using herbs to stimulate and protect the mucus layer, improve tight junctions and junctional complexes, protect the lamina propria, and stimulate acquired immunity cells, would be one way of addressing the intestinal component of "leaky gut".

# Herbs to stimulate and protect the mucus layer

Fresh Aloe (Aloe vera) leaf gel is very effective for healing erosion of the stomach or the intestines (Yusuf et al, 2004). It inhibits H. pylori and stimulates mucosal healing due to its allantoin and mucilage content. Calendula (Calendula officinalis) acts as a vulnerary and anti-inflammatory topically and internally (Al-Snafi, 2015; Mehrabani et al, 2011). The flowers also have mild antibacterial and antiviral activity and are rich in antioxidant carotenoids. Gotu kola (Centella asiatica) has a long history of traditional use for healing red, inflamed tissue. Asiatic acid, an active constituent Gotu kola, directly interacts with mitochondria and prevents the opening of the mitochondria permeability transition pore (Guo et al, 2016). Plantain leaf (Plantago major) is a demulcent herb which soothes irritated mucosal tissue and promotes mucin production and healing of the intestinal epithelial barrier. Plantain contains allantoin, chlorophyll, and flavonoids, which help heal inflamed and irritated skin, gastrointestinal tract, and urogenital tract tissue.



# Herbs to improve intestinal tight junctions

Improving tight junctions can be done with the use of **Barberry** (*Berberis vulgaris*)

Aminnezhad et al in 2016, demonstrated the which prevents damage to the mucosal ability of Marshmallow (Althea officinalis) root extract to significantly reduce biofilm formation of P. aeroginosa due to the presence of sugars and polysaccharides and mucilages in the plant extract which greatly inhibit the bacterial attachment to surfaces and biofilm formation. Berberine in Barberry (Berberis vulgaris) also effectively prevents the formation of S. epidermidis biofilm (Imenshahidi, 2016).

layer in cases of endotoxaemia gut damage, through different mechanisms including attenuation of disruption of tight junctions in intestinal epithelium (Imenshahidi, 2016). Mulberry Leaf (Morus alba L.) significantly reduces pro-inflammatory cytokines and tumor necrosis factor (TNF)- $\alpha$ , increases tight junction proteins dramatically, increases trans-epithelial electrical resistance and decreases the transmission of albuminfluorescein isothiocyanate (FITC) across the mucosal barrier (Guo et al, 2016). Mulberry leaf has the potential to ameliorate LPS-induced disruption of the gut epithelial barrier by increasing cell viability and tight junctions between cells and decreasing pro-inflammatory cytokines and oxidative damage (Guo et al, 2016). The Green Tea (Camellia sinensis) polyphenol significantly prevents the epithelial barrier dysfunction evoked by IFN-y, IL-4 (known to increase intestinal monolayers), and/or E. coli. (Watson et al, 2004)



In addition to addressing the mucosa, the biofilm of the microbiome also needs to be addressed. A biofilm is any group of microorganisms in which cells stick to each other and often these cells adhere to a surface. A biofilm is produced by the microbiome of the gut to create a biological home for themselves using a mixture of sugars and proteins. A healthy biofilm is a thin mucus allowing the passage of nutrients through the intestinal wall. A healthy gut biofilm is moistening, lubricating and antiinflammatory. An unhealthy biofilm created during dysbiosis will continue to promote the growth of pathogenic populations. Herbs like Echinacea (Echinacea purporea) (Bensch et al, 2011) and Licorice (Glycyrrhiza glabra) (Bensch et al, 2011) haven antiadhesive effects against C. jejuni. Research done by



# Herbs to stimulate acquired immunity cells

To re-establish a healthy intestinal epithelial barrier and stimulate secretion of secretory immunoglobulins, herbs can be used which modulate the immune system. Turmeric (Curcuma longa) attenuates activation of IECs as well as macrophages resulting in decreased secretion of IL-1-beta which subsequently results in disruption of tight



junctions (Wang et al, 2017). **Andrographis** (*Andrographis paniculata*) has in vitro inhibitory activity against TNF-α, IL-1β and NF-κB (Sandborn, et al, 2013). **Mastic gum** (*Pistacia lentiscus*), also known as gum mastic, comes from a tree that only grows on the Greek island of Chios. The use of this gum in human populations reduces inflammatory markers (IL-6 and CRP) associated with Crohn's disease and decreased the Crohn's activity index (Kaliora et al, 2007).

# Global approach to health

In a world of increasing populations of chronic disease states including canine cognitive disorders, cancers and allergies, in which research is showing correlations between the health of the gut and inflammation elsewhere in the body (including the brain), the health of the gut must be addressed. Taking a holistic global approach to "leaky gut" involves more than healing the intestine and using pro/ pre/post/parabiotics. The patient's overall health, diet, stress, and pesticide exposure must be addressed. A patient's digestion can be improved through the use of bitters. Adaptogens such as Cordyceps (Cordyceps sinensis) and **Eleuthero** (Eleutherococcus senticosis) will decrease the negative effects of stress on the body by modulating the HPA axis. Eating a fresh food diet, and eliminating processed foods, reduces exposure to advanced glycation end products, which play a role in creating and perpetuating "leaky gut" (Qu Wanting et al, 2017). For all the environmental toxins that cannot be avoided. supporting the organs of elimination and detoxification including the liver and kidneys, are essential. **Milk thistle** (*Silybum marianum*) is hepatoprotective, nephroprotective as well as immunostimulatory (Wilasrusmee et al, 2002). As is always with a holistic approach, there is no one formula to treat the patient with "leaky gut" and addressing the patient as a whole is essential.

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# **GIT** herbs as drugs of the future



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This article is an edited excerpt from Dr Marsden's book, "Essential Guide to Chinese Herbal Formulas - Bridging Science and Tradition in Integrative Veterinary Medicine".

#### Introduction

Research into herbal medicine is increasing logarithmically in an effort to identify new pharmaceuticals with enhanced effects relative to the drugs that are relied upon today. The constituents of interest currently occur only in plants, at too low concentrations for pharmacological action. Inside the plant and, by extension inside the herbal medicine patient, the constituents are only one voice among many that together 'sing the song' of the plant's medical influence. Besides being more concentrated, drugs of the future hoping to preserve and accentuate the benefits of these ingredients will likely have to contain more than one of them. Barbershop quartets will have to be identified within the choir that are singing the song loudest and most clearly. Such drugs do not yet exist. For the moment, veterinarians can access them only in plant form.

However, the effects are worth the effort of learning a new medical discipline. They include:

Increasing blood flow to particular tissues and organs

- Targeted anti-inflammatory effects that do not affect the whole system
- Insulin sensitization
- Resolution of chronic inflammation by reversal of endothelial dysfunction
- Halting and preventing degeneration through targeted increases in blood flow
- Normalization of smooth muscle contraction
- True immune modulation, where immunity is strengthened while destructive inflammatory responses are subdued
- Novel antimicrobials with unlimited distribution and minimal resistance
- Promotion of cellular differentiation and control of angiogenesis to induce tumor atrophy

These are just a few of the tantalizing medical possibilities arising from integrating herbs into medical practice.



# Insulin resistance: It's role in acute inflammation

Insulin resistance is of massive importance in small animal medicine, even in non-diabetic animals. Research is emerging to suggest insulin resistance is a prominent cause of acute, recurrent and chronic inflammation in small animals.

# Post-prandial hyperglycemia

Cats and dogs share a very similar metabolism to humans, such that they frequently serve as animal models for research into human metabolism and its role in inflammation. This research has disclosed that consumption of highly processed, starch-based or high-fat diets causes the appearance of a transient inflammatory post-prandial response (Margioris 2009). Although the biologic value of such a response is unclear, there is no question it occurs. It is more severe in patients with a higher body score and is mediated by potent pro-inflammatory cytokines such as interleukin-6.

Once elaborated, cytokines do not just produce inflammation but also promote generation of reactive oxygen species. C reactive protein (CRP) is one example. It is a phylogenetically old defense molecule utilized by many animal species to help increase the inflammatory response (Solter and Uhlenbruck 1982). CRP synthesis is induced in the liver by cytokines released in response to diet and has the effect of ramping up any inflammatory responses by promoting complement fixation and opsonization.

Border skirmishes on epithelial surfaces triggered by mild irritants or a few microbes suddenly have the potential to become much more incendiary and destructive under the influence of a processed starchy or high-fat diet. Multiple inflammatory

episodes occurring over time at various epithelial surfaces are the hallmark of this post-prandial inflammatory tendency. This is commonly noted in a small animal patient's medical record as a procession of '-itides'. These episodes respond to antimicrobial therapy, although the number of microflora present may not be different from a healthy animal. The difference in response is from a heightened reactivity to their presence. Just as commonly, however, inflammation remains subclinical, quietly damaging insensate tissues like the kidney and liver. Problems are only recognized on routine blood and urine screening, perhaps once functional reserves have been consumed. Examples include elevated liver enzymes, azotemia, hematuria and crystalluria.

# Post-prandial oxidative stress

Post-prandial increases in inflammation lead to oxidative stress, but so too does the meal itself as fats and starch are metabolized by liver mitochondria. If antioxidant levels are insufficient in a diet to quench them (as is typical in canned and dry foods), these reactive oxygen species provoke tissue damage that spawns more inflammation. Inflammation, in turn, adds to any oxidative stress in the body, for instance through the heightened activity of cyclo-oxygenase and lipoxygenase. In the end, a vicious cycle of inflammation and oxidative stress is created and perpetuated with each meal.

# **Development of insulin resistance**

Sustained inflammation and oxidative stress eventually can damage beta islet cells plus insulin receptor and signalling mechanisms. Obesity and insulin resistance commonly ensue. Although it is uncommon for insulin resistance to result in diabetes, it is of tremendous clinical significance. Insulin resistance impairs gluconeogenesis,

promoting heightened food consumption that in turn propagates more inflammation and oxidative stress. It also allows post-prandial hyperglycemia to endure, heightening its inflammatory consequences.

Insulin resistance paves the way for other sequelae besides inflammation and obesity. A pre-cushinoid state can be produced where glucocorticoid receptors increase in number or are otherwise up-regulated, allowing normal cortisol levels to have a heightened effect. This syndrome is common in dogs, producing symptoms of hyperadrenocorticism with no diagnostic increase in serum cortisol.

# The pro-inflammatory effect of abdominal fat

Problems deepen further as abdominal fat accumulates in response to insulin resistance. Adipose tissue, previously considered largely inert, is in fact a separate major source of inflammatory cytokines. The evolutionary advantage behind adipose tissue generating significant amounts of inflammatory mediators is not clear, but it is able to be demonstrated consistently in a variety of species. If fat stores are large, the release of cytokines is large. Not surprisingly, weight loss is associated with reversal of tendencies toward accumulation of inflammatory mediators (Bastard et al 2006). Unfortunately, weight loss is progressively more difficult as insulin resistance worsens. In addition, post-prandial inflammatory responses worsen in the obese patient and are more easily produced regardless of the nutrients consumed.



# Therapeutic intervention through diet

Satisfactory results in managing inflammation are unlikely to be obtained without addressing an animal's diet. To date, veterinarians focus on specific immune responses to individual food antigens as the leading cause of dietinduced inflammation. Clinic shelves are lined with food containing novel proteins from increasingly creative sources in an effort to address an apparent epidemic of food allergies and sensitivities. In contrast to this perception, clinical experience and research suggest that primary food allergies are relatively uncommon.

Acquisition of food allergies appears driven by chronic inflammation of the digestive tract, leading to a so-called 'leaky gut' that allows larger-sized food molecules premature entry to the lamina propria where they prime the immune system to respond to them. However, gut wall inflammation arises from inflammatory responses that are non-specific and driven by post-prandial hyperglycemia. Elimination of these inflammatory responses through use of an unprocessed, non-starch-based diet allows the gut wall to heal itself, thus eliminating the possibility of food allergies.

Non-specific inflammatory responses trump food allergies as the main diet-related problem in dogs and cats. Current research suggests the ideal dog or cat diet has a low glycemic index, such that surges in post-prandial insulin, inflammation and oxidation are minimized. Additionally, they should be an important source of anti-oxidants. When measured by these criteria, most commercial diets fail on all accounts, even so-called hypoallergenic diets.

Despite their nutritional completeness, research evidence is emerging that points to most canned and kibble diets as being potential promoters of disease. In response, the public has reached for home-cooked and raw diets for their pets, much to the chagrin of veterinarians. The veterinary profession has likely been too quick to judge, however. When compared with canned and kibbled diets, home-cooked and raw diets' greater complexity, higher antioxidant levels and longer digestion times undoubtedly lead to reductions in insulin resistance, oxidation and inflammation.



Regardless of whether relying on drugs or herbs to treat patients, a primary goal of the small animal veterinarian must include providing the owner with advice and resources on the creation of nutritionally complete, unprocessed diets.

Given the foregoing, the ideal antiinflammatory drug should be:

- Antioxidant
- Insulin sensitizing
- Anti-inflammatory

Corticosteroids, while powerful antiinflammatory drugs, actually aggravate insulin resistance and so are an inferior choice. If they are necessary to successfully manage a case, their use should at least be in tandem with an insulin sensitizing, antioxidant and anti-inflammatory herbal formula.

# **Insulin sensitizing herbs**

Three Seeds Combination (San Ren Tang) is the prime consideration for initial management of diabetes in cats. Along with an unprocessed non-starch based diet, it regularly restores eugylcemia. San Ren Tang also relieves sub-acute inflammation.

Four Marvels Combination (Si Miao San) is an acute acting anti-inflammatory formula for dogs and cats that is the treatment of choice for managing Cushings disease, whether occult or pituitary dependent. Four Marvels improves Cushings' symptoms significantly over time, often obviating the need for conventional therapy – except in primary adrenal tumors.

Coix (Yi Yi Ren Tang) is one of the main insulin sensitizing ingredients in **Four Marvels** and **Three Seeds Combinations**. It is also abundant in **Coix Combination (Yi Yi Ren Tang)**.

# Acute acting anti-inflammatory formulas

Acute inflammation becomes easy to address without drugs when processed diets are avoided. The need for anti-inflammatory drugs with their attendant side effects is obviated. Anti-inflammatory herbal formulas do not cause the same problems and have the added advantage over drugs of being insulin sensitizing and antioxidant.



Where corticosteroids must still be used to adequately control symptoms, the formula of choice for concomitant use is **Four Marvels Combination (Si Miao San)**. Four Marvels is the most commonly used herbal formula by veterinarians in North America, due to its systemic acute-acting anti-inflammatory properties that allow it to minimize the dose of anti-inflammatory pharmaceuticals. It is especially helpful for inflammation of the back, skin, liver, bladder, genital and digestive organs. Four Marvels is a powerful insulin sensitizing formula and is antioxidant.

# Chronic inflammation, degeneration and the manipulation of blood flow

Insulin resistance does not just predispose animals to acute inflammation, it also allows it to persist. Entirely different mechanisms are involved in the propagation of chronic inflammation. These mechanisms together are known as endothelial dysfunction.

# Introduction to endothelial dysfunction

A massive worldwide research effort has disclosed that endothelial dysfunction is a problem of epidemic proportions, occurring at a far higher incidence than virtually any other disease process in the world. It is a global pandemic of circulatory impairment, caused largely by the chronic consumption of a high glycemic index diet. Endothelial dysfunction is the chief cause of heart disease and systemic hypertension. In addition it is now recognized as the core problem behind a steadily growing list of other conditions, including:

- Rheumatoid arthritis
- Degenerative joint disease
- Chronic depression
- Alzheimer's disease
- Congestive heart failure
- Osteoarthritis
- Inflammatory bowel disease
- Chronic active hepatitis
- Renal failure
- Senility
- Thyroiditis

Until recently, medicine believed that inflammatory processes simply burned themselves out, resolving once all antigens that sparked the fire were eliminated. Recent research has confirmed, however, that inflammation does not naturally fizzle out, but must be 'actively resolved'.

#### Normal resolution of inflammation

The normal process of inflammation, as it should unfold, can be broken down into two distinct phases. The first phase of acute

inflammation is driven by cytokines derived from omega 6 (arachidonic) fatty acids. This first phase is characterized by:

- Increased vascular permeability
- Fibrin deposition
- Leukocyte ingress
- Endothelial activation and capillary sprouting
- Fibrin modification by extra-cellular proteases

A result is the creation of a scaffold for invasion by specialized endothelial cells.

In the second phase of inflammation, cyclo-oxygenase enzymes switch substrates, utilizing eicosanoids to manufacture a new class of compounds known as SPMs (specialized proresolving mediators). Specific examples include the aptly named resolvins, protectins and lipoxins. These new families of local mediators control the duration and magnitude of acute inflammation, as well as the return of the site to homeostasis (Serhan 2010).

Resolvins and lipoxins do not throw water on the fire of inflammation directly, but act through another compound called endothelial nitric oxide. It is endothelial nitric oxide that controls the vascularity of a tissue. It does this by:

- Reducing vascular permeability, restoring lymphatic clearance of inflammatory debris, cytokines and free radicals through Starling forces
- Reducing leukocyte-endothelial interactions to minimize chemotaxis and inflammation in the interstitium
- Heightening interstitial macrophage vigilance and resistance to infection
- Promoting extra-cellular matrix modification and repair

- Inhibiting platelet adhesion and aggregation, as well as vascular occlusion
- Inhibiting vascular smooth muscle cell proliferation (of importance in atherosclerosis)
- Promoting regression of excess vascular structures
- Promoting growth of endothelial buds that restore normal tissue vascularity, facilitating long-term repair

The above sequence of vascular events is known as 'active resolution'. This is lacking in almost all tissues suffering chronic inflammation and degeneration.

# Causes of endothelial dysfunction

Ironically, one potential cause of continued inflammation appears to be the chronic sustained use of anti-inflammatory drugs. SMPs like lipoxins are manufactured by cyclo-oxygenase, the same enzyme which is the target of non-steroidal anti-inflammatory drugs (NSAIDs) like meloxicam and deracoxib. The only NSAID that supports lipoxin synthesis is acetylsalicylic acid, a plant-derived compound whose role as an anti-inflammatory has been supplanted by more potent synthetic pharmaceuticals.

Herbs like Turmeric and Boswelia inhibit acute inflammation by suppressing lipoxygenase function, but support cyclo-oxygenase activity so that inflammation-resolving SMPs can be produced. On this basis, they are superior choices to most pharmaceuticals in managing chronic joint inflammation and degeneration. The two herbs have been used together for centuries in classical formulas to limit inflammation and pain, including in Minor Invigorate the Collaterals (Xiao Huo Luo Dan) and Angelica and Mastic (Xian Fang Huo Ming Yin).



The potential risks of drugs notwithstanding, by far the most common cause of endothelial dysfunction is insulin resistance. Insulin resistance is nearly always attended by a systemic increase in oxidative stress. Oxidative stress, in turn, damages the portions of cyclo-oxygenase and lipoxygenase that turn eicosanoids into resolvins, protectins and lipoxins.

Insulin resistance also makes post-prandial hyperglycemia more likely. Even transient increases in blood sugar lead to surges in free radical production, pro-inflammatory compound release from the liver and cyclo-oxygenase mediated production of inflammatory cytokines (Wakshlag et al 2011). If cyclo-oxygenase enzymes are making pro-inflammatory cytokines, they are not making SMPs like lipoxin.

In addition to this upstream impairment of active resolution, insulin resistance directly impedes endothelial nitric oxide production. High insulin levels lead to increased protein kinase C activity (Bohlen and Nase 2002). This, in turn, halts endothelial nitric oxide synthase (eNOS) activity and lowers nitric oxide levels further.

# Formulas to resolve chronic inflammation

Many plants have been confirmed useful in actively resolving chronic inflammatory and degenerative disorders associated with endothelial dysfunction (Recio et al 2012). Indirect benefits include insulin sensitization and protection of cyclo-oxygenase through their content of antioxidants.

Additionally, and of more direct benefit, plants bypass the deficit in SMP synthesis by directly stimulating endothelial nitric oxide synthesis. The effects on eNOS can be systemic or local (through 'organ affinities' or selective uptake). This allows the veterinary herbalist to target particular tissues and regions, depending on the formula used.

The following table lists common sites of degeneration or chronic inflammation in small animal medicine GIT disorders, plus some specific formulas to address them:

Formulas to resolve chronic inflammation in particular organs			
Target Organ	Formulas		
Colon	Agastache Combination (Huo Xiang Zheng Qi San)		
	Three Seeds Combination (San Ren Tang)		
Liver	Rambling Ease Combination (Xiao Yao San)		
Pancreas Agastache Combination (Huo Xiang Zheng Qi San)			
	Glehnia and Rehmannia Combination (Yi Guan Jian)		
	Harmonize the Stomach Combination (Ping Wei San)		
	Harmonize the Stomach with Poria Five Herb Combination (Wei Ling Tang)		
Harmonize the Stomach Combination (Ping Wei San)			
Stomach and	nd Harmonize the Stomach with Poria Five Herb Combination (Wei Ling Tang		
small intestine	Glehnia and Rehmannia Combination (Yi Guan Jian)		
	Three Seeds Combination (San Ren Tang)		

|--|

Formulas that boost circulation in specific organs			
Target Organ Indication Formulas			
Microvascular shunt	Angelica and Peony Combination (Dang Gui Shao Yao San)		
Chronic vomiting and	Rambling Ease Combination (Xiao Yao San)  Glehnia and Rehmannia Combination		
malabsorption	(Yi Guan Jian) Harmonize the Stomach with Poria Five Herb Combination (Wei Ling Tang)		
,	Indication  Microvascular shunt  Chronic vomiting and		

# Formulas to counter degeneration

Many degenerative processes are believed to stem from endothelial dysfunction. The table above lists formulas that counter degenerative processes and restore normal function in particular organs by improving blood flow.

## Other formula effects:

# Regulation of smooth muscles and motility

The targeted effects of classical Chinese herbal formulas extend to more than just the regulation of circulation. Certain formulas excel at regulating smooth muscle tone and motility in specific regions. Where signs otherwise agree, **Ginseng and Astragalus** (**Bu Zhong Yi Qi Tang**) is used for:

- Prolapse tendencies
- Incontinence
- Urethral obstruction
- Constipation and/or soft stool
- Prevention of abortion
- Abdominal distension

Rambling Ease Combination (Xiao Yao San) can normalize abdominal distension, constipation and/or soft stool. It has anti-depressant effects that, along with its motility normalizing influence, can potentially boost appetite in cats.

As a systemically acting anti-inflammatory, **Three Seeds Combination (San Ren Tang)** has a broad reach and can address:

- Cough (moist)
- Constipation
- Vomiting
- Dyspepsia
- Abdominal distension

Harmonize the Stomach with Poria and Five Herbs Combination (Wei Ling Tang) mimics the effects of cisapride in boosting feline gastrointestinal motility and appetite. It also quells vomiting. Minor Bupleurum (Xiao Chai Hu Tang) is a specific formula for the management of collapsing trachea in dogs. Together with Harmonize the Stomach with Five Herbs and Poria Combination (Wei Ling Tang), it can remove tendencies to gastric dilation and volvulus (GDV).

# Immune modulating and anti-infective formulas

The term 'immune modulating' is used charitably in veterinary pharmacology – most such drugs are really just immune suppressants. In contrast, the biochemical complexity of the classical Chinese herbal formulas in this text enables the veterinarian to simultaneously inhibit destructive autoimmune and inflammatory responses while enabling and supporting humoral immunity. They are thus superior choices to immune suppressant drugs where signs and



symptoms otherwise agree. Two formulas commonly used for their anti-infective properties are Agastache Combination (Huo Xiang Zheng Qi San) and Eliminate Damp and Harmonize the Stomach with Poria Five Herb Combination (Chu Shi Wei Ling Tang). Both formulas address infections resistant to antimicrobial pharmaceuticals due to poor drug delivery.

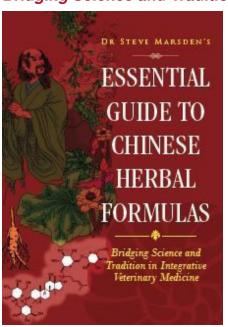
Agastache Combination handily resolves chronic or recurrent viral and bacterial infections of the gastrointestinal tract, including colitis from recurrent clostridial infections. In both cases, the improved drug delivery comes from the formula's content of aromatic herbs which stimulate vasodilation and endothelial bud growth in the target region.

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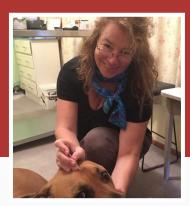
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# **Case Report**

# "Penny": The use of acupuncture in treatment of suspected megaoesophagus in a puppy





## **Abstract**

A 12 weeks young Miniature French Bulldog female puppy was presented to Hint of Thyme, Veterinary Integrative Medicine with persistent vomiting. Conventional diagnostic tests were inconclusive and conventional veterinary medicine did not offer satisfactory or successful treatment or management. Acupuncture, western herbal medicine and cold laser treatments were used to resolve regurgitation and vomiting caused by suspected congenital megaeosophagus.

The puppy arrived from mainland Australia on a plane at eight weeks of age and started to vomit as soon as she was off the plane. She also developed watery diarrhoea. She kept vomiting intermittently since, usually soon after a meal. Owner took the puppy to her regular vet for both vomiting and diarrhoea and was given Hills digestion diet (Hill's Prescription Diet I/D). This food did not stay down and diarrhoea got better with prescription of sulfadimidine 1ml/kg/ twice daily (Scourban Plus, Bayer). Vomiting persisted and the puppy lost weight of about 200g within a week from the original weight of 1.7kg. Owner took her back to the veterinary clinic (all this was during 'Covid-19 state lock down' and the vet who is normally very attentive seemed much stressed) - despite his reluctance due to puppy's poor condition, he put her under general anaesthetics for abdominal x-rays and ultrasound. He

reported no abnormalities were detected (NAD) and informed the owner he had a bad feeling that something very bad was going on within the puppy's abdomen (this comment stressed the owner to the maximum). Owner was given Black Hawk kibbles (owner was not sure what line or flavour) without any further advice or medication. She decided to discontinue feeding the diet after two days as it did not resolve the vomiting.

Owner started to cook own food for the puppy comprising of chicken, rice, pumpkin, sweet potato and bone broth which the puppy loved. She put 200g back on in a week on this diet to current weight of 1.7kg. The vomiting stopped for a week on home-made diet until owner's mum gave the puppy beef tendon for a treat and the puppy vomited again. She seemed to be vomiting only after eating, especially when she gulps food down. Her stool was pale and sloppy before the homemade diet was introduced and since the diet changed is normal colour, amount and consistency. She received second puppy vaccination (DHPP) at ten weeks of age and had been de-wormed at the same time.

# **Examination**

#### **Western Medicine Examination:**

The puppy was bright alert responsive (BAR) with body condition 3/9 (WSAVA score system), her heart rate was at 165 beats per

minute (bpm), regular and no murmur was detected. Temperature was within normal range at 38.3°C. Her mucous membranes were pink-red, with capillary refill time <2 seconds. There were no discharges from any orifices and no foul odour was detected. On palpation, wall of oesophagus felt thickened at the thoracic inlet with sensation of fluid pooling at that area.

# Traditional Chinese Medicine (TCM) examination:

Pulses were deeper and rapid.

Tongue was pink-red and moist.

No active acupoints were detected even though could not be completely sure as the puppy was in a playful mode that may have masked any responses.

# Western Medicine diagnosis:

Open – suspected differential diagnosis of megaeosophagus and/or food intolerance and/or congenital issue in cranial abdomen.

# **Traditional Chinese Medicine diagnosis:**

Eight principles: internal, hot, yang, excess. Fire in the stomach, rebellious Stomach Qi, Spleen and Stomach deficiency leading to Qi deficiency and concurrent Blood and/or Yin deficiency, Kidney Jing deficiency.

## **Treatment**

# Treatment goal:

To remove fire, tonify Qi and improve Qi and Blood flow, tonify Spleen and Stomach tonify Yin and Jing.

#### **Western treatment:**

Currently, there is no western treatment prescribed.

# Traditional Chinese Medicine treatment and results:

#### Day one

During first treatment Seirin acupuncture needles 0.25mm x 15mm were placed in the

acupuncture points PC6, PC9, LI11, GV14, KID23 and CV12 at the depth described in Table 1. The points were sedated with retention time of more than 15 minutes. ST36 was tonified with retention time of less than 15 minutes.

After the treatment the pulses were fuller.

Diet recommendation was made to keep feeding home cooked diet made into firmer balls preventing food aspiration and feeding from raised food bowl including water bowl or in upright position with smaller more frequent meals (Dodd 2020, Becker 2016, Bailey chair 2020).

# Day seven

On the second visit, owner reported puppy vomited only once during the night after engorging on kibbles that she found at mother's place. Otherwise, owner reported that the pup was fine, full of energy and behaving like a pup again. The tongue was pale-pink/pink, the pulses were fuller. There was still thickening of the oesophagus at the thoracic inlet with a pocket of air and fluid pooling (Picture 1). Body score was 3.5 (WSAVA score system). She gained about 50g with shiny coat and filling up musculature along lumbar spine and pelvic bones.



Seirin acupuncture needles 0.25mm x 15mm were placed in the acupuncture points PC6, LI11, GV14, KID23 and CV12 at the depth described in Table 1. The puppy objected to insertion of PC9 on the first visit and was not used during the second treatment. GV24 was added to the prescription to calm down the pup that became livelier for the treatment. ST40 was added to the point prescription to help move Qi and aid to remove excess fluid and phlegm from the body. The points were sedated with retention time of more than 15 minutes. ST36 was tonified with retention time of less than 15 minutes.

## Day ten

On third visit body score improved again to 4/9 (WSAVA score system). The tongue was pink and pulses fuller. She was running around wagging the tail/full body in excitement running towards me. Owner reported she was usually not this excited to see people including herself. Owner also reported vomiting/regurgitation happened only on couple of occasions when the puppy ate food too quickly.

Seirin acupuncture needles 0.25mm x 15mm were placed in the acupuncture points PC6, LI11, GV14, KID23 and CV12, GV24 and ST40 at the depth described in Table 1. The points were sedated with retention time of more than 15 minutes. ST36 was tonified with retention time of less than 15 minutes.

#### Day fourteen

During fourth visit owner reported she changed the puppy's diet to BARF diet (BARF). She reported the puppy vomited first time receiving the new diet otherwise is keeping the new food down and is still very energetic. Body condition was 4/9 and body weight increased to 1.85kg. Coat was shiny and there were no foul odours. Owner reported during one night since previous visit, the pup's resting respiratory rate went

to about 50 breaths per minute (bpm) during sleep and she heard bit of gurgling noises. Heart rate was 138 bpm, regular with no murmur detected, chest sounded were clear with gurgling noises being auscultated over the thoracic inlet. Palpation of the area produced swallowing reflex and excess salivation.



Seirin acupuncture needles 0.25mm x 15mm were placed in the acupuncture points PC6, LI11, GV14, KID23 and CV12, GV24, ST40 and ST36 at the depth described in Table 1. SP6 and SP9 were added to the prescription to drain excess fluid/phlegm and support Spleen function. The points were tonified with retention time of less than 15 minutes.

Marshmallow Root Glycetract 0.1-0.2ml orally three times a day (Marshmallow Root Glycetract Althea *officinalis* Root 1:5, Mediherb) was prescribed for its nutritive, demulcent and vulnerary actions to decrease irritation/inflammation of the oesophagus and mechanically protect its mucosa.

K-laser treatment (K-laser Cube 4 class IV laser, K-laser USA, Summus Medical Laser) (Saik JE 2018, Palm JG 2020) was performed bilaterally along spine to stimulate sympathetic ganglion from TH1 to L4 @ 495J in total and in the area of thoracic inlet @ 261J in total.

## Day eighteen

During the fifth visit owner reported there was no vomiting or regurgitation since the last visit. She still could hear some gurgling noises and seemed to have increased respiratory rate during rest on small number of occasions. The puppy was BAR and energetic. Condition score of 4/9 (WSAVA score system) with evidence of 'filling up' and growing. Her weight was 1.9kg. The thickening of oesophageal wall and fluid pooling was still present and puppy was still making occasional gurgling noises. The tongue was pale pink and moist. The pulses were deeper and compressible. Seirin acupuncture needles 0.25mm x 15mm were placed in the acupuncture points PC6, LI11, GV14, GV24, KID23 and CV12, ST40, SP6, SP9 and ST36 at the depth described in Table 1. The points were tonified with retention time of less than 15 minutes. LI4 was added to the prescription to regulate defence Qi, remove obstructions in the channel and support the Lungs. Attempt was made to needle PC9 and the needle did not stay in long again before it was shaken out.

K-laser treatment (K-laser Cube 4 class IV laser, K-laser USA, Summus Medical Laser) (Saik JE 2018, Palm JG 2020) was performed bilaterally along spine to stimulate sympathetic ganglion from TH4 to L2 @ 495J in total and in the area of thoracic inlet @ 261J in total.

Tongue colour after the treatment improved to pink and pulses were fuller.

Modified Si Ju Zi Tang (Table 2) 1/8-1/4 of teaspoon to be mixed with food twice daily was prescribed to replenish and invigorate Qi and to strengthen Spleen (Clemmons 2020, Xiangyang 2014). Hou Po is added to the decoction to promote Qi movement downward, dry dampness and resolve phlegm (Clemmons 2020, Penner 2020).

The acupuncture treatment will continue weekly for four weeks then monthly or as needed. The low level laser treatment will continue for twelve treatments in total then when/if needed. The herbal treatment will continue for twelve weeks and will be reviewed regularly then as/if needed.

Testing for myasthenia gravis at the regular vet was discussed with the owner.

Table 1. Acupuncture points prescription

(Clemmons, CIVT 2015, Matern 2012, Saik 2018, Schoen 2011, Looney 2001)

Point	Anatomical Location Insertion Technique	Effect	Indication
LI4	Between the first and second metacarpal bones, at the level of the middle of the second phalanx of the first toe in the front paw. To a depth of about 0.3 Cun, perpendicular insertion.	Dispels wind heat, frees the surface, regulates defence Qi, resolves obstructions in the channel, stimulates the distribution function of the lung	Fever

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Point	Anatomical Location Insertion Technique	Effect	Indication
LI11	At the end of the lateral cubital crease, halfway between the biceps tendon and the lateral epicondyle of the humerus with the elbow flexed.  0.5 Cun deep, perpendicular insertion.	Regulates Qi and Blood. Removes heat.  Activates the meridian and alleviates pain.  Dispels wind and heat everywhere in the body, cools and regulates blood, regulates food Qi, loosens phlegm, draws out dampness.	Tonification Point  He Sea and Earth Point.
GV14	On the midline, between the dorsal processes of the last cervical and the first thoracic vertebrae.  1.5 Cun deep, perpendicular insertion.	Local point. Decrease inflammation, resolve stagnation, move Blood, relieve pain.	Influential point of Yang energy, point of the Sea of Qi. Meeting point of all the Yang meridians.
GV24	On the dorsal midline of the skull cap 1 Cun dorsal to the inner corner of the eye.  0.5 Cun deep, oblique insertion in a rostral direction.	Calms the spirit.	Calming effect.
PC6	Medial 2 Cun above the carpal fold, between the tendons of the superficial flexor muscles of the superficial flexor digitorum muscles and flexor carpi radialis muscles, lateral across from TB5.	Master point for the chest and heart, strong point for calming the heart and spirit and for alleviating anxiety, regulates Qi and blood.	Luo network point, opener of the yin linking vessels. Problems of the thorax, calms the spirit, problems in the upper abdomen, relieves nausea and vomiting, harmonises stomach function.
	To a depth of about 0.3Cun, perpendicular insertion.		
PC9	On the third toe of the forepaw lateral to the claw fold, alternatively medial to the claw.	Eliminates heat, dispels wind.	Jing-well point, wood point.

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Point	Anatomical Location Insertion Technique	Effect	Indication
ST36	3 Cun distal to ST35, laterally at the height of the distal end of the tibial tuberosity, in a depression roughly in the centre of the tibialis cranialis muscle.  To a depth of about 1 Cun, perpendicular insertion.	Normalizes down-leading function of the stomach, supports the spleen's functions of transformation and transport, supplements Qi, calms the spirit, moves Qi along the channel.	He-sea point, earth point, a point of the sea of grain. All gastrointestinal problems, stomach or biliary colic, impaired digestion, fever.
ST40	8 Cun proximal to the lateral malleolus, directly cranial to the fibula. 1 Cun lateral to ST38 between the tibialis cranialis and the long extensor muscles of the toes. To a depth of about 1 Cun, perpendicular insertion.	Transforms and resolves phlegm and dampness, clears heat (especially heat in the stomach), calms the spirit, opens up the chest, moves Qi along the channel.	Leu-network point. Problems with phlegm in the respiratory tract, knots everywhere, mental problems phlegm in the body and below the skin.
CV12	On the ventral midline, halfway between the xiphoid process and the navel. To a depth of about 0.5 Cun, tangential insertion.	Influential point for all yang conditions, supports the stomach, lowers rebellious Qi, promotes the splenic functions of transport and transformation, dispels and transforms dampness, disperses food stagnation.	Mu-alarm point of the stomach, hui-meeting point of the bowels, intersection point with the small intestine, triple burner and stomach channels. Gastrointestinal problems, wakened digestion, diarrhoea.
KI 23	In the fourth intercostals space, 1 Cun lateral to the midline and the sternum. To a depth of about 0.2 Cun, acute angle insertion.	Lowers rebellious stomach and lung Qi, frees the thorax.	Pleuralgia, dyspnoea, cough, generalized weakness with vomiting.



Point	Anatomical Location Insertion Technique	Effect	Indication
SP6	3 Cun directly above the center of the medial tibial malleolus, on the caudal edge of the tibia, on a line between the malleolus and SP9, across from GB39.  0.4 Cun deep, perpendicular insertion.	Normalizes the SP function of transformation and transport, transforms heat as well as phlegm, calms the spirits and strengthens the blood.	Meeting point of the three yin channels of the foot. Master point of the lower abdomen and urogenital system.
SP9	On the lower edge of the medial condyle of the tibia, in a depression between the posterior edge of the tibia and the gastrocnemius muscle across from GB44.  1 Cun deep, perpendicular insertion.	Normalizes the SP function of transformation and transport, eliminates dampness, transforms and draws out phlegm and phlegm-heat, especially in the lower burner.	He-sea point, water point.  Abdominal pain, spasm, all kind of oedemas.

# Table 2. Si Ju Xin Tang decoction

(Dharmananda 2020, Marsden 2014, Penner 2020) modified with Hou po (Clemmens 2020)

Pharmaceutical Latin	Pin Yin	Actions
Rx. Ginseng	Ren Shen	Tonifies <i>Qi</i> and strengthens the Spleen and Stomach. With Bai Zhu, tonifies the transformation and transportation functions of the Spleen.  With BAi Zhu Zhi Gan Cao and Fu Ling, for Spleen and Stomach <i>Qi</i> deficiency.
(Rx. Codonopsis)	(Dang Shen)	(Tonifies the Middle Jioa and augments Qi. Substitutes for Ren Shen especially in Gu syndrome.) (With Fu Ling, for Spleen and Stomach deficiency with fatigue, a sensation of fullness in the abdomen, dizziness, lethargy, shortness of breath, anorexia and loose stools or diarrhoea. With Bai Zhu, for Spleen Qi deficiency with anorexia, loose stools and vomiting. With Fu Ling and Bai Zhu, increases the rate of natural rosette formation of lymph cells of peripheral blood vessels, Increases lymphocyte transformation rate and increases serum IgG.)

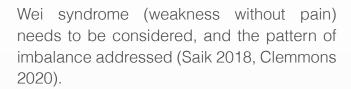


Rz. Atractylodis Macrocephalae	Bai Zhu	Strengthens the Spleen, augments Qi and dries Dampness.
Wacrocophalae		With Fu Ling and Zhi Gan Cao, for Spleen and Stomach Qi deficiency.
Poria	Fu Ling	Dries Dampness, strengthens the Spleen and moderates the drying nature of Ahi Gan Cao.
		With Ren Shen and Bai Zhu, for weak and deficient Spleen with fatigue, anorexia and loose stools.
Rx. Glycyrrhizae Preparata	Zhi Gan Cao	Harmonizes, warms and strengthens the Middle Jiao and moderates the draining properties of Fu Ling.
		With Dan Shen, for anorexia, fatigue and loose stools due to Spleen deficiency and palpitations due to Heart Qi deficiency.
		With Ren Shen, Bai Zhu and Fu ling, strengthens the Spleen and augments Qi.
Cortex Magnoliae Officinalis	Hou Po	Promotes the movement of Qi in the Middle Jiao and resolves stagnation (Resolves Food Stagnation).
		Promotes the movement of Qi downward, dries Dampness and transforms Phlegm.
		Descends Rebellious Qi, reduces Phlegm and calms wheezing.

## **Results and discussion**

Megaeosophagus is a medical condition where the oesophagus loses all tone and dilates; it cannot coordinate the movement of food into the stomach properly (Brook 2001, 2020). Megaeosophagus can be a challenging condition to manage. Treatment requires dedication and commitment and still may produce poor results. Whether it is congenital or acquired condition the conventional approach for megaeosophagus is very similar: Use of elevated feeding; placement of feeding tube; medications keep lower oesophageal sphincter opened such as silderofil; medications to stimulate smooth muscle to tighten the lower oesophageal sphincter such as metoclopramide and cisapride, medications to improve muscle tone such as bethanechol and gastroprotectives and antacids to prevent oesophageal damage by stomach juices (Brook 2001, 2020). All these modalities need to be administered on a daily basis.

Based on TCM theory, megaeosophagus is considered a Qi Deficiency, due to the inhibition of directional movement of a tubular organ. It can be also be associated with concurrent Blood or Yin Deficiency with subsequent dryness that fails to lubricate the ingesta. With acquired megaeosophagus, an exogenous (i.e. distemper virus, trauma, toxins) or endogenous (i.e. hypothyroidism, hypoadrenocorticism, myasthenia gravis) pernicious influence leading to a localized



TCM therefore offers deeper look into the root of the cause of megaeosophagus. It also offers more permanent solution in management of regurgitation without the use of conventional medications and their side-effects.

Despite of not having a definite diagnosis for the puppy's condition in this case, when managed on the conventional medicine advice she kept regurgitating/vomiting up prescribed commercial food and losing weight and energy. Once the acupuncture commenced and the dietary changes were put in place the regurgitation/vomiting rapidly decreased and stopped after three acupuncture treatments. The puppy levels of energy improved after one session of acupuncture and she started to gain weight again.

There is still thickening of the oesophagus and fluid/saliva pooling at the thoracic inlet and at this stage does not seem to be affecting the puppy's life detrimentally. Modified Si Ju Zi Tang is a TCM medicine used to replenish Qi and invigorate the function of the Spleen with modification of Hou Po to promote movement of Qi downward, dry dampness and resolve phlegm. This prescription can improve gastrointestinal function and strengthen immune function (Xiangyang 2014).

It has been documented that sympathetic ganglia overstimulation by cold laser (<15mW/cm2) to re-establish nerve communication and circulation to the area can improve the outcome of the megaeosophagus management (Saik 2018, Clemmons 2020).

In conclusion, acupuncture is a feasible option that can offer more permanent management of megaeosophagus with more permanent positive effects on the condition and fewer or none of the side effects seen with use of conventional medications. Acupuncture can offer happier life to the patient with less likelihood of developing complications by aspiration pneumonia and more peace of mind to the owner who may not need to comply with daily medications administration.

In this case there was a significant improvement in the pup's condition documented by ceasing of regurgitation, improving in body condition, tongue colour, weight gain and overall vitality.

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# **Case Report**

# "Smudgy": Herbal management of feline stomatitis

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# **Abstract**

considerable Feline stomatitis causes suffering for cats, stress for caregivers and frustration for veterinarians. Extraction of all teeth does offer relief for most cats, so long as all diseased bone is also removed, which is often not the case. However, this procedure is invasive and not affordable for many caregivers. This case study describes the use of four herbs, Agrimonia eupatoria, Arctium lappa, Smilax officinalis and Rumex crispus as part of multimodal therapy (food therapy, acupuncture and homeopathy) that offered a normal quality of life and near complete resolution for three years.

Smudgy was a timid 11 year old female spayed domestic short haired cat with a history of chronic stomatitis of the caudal oropharynx for the last three years. Her appetite, energy and pain would fluctuate, often improving temporarily with medical therapy (corticosteroids, antibiotics, analgesics). But the relief was not sustainable and she had begun to scream when opening her mouth, was reluctant to eat and losing weight. Her caregivers opted to have extraction of all teeth caudal to the canines by a boardcertified veterinary dentist six weeks prior to presentation. Biopsy indicated severe lymphocytic plasmacytic stomatitis.

# History, physical examination and diagnostics

Unfortunately, Smudgy still had severe ulcerative stomatitis when I first met her. six weeks after the dental extractions. ulceration and inflammation were restricted to the caudal commissures of the mouth and were approximately 2.0 cm<sup>2</sup> on each side. There was no gingivitis around the remaining teeth. Her appetite was excellent at the time, but she was losing weight. The rest of her physical exam was normal, including the absence of a palpable thyroid nodule. She had no coughing, sneezing, polyuria or polydypsia but she did have occasional vomiting approximately once every two weeks and had become quite restless at home. Her tongue was red, dry and small and her pulse was rapid, wiry and thin. She had a mild preference for warmer areas and there was some fur bleaching behind her ears. She was on buprenorphine as needed for analgesia. Complete blood count, chemistry and T4 were normal except for moderately increased globulins.





The severe inflammation characteristic of feline stomatitis is probably the end result of an imbalanced immune response (Stepaniuk, 2015; Plechner, 2003). But there is much debate regarding the trigger(s) of this immune response with infectious agents (a) of the underlying bone (polymicrobial bone disease) (Deforge, 2019; Deforge, 2020), (b) of the plaque biofilm (Stepaniuk, 2015) and (c) of systemic origin (particularly Bartonella spp. in cats under one year of age (Deforge, 2020) and calicivirus (Stepaniuk, 2015) most often considered the culprits. Atypical Cortisol Estrogen Imbalance Syndrome (ACEIS - which leads to deficient protective IgA for the mucous membranes) (Plechner, 2003) and oral food allergens (Rochette, 2005; McCullough, 2011) may also play a role in many cats. Regardless of the cause, inflammation is significant and often causes considerable pain and years of suffering.

## **Assessment**

Smudgy had persistent severe ulcerative stomatitis despite extraction of all teeth caudal to the canines, which wasn't surprising as only about 60% of cats with extraction of just the teeth caudal to the canines do well (Niemiec, 2018). Her chronic intermittent vomiting was probably due to inflammatory bowel disease (IBD) secondary to food allergy though early neoplasia was not ruled out as no biopsy was performed. Restlessness at home may have been due to pain and fur bleaching may have indicated Blood deficiency in Traditional Chinese Medicine (TCM).

# **Treatment plan for Smudgy**

Removal of all oral osteomyelitis, diseased bone and the remaining teeth, followed by guided bone regeneration may completely and permanently resolve stomatitis, even in cats who had full dental extractions with recurrence of stomatitis (Deforge, 2020), as may correction of ACEIS with physiologic dosing of hydrocortisone (Plechner, 2003). However, her caregivers did not want any further testing or invasive procedures so a novel protein, acupuncture and homeopathy were started at the first visit (see Appendix 3). The stomatitis was 75% improved one week later. The bilaterally inflamed areas in the caudal commissures were approximately However, the stomatitis did not improve any further - staying at this level for the next three months - with monthly acupuncture and continued novel protein and homeopathy. At this point, three months after the first visit, a herbal formula was started. Throughout this time she continued to eat well and her mouth did not appear too painful. Synthetic analgesics (buprenorphine) were relied upon for pain relief, but she did not appear to require any after the first visit. She kept losing weight though, until six weeks after the initial visit when she started to gain weight. There was no further vomiting after instituting a novel protein, but she did remain restless.

Herbal treatment goals (with corresponding herbal actions in brackets) for Smudgy were to (1) modulate her immune system (adaptogen/immune amphoteric), (2) enhance elimination of "toxins" from the body (alterative), (3) heal the oral ulcers (vulnerary), (4) decrease inflammation (anti-inflammatory), (5) decrease microbes in bone and plaque biofilm (antimicrobial), (6) improve gastrointestinal health (gastrointestinal anti-inflammatory, bitter) and nourish blood (blood tonic). (See Appendix 1)

Adaptogenic/ Immune amphoteric: Adaptogens help the body counter stress from various causes including chronic disease by bringing the endocrine and immune systems into balance (Winston & Maimes, 2007). Immune amphoterics (Winston, 2013)



(also called immune modulators) restore balance to over-functioning and underfunctioning immune systems (CIVT, 2020) and all adaptogens are immune amphoterics (Winston & Maimes, 2007) (but not all immune amphoterics are adaptogens). Because the root cause of the stomatitis is thought to be an immune imbalance, adaptogenic/immune amphoteric action is required. Burdock root's method of immune modulation may help (a) if there is an allergic component to Smudgy's stomatitis (it may suppress T helper type 2 cells (Th2), thus decreasing the inflammation from Th2-associated disorders such as allergies) (Ahmadabad et al, 2017) or (b) if there is an infectious component to her stomatitis (it may enhance the cell-mediated immune response) (Ahmadabad et al, 2017).

Historically, alterative formulas **Alterative:** were often prescribed successfully for human stomatitis (Wynn & Marsden, 2003). Alteratives are fascinating and act unlike any class of modern drug – (1) they improve absorption of nutrients (Wynn & Fougere, 2007) and (2) probably most importantly for stomatitis, they enhance the body's ability to extract "toxins" deposited in tissues, metabolize them (if necessary) and remove them from the body through the routes of elimination already in place: the liver, bowel, kidney, skin, lung and lymphatic systems via hepatic, laxative, diuretic, diaphoretic, lung tonic and lymphatic actions, respectively (Holmes, 1989; Winston, 2013; Wynn & Fougere, 2007). These toxins may be endogenous (either microbial [originating from intestinal dysbiosis] or metabolic [from liver/pancreatic/kidney insufficiency] origin) or exogenous (chemicals, metals, radiation, food allergens) (Holmes, 1989). Each alterative herb enhances multiple routes of toxin clearance from the body (Winston, Though it isn't clear what type of 2013). toxin may be involved in feline stomatitis, many of the modern etiologic theories do involve agents that could be classified as toxins (specifically the polymicrobial bone disease theory (DeForge 2019; DeForge 2020), the decreased clearance of toxins and pathogenic microorganisms due to the low mucosal IgA of ACEIS (Mantis, Rol & Corthesy, 2011; Plechner, 2003) and the involvement of food allergens (Rochette, 2005; McCullough, 2011)).

Burdock (*Arctium lappa*), yellow dock (*Rumex crispus*) and sarsaparilla (*Smilax officinalis*) are all excellent alteratives and were selected for this task: burdock primarily to draw toxins out of tissues (Holmes, 1989), sarsaparilla to take these toxins and eliminate them from the body (Holmes, 1989) and yellow dock to focus alterative action on the inflamed mucous membranes of the mouth (Ellingwood, 1919).

Burdock root is considered one of the most effective alteratives (Bone, 2003) - extracting toxins deposited in connective tissue and moving them into the circulatory system so they are free to be eliminated from the body (Holmes, 1989). While it excels at mobilizing these embedded toxins, burdock takes its time removing them from the body (Weed, 1989), primarily via the skin (diaphoretic), kidneys (mild diuretic) and bowel (mild laxative) (Bone, 2003), so the assistance of other alteratives that have faster eliminatory action is indicated to prevent an excess of toxins in circulation (Holmes, 1989).

Sarsaparilla, while not considered as strong an alterative as burdock (Weed, 1989), complements burdock's dislodging of toxins by promoting their removal via circulatory stimulation and elimination through its diaphoretic and diuretic actions (Holmes, 1989). Yellow dock's historical effectiveness for human ulcerative stomatitis due to "impure blood" (ie: microbial toxicosis) (Holmes, 1989) is said to be unsurpassed ("having no equal") (Ellingwood, 1919) - it eliminates

these toxins via its alterative actions (hepatic, cholagogue, diuretic, lymphatic and mild laxative) (Holmes, 1989; Ellingwood, 1919). As it has an affinity for inflammation of the upper gastrointestinal tract (Ellingwood, 1919), it focuses the alterative action of these herbs specifically on Smudgy's inflamed mouth.



**Vulnerary:** Agrimony's astringent action has been put to use for healing "inveterate ulcers" (Culpeper, 1653) for centuries and it is indicated for ulcers of the mouth (Wood, 2007). Its high tannin content (3-13%) (Ross, 2010) binds and precipitates proteins on the mucosal surface resulting in a temporary protective coating that (a) numbs the surface (b) decreases inflammation and (c) forms a barrier that protects against infection (Romm et al, 2010). Topical application of tannins to edentulous human mouths increases keratinization and makes the mucosa mechanically stronger (Radke et al, 2014). The astringent action on tissues may make it more difficult for bacteria to survive (Simons, 2018) and astringents have been used in human dentistry to "detoxify" gums and for plaque removal (Radke 35 al, 2014) - both actions that are likely helpful for feline stomatitis. Two of the other herbs in the formula may play a role here as well: yellow dock has astringent properties and sarsaparilla is indicated for chronic ulcers (Holmes, 1989). While burdock leaf and seed are vulnerary (the leaf is "food for old ulcers") (Culpeper, 1653), the root was used and not expected to have this action.

**Anti-inflammatory:** All four herbs provide the anti-inflammatory action much needed to quell the inflammation in Smudgy's mouth: burdock, yellow dock and agrimony (Holmes, 1989; Winn & Fougere, 2007) are traditional anti-inflammatories while sarsaparilla is an immune-regulating anti-inflammatory – a strong antioxidant that suppresses excessive immune responses (Winston, 2013).

Antimicrobial: Although all herbs selected have some antimicrobial action (burdock, agrimony, sarsaparilla, yellow dock (Weed, 1989; Wynn & Fougere, 2007; Taylor, 2005; Idris, Wintola & Afolayan, 2019) they were not chosen specifically for this action and stronger antimicrobials were not added.

**Digestive bitter:** Elimination of suspected food allergens was relied on here instead of herbs, but burdock and yellow dock are both bitter tonics and digestive stimulants - properties that are of assistance for Smudgy's chronic vomiting thought to be due to inflammatory bowel disease.

**Blood tonic:** This was achieved primarily through food (high meat diet), with assistance from the hemogenic potential of sarsaparilla and yellow dock's high iron (Holmes, 1989).

# Initiation of herbal therapy and follow-up

Three months after initial presentation, Smudgy started herbs (see Appendix 2). Her daily herbal tincture formula consisted of agrimony (*Agrimonia eupatoria* aerial parts, 0.23 ml of 1:4), burdock (*Arctium lappa* root, 0.15 ml of 1:4), sarsaparilla (*Smilax officinalis* root, 0.15 ml of 1:4) and yellow dock (*Rumex crispus* root, 0.075 ml of 1:4) divided into two doses. She did not like the tincture, would not take a higher dose and thus likely received suboptimal amounts of the herbs.



Twelve days after starting the herbs, the stomatitis was 20% improved over the last visit. This marked the first time there was any improvement since starting the acupuncture, novel protein and homeopathy three months earlier.

After another 41 days, the stomatitis was 95% resolved, with only approximately a 1-2 mm<sup>2</sup> area of non-ulcerated subtle inflammation at the caudal commissures. She had no pain opening her mouth and was eating well and no longer restless.

After nine months of herbs, chicken and venison were re-introduced into her diet and the stomatitis flared up despite herbs, acupuncture and homeopathy. Upon (a) elimination of chicken and venison and (b) increasing the herbal formula volume by 33% the stomatitis decreased by 50% at the 19 day follow-up visit and was back to baseline

(95-99% resolved) in another 21 days. The fur bleaching was no longer evident at this point. For the following three years, Smudgy's stomatitis remained 95-99% resolved but did require acupuncture, avoidance of food allergens and the herbal formula to maintain improvement. Throughout these years she ate well, was playful, did not appear painful, and seemed to be enjoying life. Sadly after three years, she developed an abdominal mass (probably intestinal) and was euthanized when her quality of life deteriorated.

## **Discussion and Reflection**

The focus of the herbal formula was on alterative action. It did give Smudgy back her life for three years, but it may have been more effective to have a stronger emphasis on immune modulation to address the underlying causes of stomatitis and perhaps to assist with prevention of neoplasia. A higher dose may also have been more effective, but this was challenging. A multimodal approach was necessary for Smudgy: although food and acupuncture helped tremendously she did need herbs to nearly resolve the stomatitis, and she required acupuncture and avoidance of food allergens to sustain this.

# **Appendices**

Appendix 1: Treatment goals, corresponding actions and herbs selected			
Treatment goals	Corresponding action	Primary herb(s) in formula for this action	Secondary herb(s) in formula for this action
balance endocrine-	adaptogen/	burdock (Hobbs,	sarsaparilla (Holmes,
immune system	immune	2014)	1989)
	amphoteric		
enhance toxin	alterative	burdock, yellow dock,	agrimony (Ross, 2010)
elimination		sarsaparilla (Bone,	
		2003; CIVT, 2020)	



Appendix 1: Treatment goals, corresponding actions and herbs selected			
Treatment goals	Corresponding action	Primary herb(s) in formula for this action	Secondary herb(s) in formula for this action
heal oral ulcer	vulnerary, astringent	agrimony (Wynn & Fougere, 2007; Culpeper; 1653)	yellow dock, sarsaparilla (Holmes, 1989)
↓ inflammation	anti-inflammatory	sarsaparilla, burdock, yellow dock, agrimony (Holmes, 1989; Wynn & Fougere, 2007; Winston, 2013)	
√microbes	anti-microbial	sarsaparilla, burdock, yellow dock, agrimony (Taylor, 2005; Idris, Wintola & Afolayan, 2019; Wynn & Fougere, 2007; Weed, 1989)	
improve GI health	anti-inflammatory	sarsaparilla, burdock, yellow dock, agrimony (Holmes, 1989; Wynn & Fougere, 2007; Winston, 2013)	
	bitter	yellow dock, burdock (I	Holmes, 1989; CIVT, 2020)
√fur bleaching	blood tonic	yellow dock, sarsaparilla (Holmes, 1989)	

Appendix 2: Prescription: herbs selected and why for 12.4lb (5.6kg) Smudgy				
Herbs selected	Primary action in formula	Additional beneficial actions for Smudgy	Smudgy dose range (ml/day)*	Dose given (ml/day) divided into 2 doses
burdock ( <i>Arctium lappa</i> ) root 1:4	alterative (Bone, 2003)	immune amphoteric, anti-inflammatory, antimicrobial, bitter (CIVT, 2020; Holmes, 1989; Hobbs, 2014; Weed, 1989)	0.25-0.6	0.15
yellow dock ( <i>Rumex crispus</i> ) root 1:4	alterative (Bone, 2003)	astringent, anti- inflammatory, antimicrobial, bitter (Holmes, 1989; Idris, Wintola & Afolayan, 2019)	0.35-0.7	0.075
sarsaparilla ( <i>Smilax officinalis</i> ) root 1:4	alterative (CIVT, 2020)	immune modulator, anti-inflammatory, antimicrobial (Holmes, 1989; Winston, 2013; Wynn & Fougere, 2007)	0.5-1.0	0.15



Appendix 2: Prescription: herbs selected and why for 12.4lb (5.6kg) Smudgy				
Herbs selected	Primary action in formula	Additional beneficial actions for Smudgy	Smudgy dose range (ml/day)*	Dose given (ml/day) divided into 2 doses
agrimony ( <i>Agrimonia</i> <i>eupatoria</i> ) aerial 1:4	vulnerary/ astringent (Wynn & Fougere, 2007; Culpeper, 1653)	alterative, anti- inflammatory, antimicrobial (Wynn & Fougere, 2007; Ross, 2010)	0.35-0.7	0.23

Total dose given: 0.6mL/day (0.3mL PO q 12 hours)

<sup>\*</sup>using 'Human Phytomedicine Dosage Chart' and 'Dosing Principles' from College of Integrative Veterinary Therapies

Appendix 3: Food, Acupuncture and Homeopathy for Smudgy		
Food	Novel protein (raw rabbit with ground bone, liver, heart, kidney and vegetables but no synthetic supplements). Novel protein was started based on the observation of frequent food allergies in cats with stomatitis and that chronic antigenic stimulation may play a role in the feline stomatitis disease process (Rochette, 2005)	
Homeopathy	Natrum muriatricum 30C daily	
Acupuncture	2 points (ST44 to clear Stomach Fire and LI4 to direct treatment to her face) were used for most sessions, although other points (HT8, LIV3) were occasionally added in later. Laser acupuncture was used (10 seconds of Nogier A" [double prime] per point).	

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## Western herb - Althaea officinalis (Marshmallow)

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Common name: Marshmallow

Family: Malvaceae

**Distribution:** Native to Europe and Asia.

Parts used: The fleshy part of the roots,

occasionally the leaves.

**Active constituents:** Mucilage, asparagines, tannins, flavonoids and phenolic acids.

Clinical actions: Demulcent, vulnerary,

diuretic and nutritive.

**Energetics:** Sweet, bitter and cool.

**Veterinary indications:** Traditionally used for 'diseases of the mucous tissues', marshmallow root has clinical application for veterinary patients with:

- Digestive complaints, especially gastroenteritis, gastric ulcers, colitis and diarrhoea
- Urinary tract inflammation, including cystitis, nephritis and urethritis
- Stomatitis, laryngitis, bronchitis and other chronic coughs
- Topically for ruptured abscesses, ulcers and open wounds

In reference to the gastrointestinal tract, demulcent herbs are used to lubricate and protect the buccal, pharyngeal, oesophageal and gastric mucous membranes by adhering to the mucosa. This may be as a preventative action or to alleviate inflammation and irritation. Demulcent herbs also have the potential to act as a prebiotic and assist in normalising the microbiome, therefore reducing epithelial inflammation.

**Cautions and contraindications:** None reported, AHPA Class 1.

**Herb-drug interactions:** Theoretical concern for reduced absorption of drugs, glucose and other soluble molecules from the gastrointestinal tract.



- Dried herb: 25-300mg/kg, divided; Infusion: 5-30g per cup of water, administered at a rate of ½ - ½ cup per 10kg, divided.
- Tincture (usually in 25-30% ethanol or glycetract): 1:2 – 1:3: 0.5-1.5mL per 10kg, divided and diluted or combined with other herbs. Ideally glycetract is used.
- Note that decocting destroys mucilage and thus cold infusion is best.

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#### Monograph

## Acupuncture point - ST 36 - Zu San Li (Hou San Li)





ST 36 Hou San Li (hindleg 3 miles)

Earth

Use: BUILDS QI AND BLOOD,
TONIFICATION OF DEFICIENT
PATIENTS, most important distal point for
GI problems; pelvic limb paralysis,
acupuncture analgesia, homeostatic effects
in endocrine disorders such as degenerative
myelopathy, metabolic disorders

Comments: The Yang Ming channels
represent the areas in the body where Yang
QI consolidates. As a major point on this
channel, ST 36 is used to generate Yang Qi
when it is lacking. From this Qi, Blood can
be manufactured. Points to use in
combination with ST 36 in the generation of
QI and Blood are LI 4 and LI 10. ST 36 also
has an important consolidating effect on the
Yang QI, allowing it to help promote the
downbearing of Qi and a resultant reduction
of hypertension.

He Sea point, Earth point, Horary point on the Stomach channel, Master point for the abdomen and the gastrointestinal tract

**Effect:** Normalizes the descending function of the Stomach, supports Spleen transformation and transportation, expels Cold, lifts Yang, supplements Qi, nourishes Yang Qi, Blood and Yin, tonifies Qi and Blood, regulates Nutritive and Defensive Qi, calms the Spirit, moves Qi in the Stomach channel, homeostatic effect on endocrine disease and metabolic disorders

Indications: Used for all gastrointestinal problems, stomach or biliary colic, vomiting, gastric ulcers, food stasis, impaired digestion, constipation, diarrhea, abdominal pain, local stifle point, pelvic limb, tibial and fibular paralysis, anorexia, lethargy, asthma, stimulates Wei Qi, fever, acupuncture analgesia

Comments: A major point of the Stomach channel, a Yang Ming channel in which Yang Qi consolidates, ST36 is used to generate Yang Qi from which Blood and Qi can be generated. Combination with LI10 (Shou San Li) on the foreleg augments this action. Additionally, by virtue of its consolidating effect on Yang Qi, it can be useful in reducing blood pressure when treating hypertension.

Because of its Qi tonifying ability, it is a useful point in disorders with weakness. In birds, its immune tonifying actions arise from the ability to regulate Nutritive and Defensive QI, strengthening the Wei Qi and immune system.

Innervation: Deep Peroneal nerve

**Location:** 3 cun distal to ST35, lateral to the distal aspect of the tibial tuberosity, in a depression approximately in the center of the cranial tibial muscle. Described in Xie as "long linear point"

**Technique:** Perpendicular insertion to a depth of about 1 cun. I usually needle this point aiming the needle longitudinally in a proximal to distal direction, which also stimulates ST37-39. I find I get better needle retention versus placing the needle perpendicularly. Described in Xie as "oblique insertion: dry needle depth 0.5-1 cun"

Moxibustion of this point can be especially useful.



Additional comments: When you use palpation, and you are looking for active or deficient points, many times you will be able to feel a depression in this area, especially in cases of Spleen deficiency. Find the tibial tuberosity, move your finger laterally to the belly of the cranial tibial muscle, and see if you can detect a dent or sensitive area in the cranial tibial muscle. If you have an excess condition, e.g. stifle inflammation, or enteritis, this area may feel swollen and/or hot, the patient may move away from you or react when you press here. It is very common to palpate a depression in the cranial tibial muscle here as many of our patients eating processed foods have a deficient Spleen Qi.

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#### Monograph

### Chinese herbal formula - San Ren Tang (Three Seeds Combination)

#### **Dr Steve Marsden**

DVM, ND, MSOM, GDVA, GDVCHM, Dipl.AC, Dipl.CH, CVA, AHG Alberta, Canada



This monograph is an excerpt from Dr Marsden's book, "Essential Guide to Chinese Herbal Formulas- Bridging Science and Tradition in Integrative Veterinary Medicine"



#### History

Three Seeds Combination is also known as San Ren Tang (Three Seeds Decoction) and was first described in the Systematic Differentiation of Warm Diseases written by Wu Ju-Tong in 1798. While the formula was developed to address acute systemic contagions in humans, it is one of the quintessential cat formulas of veterinary herbal medicine, as well as a main formula to address the ubiquitous problem of Damp Heat (i.e. **diet driven inflammation**) in small animals.

When "Damp" accumulates, it obstructs the movement of Qi, and generates Heat. Obstruction of Lung Qi movement (or circulation) leads to **coughing**; obstruction of movement in the middle of the body leads to **vomiting**; and obstruction of the lower abdomen can result in **constipation** or **disordered micturition**.

In cats, problems in all three of these areas commonly occur over time in the same patient, making the formula an exceptional feline remedy. Through its inclusion of three different seeds, San Ren Tang restores normal function in all three of these areas. Chinese medicine believes that as the normal descent of Lung Qi is restored, Damp is guided out of the body through the Kidneys and Bladder.

Dampness accumulation and Damp Heat in Chinese medicine are tantamount to diet driven inflammation in conventional medical terms, particularly at epithelial surfaces with associated smooth muscle. These inflammatory tendencies often occur in association with insulin resistance. Thus, from a western medical perspective, San Ren Tang is anti-inflammatory; regulates peristalsis; and is insulin sensitizing.

Two other formulas, **Wei Ling Tang** and **Si Miao San** also have these general effects, but to varying degrees.

**Si Miao San** is an acute acting antiinflammatory that pulls circulation away from epithelial surfaces in the process. It is insulin sensitizing, but its peristalsis regulating effects are comparatively weak. It does not directly enhance digestive efficiency and absorption.

Wei Ling Tang enhances digestion and absorption by enhancing mucosal blood flow, and epithelial blood flow in general. It is useful for actively resolving chronic smouldering inflammation of the urinary and digestive tracts, and for enhancing cutaneous perfusion to combat yeast overgrowth and mild pyoderma. Its anti-inflammatory effects are relatively mild, but it strongly regulates peristalsis to stop vomiting and small bowel diarrhea. Wei Ling Tang is an insulin sensitizer, though not as strong as Si Miao San.

San Ren Tang is intermediate between these two formulas. Like Si Miao San, It is a reasonably strong anti-inflammatory, yet like Wei Ling Tang it helps to actively resolve chronic inflammation by enhancing epithelial perfusion. Like Si Miao San, it provides only modest support for enhancing digestion and absorption, but like Wei Ling Tang, it strongly regulates and normalizes peristalsis. San Ren Tang is a strong insulin sensitizer.

Formula	Wei Ling Tang	San Ren Tang	Si Miao San
Insulin Sensitization	Mild	Strong	Strong
Anti- inflammatory	Mild	Strong	Very Strong
Peristalsis Regulation	Strong	Strong	Mild
Assimilation	Strong	Mild	Mild

Because the inflammatory processes the formula addresses are diet driven, any improvement with the use of San Ren Tang signals the need for a diet change toward something that is more insulin-sensitizing for the animal. Generally in carnivores, this means a diet that is minimally processed and not very starchy. High fat diets can also be aggravating in animals confirmed to be suffering from Damp Heat by their response to San Ren Tang.

#### **Chief Indications**

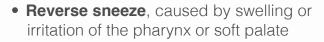
While effective in both dogs and cats, Three Seeds Combination is especially suited to feline medicine because of its mild taste and because the diseases it treats either co-exist or all figure prominently in the past medical history of feline patients.

Versions of San Ren Tang made for use in humans are not very effective in animals. Only veterinary versions made according to the originally published recipe appear sufficiently effective for animal use.

Human formulas are often over 80 percent Coix. Coix, inhibits interstitial nitric oxide synthesis as well as superoxide production and release by macrophages, making versions for human use strongly anti-inflammatory. Underrepresented in versions for human use, however, are the herbs that regulate peristalsis and smooth muscle function, making these versions of limited benefit for managing diarrhea, coughing and vomiting in animals.

Inflammatory conditions affecting all major epithelial surfaces of the body benefit from San Ren Tang, including especially the respiratory, gastrointestinal, and urinary tracts; the conjunctiva; and the skin.

**Respiratory** conditions that respond to San Ren Tang include:



- Naso-pharnygeal irritation and inflammation, including from intranasal vaccines
- Excess mucous or congestion of the sinuses, trachea and bronchi (e.g. feline asthma)

#### Cough

- o Magnolia bark is also a calcium channel blocking antispasmodic
- o Prunus is an anti-tussive
- Sinus congestion with nasal whistling or wheeze

**Gastrointestinal** conditions that respond to San Ren Tang include:

- Constipation or even mild megacolon, particularly in cats
  - Magnolia bark relieves smooth muscle spasm while the oils of Apricot seed serve as a mild intestinal lubricant
  - o For more severe constipation and megacolon, particularly in young or middle-aged animals, combine San Ren Tang with low doses of cathartics such as Cascara Combination (Natural Path Herb Company) to restore bowel movements.

#### Colitis and gastritis

- Cardamon and Coix both have anti-inflammatory effects on the intestinal tract
- o Unlike **Wei Ling Tang**, however, San Ren Tang does not increase small intestine mucosal blood flow to improve absorption. Use San Ren Tang for chronic large bowel diarrhea only

**Urinary** conditions that respond to San Ren Tang include:

#### Cystitis

- Subacute or chronic
- Prevention of recurrence
- Inhibition of crystal formation
  - San Ren Tang appears to inhibit crystal formation, not through manipulation of pH, but by reduction of urinary tract inflammation
  - The amount of proteinaceous debris that can serve as a nidus subsequently declines
- o San Ren Tang is a mildly calming formula through its content of Lophatherum, and may therefore be of benefit in the treatment and prevention of **cystitis where agitation appears to be a factor**, and symptoms otherwise agree

#### • Renal failure

- o Use in cases, such as **protein losing nephropathies** where urine protein creatinine ratios are greater than 3.5, signalling inflammation as a likely contributing factor to renal pathology
- o Coix has a clinical reputation for promoting renal filtration while reducing inflammation, making it ideally suited to such cases
- o Patients that benefit often don't respond well, or only initially, to aggressive fluid therapy
- o San Ren Tang is likely to aid those renal failure animals failing to respond to, or aggravated by, **Rehmannia Eight**
- San Ren Tang is entirely compatible with medications routinely used in renal failure, such as hypotensive drugs
- San Ren Tang to even greater effect with versions of **Minor Bupleurum** containing **Qin Jiao**

**Skin** conditions that benefit from San Ren Tang include:

- Allergic dermatitis, whether presenting as military dermatitis or a papular rash of the temporal region of cats
- Otitis externa associated with excess wax production
- Seborrhea oleosa
- Hyperesthesia

A hallmark trait of animals benefiting from San Ren Tang is **profuse conjunctival discharge** secondary to **conjunctivitis**.

#### **Diabetes**

San Ren Tang addresses Damp Heat accumulation, which is tantamount, in turn, to inflammation arising from use of low glycemic index diets, with subsequent insulin resistance. San Ren Tang owes some of its efficacy as an anti-inflammatory to its ability to **increase insulin sensitivity**, making it also of value in the treatment of **type II diabetes mellitus**. Coix markedly increases insulin sensitivity and has thus been shown to reduce adipose tissue weight, leptin, and insulin levels in Metabolic Syndrome.

When used in tandem with a low carbohydrate and minimally processed diet, San Ren Tang **routinely restores euglycemia** in cats, although it may also provide this benefit to animals maintained on low carbohydrate high protein kibble. Eventually San Ren Tang can also be discontinued, yet the patient will remain euglycemic, as long as dietary improvements are maintained.

San Ren Tang works so rapidly in these animals that within a week of initiating therapy, any animal also receiving insulin should have its blood glucose checked routinely at the time of anticipated nadir, in order to avoid hypoglycaemia. The formula itself never causes hypoglycaemia, but instead corrects the diabetic tendency, making insulin administration in type II patients rapidly unnecessary.

Insulin doses should be adjusted downward as needed. Failure to do so may result in overswings, resulting in apparent hyperglycemia being noted prior to injections. Within two to eight weeks, insulin will have to be discontinued in many patients.



#### **Lumbosacral Disc Disease**

San Ren Tang has a surprising ability to address disc prolapse at or near the lumbo-sacral junction. The **pain is not as pronounced** as the animal's **ataxia** and **paralysis**. They almost invariably have urinary symptoms, such as **abnormal micturition, retained urine,** and an **overflow bladder**. They may also have **urinary tract infections** or **urolithiasis**, often not previously recognized, but **concurrent with the disc prolapse**. Coix likely assists in the anti-inflammatory effects on nervous tissue and is a major component of a formula used in Japan for the treatment of **neuritis**.

#### Formula Design

Three Seeds Combination benefits from strong synergies amongst its constituent herbs:

Xing Ren	Apricot seed	
Yi Yi Ren	Coix seed	
Hua Shi	Talc	
Ban Xia	Pinellia rhizome	
Bai Dou Kou	Round Cardamon	
Dan Zhu Ye	Lopatherum	
Hou Po	Magnolia bark	
Tong Cao	Rice Paper pith	

As the name suggests, the formula contains three seeds, each of which unblocks the descent of Qi in a different burner, or stratum, of the body. Apricot descends Lung Qi out of the upper burner (body), relieving coughing. Cardamon descends Stomach Qi in the middle burner (body) to relieve vomiting. Restoration of the descent of Lung Qi propels Dampness before it, which Coix then guides to the Kidneys and Bladder in the lower burner (body).

Each of these three seeds assists one of the others, creating a synergistic action within the formula. Apricot relieves constipation in the lower burner. Coix supports Cardamon in reducing Dampness formation in the middle burner. Cardamon helps to open the chest and normalize Lung Qi movement in the upper burner. Coix also has an additional role in the lower burner, relieving diarrhea and particularly colitis.

Coix and Cardamon also interact another way. Strongly aromatic Cardamon develops and recruits the Wind Damp expelling effects of Coix to address invasions of the Tai Yang (dorsum), characterized by body aches and even paresis.

The other herbs also facilitate the downward movement of Qi and fluids. Pinellia echoes and amplifies the descending actions of all three seeds, by helping to quell coughing and vomiting while propelling Dampness to the Kidneys. Magnolia relieves bloat, constipation and inappetence by mobilizing Qi that has become stagnant from obstructing Dampness in the abdomen. Rice Paper, Lopatherum and Talc further promote the elimination of Damp by the Kidneys and Bladder while providing a gentle cooling effect. Rice Paper also helps guide Lung Qi downward.

#### **Supporting Symptoms**

The ability of the formula to address Damp Heat is reminiscent of **Four Materials**  **Powder (Si Miao San)**, but Three Seeds Combination is designed for patients where the Heat signs are not strongly developed and often restricted to:

- Itch
- Mild agitation
- Hematuria
- Mild fever or heat intolerance
- Colitis

Dampness signs and their sequelae predominate instead and include:

- Loud purr, sometimes associated with exaggerated swallowing
- Greasy coats
- Moist or productive coughs
- Snoring and reverse sneezing
- Profuse eye discharges
- Chronic vomiting of slimy material
- Dysuria
- Crystalluria
- Inappetence
- Abdominal distention
- Constipation

Many of these signs are present simultaneously.

**The tongue** is usually lavender, wet and swollen, although it can be a mild red color.

The pulse is usually toned.

#### **Cautions and Contraindications**

San Ren Tang is a generally safe formula when used appropriately and has no particular contraindications.

It can aggravate Yin deficiency patients with its drying qualities.

San Ren Tang is used in both dogs and cats.

#### **Research updates**

#### **Abstracts**

### Fecal microbiome in healthy dogs impacted by Metronidazole for four weeks

Pilla R, Gaschen F P, Barr J W, Olson E, Honneffer J, Guard B C, Blake A B, Villanueva D, Khattab M R, AlShawaqfeh M K, Lidbury J A, Steiner J M, Suchodolski J S, 'Effects of metronidazole on the fecal microbiome and metabolome in healthy dogs', 2020 Aug, *J Vet Intern Med.* 2020; 1–14.

#### **Abstract**

**Background:** Metronidazole has a substantial impact on the gut microbiome. However, the recovery of the microbiome after discontinuation of administration, and the metabolic consequences of such alterations have not been investigated to date.

**Objectives:** To describe the impact of 14-day metronidazole administration, alone or in combination with a hydrolyzed protein diet, on fecal microbiome, metabolome, bile acids (BAs), and lactate production, and on serum metabolome in healthy dogs.

**Animals:** Twenty-four healthy pet dogs.

Methods: Prospective, nonrandomized controlled study. Dogs fed various commercial diets were divided in three groups: control group (no intervention, G1); group receiving hydrolyzed protein diet, followed by metronidazole administration (G2); and group receiving metronidazole only (G3). Microbiome composition was evaluated with sequencing of 16S rRNA genes and quantitative polymerase chain reaction (qPCR)-based dysbiosis index. Untargeted metabolomics analysis of fecal

and serum samples were performed, followed by targeted assays for fecal BAs and lactate.

**Results:** No changes were observed in G1, or G2 during diet change. Metronidazole significantly changed microbiome composition in G2 and G3, including decreases in richness (P < .001) and in key bacteria such as Fusobacteria (q < 0.001) that did not fully resolve four weeks after metronidazole discontinuation. Fecal dysbiosis index was significantly increased (P < .001). Those changes were accompanied by increased fecal total lactate (P < .001), and decreased secondary BAs deoxycholic acid and lithocholic acid (P < .001).

**Conclusion and Clinical Importance:** Our results indicate a minimum four-week effect of metronidazole on fecal microbiome and metabolome, supporting a cautious approach to prescription of metronidazole in dogs.

CIVT members can log in to the CIVT website <u>HERE</u> to read the full paper in the Latest News section.

## Raw food may positively impact atopic dermatitis in dogs

Anturaniemi J, Zaldívar-López S, Savelkoul H F J, Elo K, Hielm-Björkman A, 'The Effect of Atopic Dermatitis and Diet on the Skin Transcriptome in Staffordshire Bull Terriers', *Front Vet Sci.* 2020 Oct; 7:552251

#### **Abstract**

Canine atopic dermatitis (CAD) has a hereditary basis that is modified by interactions with the environment, including



diet. Differentially expressed genes in non-lesional skin, determined by RNA sequencing before and after a dietary intervention, were compared between dogs with naturally occurring CAD (n = 4) and healthy dogs (n = 4). The dogs were fed either a common commercial heat-processed high carbohydrate food (kibble diet) (n = 4), or a non-processed high fat food (raw meat-based diet) (n = 4).

At the end of the diet intervention, 149 differentially expressed transcripts were found between the atopic and healthy dogs. The main canonical pathways altered by the dysregulation of these genes were angiopoietin signaling, epidermal growth factor signaling, activation of angiogenesis, and alterations in keratinocyte proliferation and lipid metabolism. On the other hand, 33 differently expressed transcripts were found between the two diet groups, of which eight encode genes that are annotated in the current version of the dog genome: immunoglobulin heavy constant mu (IGHM), immunoglobulin lambda-like polypeptide 5 (IGLL5), B-cell antigen receptor complexassociated protein beta chain (CD79B), polymeric immunoglobulin receptor (PIGR), cystathionine β-synthase (CBS), argininosuccinate synthase (ASS1), secretory leukocyte peptidase inhibitor (SLPI), and mitochondrial ribosome recycling factor (MRRF). All genes were upregulated in the raw diet group.

In conclusion the findings of this study suggest alterations in lipid and keratinocyte metabolism as well as angiogenesis in the skin of atopic dogs. Additionally, a possible enhancement of innate immunity and decrease in oxidative stress was seen in raw food fed dogs, which could have an important role in preventing hypersensitivities and disturbed immunity at a young age. CIVT members can log in to the CIVT website HERE to read the full paper in the Latest News section.

## Medium-chain triglycerides improve cognitive abilities in epileptic dogs

Berk B A, Packer R M A, Law T H, Wessmann A, Bathen-Nöthen A, Jokinen T S, Knebel A, Tipold A, Pelligand L, Volk H A, 'Medium-chain triglycerides dietary supplement improves cognitive abilities in canine epilepsy', *Epilepsy Behav.* 2020 Nov; 107608

#### Abstract

**Objective:** Cognitive impairments (CI) have recently been identified in canine epilepsy patients. A medium-chain triglyceride (MCT) enriched diet has been demonstrated to improve cognition in aged dogs and seizure control in canine epilepsy. This study evaluates the short-term effects of MCT-oil consumption on cognitive abilities in dogs with epilepsy, a naturally occurring animal model.

Methods: A six month multicenter, prospective, randomized, double-blinded, controlled crossover diet trial was conducted comparing dietary supplementation (DS) of MCT oil to a control oil. Allocation to dietary oil supplements, consisting of 9% total caloric intake, was block-randomized and supplemented into each dogs' diet for three months followed by a respective switch of DS-oil for a further three months. Non-invasive cognitive tests and a validated psychometric tool were utilized to evaluate cognitive function and perturbations associated with dietary intervention.

**Results:** 29 dogs completed the trial, of which 18 completed non-invasive cognitive testing. Spatial-working memory (P = 0.008), problem-solving ability (P = 0.048), and owner-reported trainability (P = 0.041) were significantly improved during MCT-oil supplementation compared to control-DS.

**Significance:** MCT-oil DS improves cognition in dogs with epilepsy when compared to a control-DS. MCT supplementation may represent a promising option to address CI associated with epilepsy.



CIVT members can log in to the CIVT website <u>HERE</u> to read the full paper in the Latest News section.

## Nutritional management of chronic enteropathy in dogs and cats

Kathrani A, 'Dietary and nutritional approaches to the management of chronic enteropathy in dogs and cats', *Vet Clin North Am Small Anim Pract.* 2021 Jan; 51(1):123-136.

#### **Abstract**

Nutrition can influence those functions of the gastrointestinal tract that can be adversely affected in chronic enteropathy, such as microbiota, mucosal immune system, intestinal permeability, and motility. Diet serves as a possible risk factor in disease pathogenesis and as a target for treatment in chronic enteropathy. Malnutrition is prevalent in people with inflammatory bowel disease and negatively affects outcome. Approximately two-thirds of dogs with protein-losing enteropathy due to chronic enteropathy or lymphangiectasia are underweight. Commercial diets and homeprepared diets have been used successfully in the management of chronic enteropathy. Fat restriction is the main dietary strategy for intestinal lymphangiectasia.

The full paper will be published in January 2021, keep an eye out for an update in the CIVT newsletter.

## Higher prevalence of dogs with both hypoadrenocorticism and chronic gastrointestinal disease

Hauck C, Silke S, Schmitz SS, Iwan A, Burgener IA, Wehner A, Neiger R, Kohn B, Rieker T, Reese S, Unterer S, 'Prevalence and characterization of hypoadrenocorticism in dogs with signs of chronic gastrointestinal disease: A multicenter study', *J Vet Intern Med.* 2020 July; 34:1399–1405.

#### **Abstract**

**Background:** Dogs with hypoadrenocorticism (HA) frequently show signs of gastrointestinal disease (SGD). The prevalence of dogs presented for chronic SGD with HA is unknown.

**Objectives:** The aims of this study were to determine the prevalence of HA in dogs with chronic SGD and to identify clinical and laboratory variables for HA in this population.

**Animals:** One hundred fifty-one dogs with chronic SGD.

Methods: In this multicentered prevalence study a standardized workup was performed in prospectively enrolled dogs with SGD > 3 weeks duration. Basal serum cortisol concentration was measured in every dog with ACTH stimulation test (ACTHST) if basal serum cortisol concentration was <3 μg/dL.

**Results:** Basal serum cortisol concentration was <3  $\mu$ g/dL in 80/151 (53%) dogs, <2  $\mu$ g/dL in 42/151 (28%) dogs, and < 1  $\mu$ g/dL in 9/151 (6%) dogs. In 6/151 dogs HA was diagnosed based on ACTHST (stimulated serum cortisol concentration < 2  $\mu$ g/ dL), a prevalence of 4%. There was no difference in history, physical examination, and laboratory variables between dogs with HA and those with other causes of chronic SGD. In 4/6 dogs with HA, there was melena or hematochezia indicating gastrointestinal blood loss. Hyperkalemia, hyponatremia, or both was not observed in any dog.

Conclusion and Clinical Importance: The prevalence of HA among dogs with chronic SGD is higher than in the general population. Based on these results, testing adrenal function should be performed as a standard screening test in dogs with chronic SGD to differentiate between HA and chronic enteropathies.

CIVT members can log in to the CIVT website HERE to read the full paper in the Latest News section.



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