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JIVT: An introduction

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Wound Healing Properties of Calendula Officinalis and its Application in Veterinary Medicine: A Review of Recent Literature

Nagisa Hiraoka, BVSc

Introduction
Calendula officinalis, also known as marigold, is an herb recognised for its anti-inflammatory and vulnerary qualities (British Pharmacopoeia 1996). Indigenous to Eastern Europe and the Mediterranean, C. officinalis has been a respected herb since ancient times and was popular in Ancient Greece and in early Indian and Arabic cultures for its medicinal qualities (Braun and Cohen 2005). C. officinalis flowers are used primarily, although the stems, younger leaves, seeds and roots are also thought to have medicinal properties (Bone 2003, Braun and Cohen 2005, Wynn and Fougere 2007).

A wound is defined as trauma to any of the tissues of the body, especially when caused by physical means and with interruption of continuity (Stedman 2000). Acute wounds heal in a very orderly and efficient manner characterised by four distinct but overlapping phases: haemostasis, inflammation, proliferation and remodelling (Diegelmann and Evans 2004). In pathologic conditions, this efficient and orderly process is lost and the tissues are locked into a state of chronic inflammation and healing can only proceed once inflammation is controlled (Diegelmann and Evans 2004).

Recent studies have evaluated the effect of C. officinalis on wound-healing activity and there is growing evidence of its positive effects on the inflammatory and proliferative phases of the process. This paper reviews the last five years’ scientific research conducted on the wound-healing effects of C. officinalis. Research on the anti-inflammatory effects of C. officinalis has been included in this review in light of the overlapping nature of wound healing and anti-inflammatory processes of the body. While the majority of studies performed on C. officinalis are aimed at human patients, many in vivo experiments are performed on animal models. This allows data to be extrapolated to veterinary patients with relative ease and relevance. The review aims to critically evaluate recent scientific literature to determine whether C. officinalis can be effectively and safely used for medical treatment in veterinary patients. An evidence table is provided to summarise clinically relevant components of each study evaluated in this paper (see Table 1).

Wound Healing Activity of C. Officinalis

C. Officinalis and Angiogenesis
As cells and tissues are inherently dependent on the vasculature to supply nutrients and oxygen in exchange for metabolites, formation of new blood vessels is critical for normal wound healing (Demidova-Rice, Durham and Herman 2012). The process of angiogenesis usually occurs in the proliferative phase of wound healing after the inflammatory phase has ended (Diegelmann and Evans 2004).

A recent randomised, controlled trial on rats found that C. officinalis significantly improved angiogenic activity in wound healing. Parente et al (2011) evaluated the wound healing activity of Brazilian grown C. officinalis ethanolic extract by inducing cutaneous wounds in 12 rats. They were randomly divided into two groups: topical treatment with C. officinalis (1% ethanol extract) or control (distilled water) for seven days. Skin samples of the cutaneous wounds were collected. Histological assessment revealed a statistically significant increase in the number of blood vessels in rats treated with C. officinalis compared to the control group. Although pro-angiogenic factors such as vascular
endothelial growth factor (VEGF) are thought to be involved in post-injury angiogenesis (Demidova-Rice, Durham and Herman 2012), the expression of VEGF in the cutaneous wound sections of this study was insignificant. The authors suggest angiogenesis induced by C. officinalis may be associated with other pro-angiogenic factors.

In the same study, Parente et al also examined the angiogenic activity of C. officinalis in the chorioallantoic membrane (CAM) of 90 embryoated eggs. Histological analysis of the CAMs 48 hours after treatment with C. officinalis extract, C. officinalis dichloromethane fraction and C. officinalis hexamin fraction revealed a statistically significant increase in vessel numbers in all eggs treated with C. officinalis (extract and fractions) when compared to the solvent control. Interestingly, when inflammatory activity was histologically assessed, only a discrete number of inflammatory cells were present in the CAMs of all treatment groups. Although C. officinalis is known to have anti-inflammatory properties, the authors conclude the angiogenic activity of C. officinalis is not related to inflammatory activity.

The combined findings in the study by Parente et al (2011) suggests that C. officinalis may have a direct influence on wound healing via increased angiogenic activity in cutaneous wounds. Although inflammation was not considered to be related to angiogenic activity, this factor was evaluated only once in CAM samples collected at the time of evaluation for angiogenesis. It is possible that the inflammatory phase of wound healing had subsided considerably by the time samples were collected.

A 2012 study by Parente et al evaluated the effect of C. officinalis on 36 rats on days 4, 7, and 14 following skin-wound induction. The aim of the study was to evaluate the effect of C. officinalis on the inflammatory phase and the proliferative phase of the healing process. The rats were randomly divided into two groups: treatment animals were treated with C. officinalis extract solution and control animals were treated with distilled water. Samples of cutaneous wounds were collected for histological and immunohistochemical analysis. Although complete healing was evident in both groups by day 14, microscopic evaluation of treated animals on days 4 and 7 showed a significant decrease in fibrin and hyperaemia compared to the control group, reflecting the anti-inflammatory effects of C. officinalis extract. Furthermore, immunohistochemical analysis on wound samples on days 4 and 7 showed a significant increase in collagen in the group treated with C. officinalis compared to the control group. This indicates a positive role of the extract on both the inflammatory and proliferative phases of cutaneous wound healing in rats. Although the authors state this study was a randomised controlled trial, additional evaluation in a double-blind placebo controlled trial is necessary to prevent the introduction of bias before a firm conclusion can be reached.

C. Officinalis and Collagen

The role played by collagen in wound healing is well recognised. When tissues are disrupted following injury, collagen is needed to repair the defect and restore anatomic structure and function (Diegelmann and Evans 2004). Recently conducted studies have evaluated the effects of C. officinalis on collagen content of experimentally injured skin in rats. Chandran and Kuttan (2008) evaluated the effect of C. officinalis flower extract against thermal burns in rats. It was found that oral administration of C. officinalis (at 20mg/kg, 100mg/kg and 200mg/kg) significantly increased hydroxyproline and hexosamine content in the granulation tissue of burned rats, showing the effectiveness of the extract in enhancing collagen content in thermally injured tissue. The authors postulate this could be due to increased synthesis or decreased catabolism of collagen due to flavonoids in C. officinalis which can produce artificial cross linkages between collagen molecules. While the study’s findings lend support to the use of C. officinalis flower extract to promote wound healing, the authors do not indicate whether the trial was randomised or blinded. Due to these methodological limitations, a firm conclusion cannot be reached using this study alone.

More recently, a randomised controlled trial was performed by Naeini et al (2012) to evaluate the effect of C. officinalis on collagen content in skin wounds of rats. It was found that topical application of 7% C. officinalis gel produced a statistically significant increase in collagen production compared to control and placebo groups. Interestingly, 5% and 10% C. officinalis gel seemed to be less effective. While the reason for this remains unknown, the authors of this study postulate that low concentrations of C. officinalis gel have no effect.
and that high concentrations may have cytotoxic effects. Although rats were randomised in this study, the author does not mention whether it was blinded. Therefore methodological limitations exist in this study.

Studies conducted by Chandran and Kuttan (2008) and Naeini et al (2012) support the use of C. officinalis for its wound healing properties. While Chandran and Kuttan (2008) observed improved wound healing in all treatment groups administered C. officinalis extract orally (at 20mg/kg, 100mg/kg and 200mg/kg), it is interesting to note that Naeini et al (2012) observed improvement only in rats treated topically with 7% C. officinalis gel. Further insight on the possible cytotoxic effects of C. officinalis may be provided by assessing the effects of the gel preparation used by Naeini et al (2012) on the experimental model of thermal injury in rats used in the study by Chandran and Kuttan (2008). Alternatively, the efficacy of C. officinalis extract may be better evaluated through administration of oral preparations (20mg/kg, 100mg/kg, 200mg/kg) as prepared by Chandran and Kuttan (2008) to the animal models used in the study by Naeini et al (2012).

Although there has been some suggestion of the anti-tumour cytotoxic effects of C. officinalis in mice (Jimenez-Medina et al 2006), the results were not stated to be statistically significant and therefore this effect of C. officinalis remains inconclusive. However, the anti-metastatic effect of C. officinalis was explored by Preethi et al (2009) and showed interesting results. Mice injected with melanoma cells were divided into three groups; Group 1 received no treatment, Groups 2 and 3 were injected with melanoma cells, with Group 3 animals being administered 250mg/kg C. officinalis extract orally for ten consecutive days. Preethi et al (2009) conclude that administration of C. officinalis flower extract significantly inhibited lung tumour colonies and increased the lifespan of tumour-bearing animals. However, the study reveals some conflicting results. In contrast to a previous study that found C. officinalis extract to increase collagen production in experimental thermal burns (Preethi et al 2008), this study found C. officinalis reduced collagen synthesis in tumour-bearing mice thereby reducing lung fibrosis. Difference in the oral dosage of C. officinalis extract was 200mg/kg and 250mg/kg, respectively. Further research is warranted before any conclusions can be reached. The effect of C. officinalis on VEGF was also conflicting – C. officinalis extract decreased the level of serum VEGF in tumour bearing mice, while a more recent study by Parente et al (2011) found levels of VEGF to be insignificant when C. officinalis was applied topically on cutaneous wounds.

Anti-inflammatory Activity of C. Officinalis

In the British Herbal Pharmacopoeia (1996), the first listed action of Calendula is anti-inflammatory. As outlined earlier, inflammation is one of the four distinct phases of wound healing and healing can proceed only after inflammation is controlled (Diegelmann and Evans 2004). Several recent studies have focused on the effect of C. officinalis on experimentally induced inflammatory conditions in animal models which provide some insight on the therapeutic potential of C. officinalis in veterinary medicine.

Experimentally Induced Paw Oedema

Preethi et al (2009) evaluated the anti-inflammatory activity of C. officinalis flower extract in acute and chronic models of inflammation in mice. Carrageenan or dextran injection was used to induce acute paw oedema and formalin injection was used to induce chronic paw oedema in a total of 72 mice. Within the carrageenan, dextran and formalin groups, there was a control group, positive control group and groups given oral administration of either 250mg/kg or 500mg/kg C. officinalis extract. To assess the effect of oral C. officinalis, the thickness of the paw was measured before and after induction of paw oedema, hourly for six hours in carrageenan and dextran groups and daily for six days in the formalin group. It was shown that treatment with C. officinalis extract significantly reduced paw oedema induced by carrageenan, dextran and formalin, that is, in both acute and chronic inflammation models. Although carrageenan, dextran and formalin are thought to induce inflammation through different mechanisms, C. officinalis extract showed anti-inflammatory activity irrespective of the induction agent used.

Although this study provides some evidence of anti-inflammatory activity of C. officinalis, the authors did not indicate whether animals were randomly assigned to groups or whether this study was blinded, thus allowing for the possible introduction of bias. Additional evaluation in a double-
blind placebo controlled trial is necessary before a firm conclusion can be reached with regards to the systemic use of C. officinalis to treat acute and chronic inflammatory conditions in veterinary patients.

**Experimentally Induced Oral Mucositis**

Mucositis is a possible side effect of veterinary radiotherapy and symptoms of oral mucositis can begin as early as the second week of radiotherapy (Collen and Mayer 2008). Management involves a range of interventions such as diet, local anaesthetics and analgesics (Collen and Mayer 2008). While the most severe cases of mucositis typically heal within two to four weeks following completion of therapy, it is likely veterinary patients experience considerable discomfort when mucositis develops. A randomised controlled clinical study on the effects of C. officinalis flower extract on radiation-induced oropharyngeal mucositis was performed recently on human patients and showed encouraging results (Babaee et al 2013). There was a statistically significant decrease in oral mucositis scores in patients treated with C. officinalis compared to placebo. Furthermore, of the 40 human patients randomly assigned to C. officinalis extract mouthwash or placebo, three patients treated with C. officinalis did not demonstrate oral mucositis after radiotherapy in the seven-week treatment period.

Although human patients were evaluated in this study, there has been evidence of the beneficial effects of topical C. officinalis on oral mucositis in experimental animal models. Tanideh et al (2013) assessed the topical application of C. officinalis extract on the healing activity of oral mucositis induced by 5-fluorouracil (5-FU) in hamsters. Sixty hamsters were randomly divided into four groups, to receive either no treatment, gel base only, or 5% or 10% C. officinalis gel. Following induction of mucositis by the intraperitoneal administration of 5-FU on days 0, 5 and 10, the cheek pouch mucosa in each hamster was irritated by superficial scratching with the tip of a sterile needle. Once maximum severity of oral mucositis was observed, treatment was initiated with the topical application of C. officinalis gel once daily. Over the course of five days, there was a statistically significant improvement in macroscopic and microscopic oral mucositis scores in both 5% and 10% C. officinalis gel groups. Weight gain in these groups was also statistically significant. The authors conclude that daily application of C. officinalis extract in gel form can significantly reduce oral mucositis induced by 5-FU in mucosa cheek pouches of hamsters.

The findings by Tanideh et al (2013) support the potential use of C. officinalis extract in treating radiation-induced oral mucositis in veterinary patients. However, the results of this study are in disagreement with those found by Naeini et al (2012). Although Naeini et al (2012) focused on cutaneous lesions and Tanideh et al (2013) focused on mucosal lesions and although the inciting cause of the lesions differed greatly, it is interesting to note that 5% and 10% gel preparations had a significant effect in mucosal healing in the study by Tanideh et al (2013) whereas 5% and 10% gel had minimal effect on cutaneous healing in the study by Naeini et al (2012). The different results observed in the two studies reflect the importance of standardising treatments in order to provide reliable data of therapeutic intervention. The difference in extract preparation and gel base in these two studies may explain the conflicting results.

**Experimentally Induced Ulcerative Colitis in Dogs**

One of the traditional uses of C. officinalis is for the treatment of gastrointestinal ulcers (Wynn and Fougere 2007). A study by Mehrabani et al (2011) investigated the effect of C. officinalis extract in the treatment of experimentally induced ulcerative colitis in dogs. Ulcerative colitis was induced with a 6% acetic acid enema in ten German Shepherds dogs. Once ulcerative colitis was macroscopically and microscopically confirmed, the dogs were randomly divided into two groups: Group A received C. officinalis extract (40% solution, 3mL/day for 30 days) via enema and Group B received a saline enema (3mL/day). Although the authors report statistically significant mucosal healing after 30 and 45 days of treatment with C. officinalis, the results from the placebo group are not included in the report. Comparison to placebo would have provided a clearer view of the effects of C. officinalis. Therefore, the effects of C. officinalis on ulcerative colitis in dogs cannot be extrapolated from this study due to the limitations of study design (lack of appropriate placebo and blinding, lack of information on C. officinalis preparation used). Further research is warranted before a firm conclusion can be reached.
<table>
<thead>
<tr>
<th>Condition</th>
<th>Study Design</th>
<th>Author/Year</th>
<th>Number of Subjects</th>
<th>Statistically Significant</th>
<th>Route of Administration</th>
<th>Extract Preparation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cutaneous Wounds</td>
<td>RCT, nonblind</td>
<td>Naeini et al 2012</td>
<td>65 Rats</td>
<td>Yes</td>
<td>Topical, 5%, 7% and 10% gel</td>
<td>Fresh flowers extracted with ethanol 70% by masturation Gel base: carbopol and sodium hydroxide</td>
</tr>
<tr>
<td>Cutaneous Wounds</td>
<td>RCT, blind</td>
<td>Parente et al 2011</td>
<td>90 embryonated eggs</td>
<td>Yes</td>
<td>Topical, 1% aqueous solution</td>
<td>Dry flowers extracted with ethanol 70% by masturation; diluted to 1% for topical application</td>
</tr>
<tr>
<td>Cutaneous Wounds</td>
<td>RCT, blind</td>
<td>Parente et al 2012</td>
<td>36 rats</td>
<td>Yes</td>
<td>Topical, 1% aqueous solution</td>
<td>Dry flowers extracted with ethanol 70% by masturation; diluted to 1% for topical application</td>
</tr>
<tr>
<td>Thermal burn</td>
<td>Non-randomised, nonblind</td>
<td>Chandran and Kuttan 2008</td>
<td>54 rats</td>
<td>Yes</td>
<td>Oral 20mg/kg 100mg/kg 200mg/kg</td>
<td>Fresh flowers extracted with ethanol by masturation</td>
</tr>
<tr>
<td>Anti-metastasis</td>
<td>Non-randomised, nonblind</td>
<td>Preethi et al 2010</td>
<td>36 mice</td>
<td>Yes</td>
<td>Oral 250mg/kg</td>
<td>Fresh flowers extracted with ethanol by masturation</td>
</tr>
<tr>
<td>Oedema (inflammation)</td>
<td>Non-randomised, nonblind</td>
<td>Preethi et al 2009</td>
<td>72 mice</td>
<td>Yes</td>
<td>Oral 250mg/kg 500mg/kg</td>
<td>Fresh flowers extracted with ethanol by masturation</td>
</tr>
<tr>
<td>Oral Mucositis</td>
<td>RCT, blind</td>
<td>Tanideh et al (2013)</td>
<td>60 hamsters</td>
<td>Yes</td>
<td>Topical, 5% and 10% gel</td>
<td>Dry and powdered flowers extracted with ethanol 80% Gel base: sodium carboxymethyl cellulose, glycerol</td>
</tr>
<tr>
<td>Ulcerative Colitis</td>
<td>RCT, nonblind</td>
<td>Mehrabani et al 2011</td>
<td>10 dogs</td>
<td>No</td>
<td>Enema, 3mL/day</td>
<td>40% C. officinalis solution (no further details)</td>
</tr>
</tbody>
</table>
Conclusion
Studies on the effects of C. officinalis in experimental animal models may provide useful insights into the therapeutic properties of this medicinal herb on veterinary patients. Recent studies indicate that angiogenesis and collagen synthesis may play an important role in the wound-healing activity of C. officinalis. Angiogenesis and collagen deposition play a vital part in the proliferative phase of wound healing. These properties, in conjunction with potential anti-inflammatory properties, suggest C. officinalis has multiple beneficial actions on wound-healing activity. Thus, C. officinalis may be useful in clinical cases where promotion of wound healing is necessary.

Traumatic wounds, thermal injury and radiotherapy-induced oral mucositis may be some conditions in which C. officinalis extract is indicated in veterinary patients. However, clinical studies reviewed in this paper have varied greatly in quality with many limited by lack of standardisation of preparations and variability in dosing regimes. While wound healing activity was supported by the majority of authors, one author suggested C. officinalis may have cytotoxic effects. Furthermore, one recent study described anti-metastatic effects of C. officinalis and provided some contradictory evidence on its effects on collagen synthesis and VEGF. Further studies using standardised preparations and predetermined dosing regimes are warranted to clarify contradictory findings.

In conclusion, there is growing evidence for the use of C. officinalis flower extracts for their therapeutic properties. Although exact mechanisms of action are still unclear, the available evidence on the wound healing and anti-inflammatory actions of C. officinalis appear promising. Ongoing research and well-conducted clinical trials are warranted to further demonstrate efficacy and safety of this herb.

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Case Report
Minnie – Chronic Active Hepatitis and Diabetes Mellitus
Kathleen Boehme, DVM

Abstract
A senior canine with a diagnosis of chronic active hepatitis and diabetes mellitus, presented for alternative treatment due to the side effects and poor resolution of her condition on conventional medication. This case was successfully treated for the presenting concerns with a series of Chinese herbal formulas and dietary modification.

Signalment
Minnie is a 14.5 year old, 23 pound (~10kg), female spayed Bichon Frise.

Diagnosis
Minnie was diagnosed with chronic active hepatitis (CAH) via laparoscopic liver biopsy on 5/19/11. She was initially started on prednisone 10mg bid, azothiaprine 25mg bid and ursodeoxycholic acid 250mg sid. She developed diabetes mellitus and steroid hepatopathy as sequelae to corticosteroid use. Her medications were switched to budesonide (another corticosteroid) and cyclosporine in an effort to control the CAH yet minimize side effects to medication. In spite of this, she continued losing weight and muscle mass, was lethargic and had developed chronically loose stools and progressing anorexia. Her owners were looking for an alternative treatment as they felt the medication was making her much worse.

Minnie’s previous issues included: epilepsy treated with K+ bromide years earlier, two episodes of back pain responsive to short courses of prednisone and mild chronic kidney changes documented on her ultrasound of 4/25/11. She ate Z/D, a dry kibbled, hydrolyzed diet. Flagyl 125mg bid was added and her diet was changed to canned W/D for the chronic loose stools and showed partial improvement. Minnie continued to do poorly so the budesonide was discontinued. At this point, her energy started to come back slightly. The dates medications were changed are noted under Table 1.

Table 1. Laboratory values prior to the integrative appointment

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>ALP (5-131)</td>
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<td>419</td>
<td>1387</td>
<td>1364</td>
<td>2185</td>
<td>1662</td>
<td>585</td>
<td>204</td>
<td>220</td>
</tr>
<tr>
<td>ALT (12-118)</td>
<td>447</td>
<td>728</td>
<td>400</td>
<td>337</td>
<td>570</td>
<td>579</td>
<td>370</td>
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<td>71</td>
</tr>
<tr>
<td>Glucose (70-138)</td>
<td>91</td>
<td>105</td>
<td>128</td>
<td>201</td>
<td>645</td>
<td>283</td>
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<td>BUN (6-31)</td>
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<td>21</td>
<td>28</td>
<td>15</td>
<td>20</td>
<td>19</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td>HCT (36-60)</td>
<td>55%</td>
<td>40%</td>
<td>31%</td>
<td>40%</td>
<td>48%</td>
<td>47%</td>
<td>47%</td>
<td>49%</td>
<td></td>
</tr>
</tbody>
</table>
1. Flagyl, amoxicillin, denamarin added 4/25/11 after ultrasound

2. Prednisone and azothiaprime added 6/7/11 after liver biopsies

3. Prednisone decreased to 5mg bid after results obtained

4. Azothiaprime discontinued, cyclosporin started after results

5. Prednisone weaned off, budesonide started after these results

6. Integrative appointment and San Ren Tang started at these results.

On presentation for her Integrative appointment on 2/20/12, Minnie was worried but friendly. She had halitosis, 2/6 systolic heart murmur, generalized seborrhea oleosa, otitis and hearing loss, thin hair coat, multiple subcutaneous lipomas, cataracts and grade 4/9 BCS and soft stool. Her Traditional Chinese Medicine (TCM) exam revealed wiry, deep pulses and a fairly normal pink tongue.

Given the clinical symptoms past and present, she was given the diagnosis of Spleen Deficiency leading to Damp Heat accumulation in the Liver and Lower Burner. Given the pulse, there was evidence of stagnation. At this point, her Spleen Qi Deficiency was evident in the weight loss and anorexia. The Damp Heat was apparent in the chronic colitis, hepatic inflammation and diabetes mellitus. Please refer to the table of clinical signs in the appendix that correlate with her physical exam findings.

Treatment
It was essential to change Minnie’s diet and turn around the cycle of inflammation that it promoted. At this point, she was anorexic but would eat some freeze-dried raw proteins. She would often eat something once or twice then stop. We did not worry about balancing her diet initially. Our goal was to include lean protein and Damp-draining vegetables. Once her Spleen was functioning and the Heat was cleared, we would focus on balancing her diet.

San Ren Tang was dispensed for Minnie due to its ability to drain Dampness from all three Burners, transform Phlegm and clear Heat (Marsden 2009). Xing Ren descends Lung and Large Intestine Qi. Yi Yi Ren is somewhat cooling, bland, supports the Spleen and leeches Dampness from the Lower Burner, thus moderating diarrhea. Bai Dou Kou transforms Damp and dries the Spleen and Stomach. Ban Xia dries Dampness and transforms Phlegm in the Middle Burner and helps descend Stomach Qi. Dan Zhu Ye has a gentle, mild Heart Fire cooling effect (secondary to Damp Heat). Huo Po moves Qi down and promotes peristalsis. Finally, Tong Cao leeches Dampness and has a mild diuretic effect. Some formulations contain Hua Shi which promotes urination and clears Heat. Minnie was prescribed a starting dose of 1/3 tsp bid for until her recheck in two weeks.

Before the owners instituted her treatment plan, she presented three days later on 2/23/12 for agitation, pacing at night, increased drinking and urination. Her physical exam showed a right-sided head turn and Horner’s syndrome (facial nerve paralysis). She had vision and no proprioceptive deficits. Her pulses were weak. Laboratory work showed an increase in glucose of 513 (normal 70-138) and a urinary tract infection with Proteus mirabilis. Minnie’s TCM diagnosis was long-standing Damp Heat damaging Yin and leading to Yin deficiency. This predisposed her to Internal Winds that can manifest as restlessness, agitation, seizures or, in Minnie’s case, Horner’s syndrome. At this point, Zhi Di Bai Huang Wan at 1/3 tsp bid was added to clear Heat and support her kidneys. It clears empty Heat, cools Blood, nourishes Blood and Yin, nourishes Kidney Yin, tonifies Spleen and drains Damp (Marsden, 2009). It addresses Kidney and Liver Yin deficiency that led to Empty Fire.

Zhi Di Bai Huang Wan consists of Zhi Mu which nourishes Yin and clears Empty Heat. Huang Bai cools empty Fire. Shu Di Huang nourishes Yin of the lower burner and cools Blood agitated by empty Heat. Shan Yao nourishes the Middle Burner. Shan Zhu Yu tonifies Liver Yin. Fu Ling drains Damp from the Middle Burner and balances Shan Yao. Ze Xie drains Damp from the Lower Burner. It balances Shu Di Huang so it does not become too dampening. Mu Dan Pi cools and moves Liver Blood.

The importance of diet was stressed again. A short course of orbax was started at the same time as the herbs because of her positive urine culture. Oral antibiotics are bitter and cooling from a TCM perspective and so were considered likely to help with
the Heat signs. Cyclosporin was decreased to sid. A recheck was set up for two weeks later.

Results: Minnie’s recheck exam on 3/8/12 showed her seborrhea had improved as had her stranguria and pollakiuria. Thus, her Damp and Damp Heat signs had also improved. Her Horner’s syndrome, colitis and appetite were unchanged, but she was maintaining her weight. Her pulses were quite weak. The owners admitted they only started San Ren Tang and orbax, but not Zhi Di Bai Huang Wan. This explained why we did not see appreciable improvement in the empty Heat signs. The plan at this point was to stop orbax and begin Zhi Di Bai Huang Wan. Urinalysis and culture confirmed resolution of her infection.

Two weeks later on 3/22/12, she was feeling and eating better but her appetite was still finicky. Four weeks later on 4/16/12 her stools had improved. She was eating primarily chicken and beef. A multivitamin was added. Two months after being on both herbal formulas, on 5/19/12, her attitude and appetite had improved significantly. Her stool was consistently normal. Minnie’s laboratory work was normal except for BUN elevation at 52 (normal 6-31). See Table 2, laboratory work results starting at the onset of herbal formula supplementation. Her tongue was pink and pulses were slippery. She had gained a pound. We continued to wean her cyclosporine dose.

Minnie was examined on 8/25/12. She was still doing well but the owners reported she seemed stiffer on rising, her vision and hearing seemed to be progressively diminishing and at times she appeared confused. She was eating a balanced dehydrated raw diet and her appetite was excellent. She had gained another pound. On physical exam she had a crouched posture in the rear and a thinning hair coat. Her Horner’s syndrome had resolved by about 80%. Her pulses were deep and weaker than at her previous visit. Her tongue was pink. From a TCM standpoint, we were starting to see diminishing KI Qi and a cooling of her body. The mental confusion, hind-end weakness and progressing sensory decline supported this. Her BUN was stable and her creatinine remained normal. Cyclosporin was discontinued. Zhi Di Bai Huang Wan was decreased to sid. Fu Zi is a hot and spicy Yang tonic. Rou Gui and Fu Zi are the warming spark behind Rehmannia 8. When Yin and Yang are mixed together, Qi is generated.

On 12/15/12, Minnie was still receiving San Ren Tang, Zhi Di Bai Huang Wan and Ba Wei Di Huang Wan, all sid. She also received K+ bromide sid and 7 units of NPH insulin bid. She was no longer on any immunosuppressive medication or ursodeoxycholic acid. The lameness and Horner’s syndrome had resolved. Her appetite was good, her stool was normal and her weight was stable at 25.5 pounds (~11.6kg). Her pulses were now palpable, somewhat toned. Her tongue was pink. Zhi Di Bai Huang Wan was discontinued at this visit.

Minnie was finally examined on 3/7/13. She was now 15.5 years old. Her attitude and appetite were good, her weight was stable and her owners were happy. She slept soundly through the night. She slept on a bed or in the sun. Although her lameness had resolved, she still had a crouched posture in the rear, poor stamina and, at times, mental confusion. There was no change in her murmur. Radiographs were normal except for a mild increase

Shu Di Huang tonifies Blood and Yin (Lower Burner) and Shan Yao preserves Yin by containing it. It is an astringent herb. Shan Zhu Yu is another astringing herb that is warming and acts as a Liver Blood and Yin tonic. Fu Ling drains Damp from the Middle Burner. Ze Xie drains Damp from the Lower Burner. Mu Dan Pi moves Blood. Rou Gui is a Yang tonic for the Lower Burner. Fu Zi is a hot and spicy Yang tonic. Rou Gui and Fu Zi are the warming spark behind Rehmannia 8. When Yin and Yang are mixed together, Qi is generated.
in vascular congestion on her thoracic view. On her TCM exam, her tongue was pink, her pulses deep and weak, thin and toned. She showed more overt signs of Kidney Qi deficiency in the weakness, poor stamina, sensory loss and mental confusion. Her Blood stasis sign, lameness, had not recurred. We discontinued San Ren Tang and opted to increase Ba Wei Di Huang Wan to bid. The owners were instructed to watch for signs of Heat or Dampness recurring. Specifically, they were to call if they saw signs of colitis, stranguria, pollakiuria, agitation and restlessness. If Minnie develops Heat signs we will restart Zhi Di Bai Huang Wan. We planned talk on the phone in two weeks and examine Minnie in three weeks. At that time I would do laboratory work, including a fructosamine.

1. Laboratory work just prior to starting San Ren Tang. Zhi Di Bai Huang Wan added 3/12
2. Ba Wei Di Huang Wan was added 10/25/12

Discussion
From a Western perspective, Minnie was quite a complicated case with many seemingly unrelated symptoms. From a TCM perspective, most of her symptoms could be explained as coming from a single root. The diet Minnie had originally been on was low in protein and very high in carbohydrates. Over time, this led to the unusable substance, Damp, causing diminished flow of Qi and Blood and subsequent friction which manifests as Heat formation. Dampness can accumulate in the Liver causing hepatomegaly and Wind Cold Damp invasions can cause back pain (Marsden 2011). From a Western perspective, high carbohydrate diets and weight gain promote non-specific inflammation and insulin resistance, in other words, metabolic syndrome (Marsden 2009). This Heat, or inflammation, led to multiple diagnoses over the years depending on where the Dampness accumulated. Diagnoses ranged from atopy, back pain, colitis and finally to CAH (Marsden 2009). This Heat, or inflammation, can exacerbate the condition and increased the inflammatory process. We saw an improvement in liver enzymes as her diabetes and increasing anorexia forced the owners into feeding primarily protein as this was all she would eat. Fortunately, this is exactly what she needed to start to reverse the root of her metabolic syndrome. This, combined with weaning Minnie off of steroids, improved liver values even before an herbal formula was started. Unfortunately, it was not soon enough to prevent damaged Yin from leading to empty Heat. In Minnie this manifested as Horner’s syndrome and mental agitation.

Biomedical indications for the initial choice of San Ren Tang include its use in the treatment of hepatitis, cholecystitis and gastroenteritis in humans (Chen & Chen 2009). Coix seed present in San Ren Tang has blood lipid-reducing properties and the capacity to increase antioxidant effects to help prevent chronic disease (Yu F et al 2011). In rats, coix supplementation may play a role in improving the symptoms of metabolic syndrome by increasing the efficiency of glucose uptake by specific cells and decreasing the expression of adipogenesis factors (Ha Do & Bae 2010).

In addition to TCM evidence for the choice of adding Zhi Di Bai Huang Wan for the Empty Heat and Yin deficiency, there is Western biomedical evidence to support its use. It has been studied and found to benefit human cases of diabetes mellitus and dryness in geriatric patients (Chen & Chen 2009). The formula is also indicated for chronic neuritis in humans (Chen & Chen 2009). Shu Di Huang and Mu Dan Pi have anti-inflammatory and antimicrobial effects. The compound 2,5-dihydroxyacetophenone isolated from Shu Di Huang inhibits inflammatory responses in macrophage lines (Han & Park 2012). Shu Di Huang is hepatoprotective and has diuretic effects (Chen & Chen 2001). In mice, Shan Zhu Yu levels out the post-prandial glucose spike after ingestion of glucose. It has anti-inflammatory and antibiotic properties (Chen & Chen 2001). Shan Yao and Zhi Mu lower blood glucose in mice (Chen & Chen 2001).

These herbal formulas were effective in resolving the original concerns regarding Dampness, Damp Heat and Empty Heat caused by Yin deficiency. The dietary changes helped stop the ongoing cycle of Spleen deficiency creating Dampness. Zhi Di Bai Huang Wan is extremely cooling and as time elapsed became too cooling for Minnie. Ba Wei Di Huang Wan was added to continue Kidney tonification and to add warmth to her aging body as the other herbs were weaned. This was safe to do as her Damp-promoting diet and medications had been discontinued.

The gradual decline in Essence over the life of a pet results in the commonly recognized signs of Kidney Qi deficiency. These include cognitive dysfunction, lower back and rear limb weakness and
deafness. Being both a Yin and Yang tonic, Ba Wei Di Huang Wan can help generate Qi. Western biomedical indications for this formula include those listed above for Zhi Di Bai Huang Wan as they share several herbs. An additional herb contained in Ba Wei Di Huang Wan is Rou Gui. It improves low-back weakness in human patients (Chen & Chen 2001). Cinnamaldehyde, a major constituent in Rou Gui, has antihyperglycemic and antihyperlipidemic actions in mice (Li & Sun 2012). Fu Zi improved cardiovascular function in animal experiments (Chen & Chen 2001).

Conclusion
Minnie’s case is a perfect illustration of the limitations of Western Medicine in some patients. The fragmented and rigid approach did not permit a global view of Minnie’s physiology and, when she worsened on her medication, there were no viable alternatives. Looking at her condition from a TCM approach allowed for individual variation and a treatment plan tailored to what her body was exhibiting, including her responses to medication. This case showed how stepping back, taking all signs and symptoms into account, not just CAH, can lead to resolution of several clinical problems through the use of dietary modification and Chinese herbal formulas. Her diabetes stills needs to be monitored and managed carefully, and she is still on insulin.

Table 2. Laboratory Values as Herbal Formulas Instituted

<table>
<thead>
<tr>
<th>Normal Values</th>
<th>2/20/2012¹</th>
<th>5/18/2012</th>
<th>8/25/2012</th>
<th>1/22/2013²</th>
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</thead>
<tbody>
<tr>
<td>ALP (5-131)</td>
<td>200</td>
<td>92</td>
<td>70</td>
<td>114</td>
</tr>
<tr>
<td>ALT (12-118)</td>
<td>71</td>
<td>60</td>
<td>66</td>
<td></td>
</tr>
<tr>
<td>Glucose (70-138)</td>
<td>513</td>
<td>188</td>
<td>275</td>
<td>342</td>
</tr>
<tr>
<td>BUN (6-31)</td>
<td>26</td>
<td>52</td>
<td>54</td>
<td>35</td>
</tr>
<tr>
<td>HCT (38-60)</td>
<td>49%</td>
<td>47%</td>
<td>50%</td>
<td>52%</td>
</tr>
</tbody>
</table>

References


Appendix

Ultrasound Report: 4/25/11

Conclusion:
1. Hepatomegaly with diffusely hyperechoic liver parenchyma. Consider primary liver disease such as hepatitis (infectious, inflammatory) or infiltrative neoplasia (e.g. lymphoma or mast cell neoplasia).


Recommendations:
Ultrasound-guided fine needle aspirate or liver biopsy is necessary for a definitive diagnosis. Alternatively, empirical therapy for hepatopathy could be pursued. If recheck blood work is not improved, consider biopsy.

Radiologist:
Dr Seth Wallack DVM DACVR
Laparoscopic Liver Biopsy Report 5/19/11
Specimen: laparoscopy-derived biopsies of liver

Microscopic Description:
Multiple representative sections are examined. There is some variation among the samples. Several of the fragments demonstrate variable degrees of hepatocellular cytoplasmic vacuolation and swelling. The most severely affected sample features loss of normal lobular architecture with prominence of thick portal tracts surrounded by dissecting fibrosis. The inflammation has a patchy distribution but is also perivascular and periportal and comprised of lymphocytes and neutrophils predominantly. In several other samples there are prominent mixed cellular infiltrates around portal tracts. Some of the infiltrates appear to represent immature leukocytes (extramedullary hematopoiesis) but they are also mixed with lymphocytes and neutrophils. In some samples there are areas of mild bile duct hyperplasia with small numbers of lymphocytes cuffing the bile ducts.

Diagnosis:
Liver - diffuse low grade, patchy, vacuolar hepatopathy; regional areas of chronic dissecting fibrosis and nodular hyperplasia; regional areas of moderate to marked lymphocyte and neutrophilic hepatitis; mild lymphocytic portal hepatitis and bile duct hyperplasia.

Pathologist:
Taylor Spangler DVM DACVP
Copper, iron and zinc levels in biopsy specimen within normal ranges
CSU Veterinary Diagnostic Laboratory 5/20/11
No growth in aerobic or anaerobic liver cultures reported 5/25/11.
Table Listing Minnie’s Clinical and Biomedical Symptoms on Exams and Corresponding TCM Diagnoses

<table>
<thead>
<tr>
<th>A</th>
<th>B</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Exam and Lab Work Findings 2/20/12</strong></td>
<td><strong>Possible TCM Diagnosis</strong></td>
</tr>
<tr>
<td>halitosis</td>
<td>Damp Heat</td>
</tr>
<tr>
<td>heart murmur</td>
<td>Blood and Qi Stasis</td>
</tr>
<tr>
<td>seborrhea oleosa</td>
<td>Damp</td>
</tr>
<tr>
<td>otitis externa</td>
<td>Damp Heat</td>
</tr>
<tr>
<td>lipomas</td>
<td>Damp</td>
</tr>
<tr>
<td>cataracts</td>
<td>Damp</td>
</tr>
<tr>
<td>muscle wasting</td>
<td>Spleen deficiency, Yin deficiency</td>
</tr>
<tr>
<td>deafness</td>
<td>KI Qi deficiency</td>
</tr>
<tr>
<td>weak in rear</td>
<td>KI Qi deficiency, TBO</td>
</tr>
<tr>
<td>thin hair coat</td>
<td>Blood deficiency</td>
</tr>
<tr>
<td>colitis</td>
<td>Damp Heat</td>
</tr>
<tr>
<td>diabetes mellitus</td>
<td>Damp Heat, +/- Yin deficiency</td>
</tr>
<tr>
<td>chronic active hepatitis</td>
<td>Damp Heat with Liver Qi stagnation</td>
</tr>
<tr>
<td><strong>Exam Findings 2/23/12</strong></td>
<td><strong>Possible TCM Diagnosis</strong></td>
</tr>
<tr>
<td>agitation, pacing</td>
<td>Empty Heat secondary to Yin deficiency, TBO</td>
</tr>
<tr>
<td>Horner’s Syndrome</td>
<td>Wind Invasion,Empty Heat secondary to Yin deficiency</td>
</tr>
<tr>
<td>Urinary tract infection with stranguria</td>
<td>Damp Heat</td>
</tr>
<tr>
<td><strong>Exam and Lab Work Findings 8/25/12</strong></td>
<td><strong>Possible TCM Diagnosis</strong></td>
</tr>
<tr>
<td>thin, deep, weak pulse</td>
<td>KI Qi deficiency, Blood deficiency</td>
</tr>
<tr>
<td>weaker hind</td>
<td>KI Qi deficiency, Blood deficiency, TBO</td>
</tr>
<tr>
<td>progressing sensory loss</td>
<td>KI Qi deficiency</td>
</tr>
<tr>
<td>cognitive dysfunction</td>
<td>KI Qi deficiency, TBO, Yin deficiency</td>
</tr>
<tr>
<td>mild BUN elevation</td>
<td>KI Qi deficiency</td>
</tr>
</tbody>
</table>
Case Report

Chinese Herbal Therapy in a Dog with Conjunctivitis, Otitis and Diarrhea

Rowena Barrett, BSc BVMS

Abstract

Chinese herbal therapy, acupuncture and dietary changes were used successfully to treat a young Bernese Mountain Dog with inflammatory symptoms in a number of different organ systems. This patient had clinical signs of conjunctivitis, otitis externa, possible balanoposthitis (evidenced by profuse preputial discharge) and diarrhea (large volume of stools with mucous). In Traditional Chinese Veterinary Medicine, the formulas used in this case; San Ren Tang and Si Miao San treat Damp Heat while providing Spleen support. The formulas were used consecutively not concurrently, San Ren Tang first, then Si Miao San. Herbs and chemical constituents of these formulas have been identified as having anti-inflammatory activity against various inflammatory mediators including nitrous oxide, tumour necrosis factor α and inter-leukin 6. Damp Heat, a pattern diagnosis in TCVM may provide an alternative explanation and treatment strategy for some cases of inflammatory bowel conditions including food allergy in the dog.

Introduction

Inflammation is a necessary process within the body, it brings cells and other substances to a damaged area to help tissue repair and remove infected or damaged cells. Inflammation within the body may be caused in many ways, including physical or chemical damage to tissues, microbial invasion and even by the bodies’ own immune response (Karin et al 2006). Excessive inflammation can, however, be damaging. It can lead to pain, erythema, tissue necrosis, abnormal granulation formation and excessive exudation or secretions (Karin et al 2006). The inflammatory process is very complex involving many inflammatory mediators and pathways (Wang et al 2012). Chinese herbal formulas provide a way of treating inflammation that is mediated by multiple targets through multiple active ingredients (Wang et al 2012). The inflammatory process in China of treating inflammatory conditions and research is now being undertaken into how individual Chinese herbs modulate inflammation (Wang et al 2012). It is thought that, by blocking key inflammatory mediators, such as tumour necrosis factor α (TNF-α), it may be possible to inhibit or reduce the inflammatory response (Feldman and Maini 2003). Herbs in the formulas used in this case have been shown in vitro to inhibit TNF-α as well as other pro inflammatory mediators such as inter-leukin 6 (IL-6) and nitrous oxide (NO). Nitrous Oxide is a substance that has an important role in terms of the body’s biochemistry (Achike & Kwan, 2003). In low concentrations it dilates blood vessels, improves circulation and therefore may help to resolve inflammation (Achike & Kwan, 2003). Nitrous Oxide is converted from L-arginine by Nitrous Oxide Synthase (NOS). NOS is found in various body tissues and functions to produce small amounts of NO as required. Inducible NOS (i NOS) can be activated by inflammatory cytokines and results in large concentrations of Nitrous Oxide that can damage body tissues and perpetuate acute and chronic inflammation (Achike & Kwan, 2003).

From a Western point of view, Jake’s persistent diarrhoea with mucous could have been a manifestation of a food intolerance or food allergy or idiopathic inflammatory bowel disease (IBD). Food allergy like IBD is an abnormal immunologically based response by the mucosal immune system to antigens’ in food or bacteria present in the gastrointestinal tract (Sampson, 2004). Common allergens for dogs include, cow’s milk, eggs, meat protein from beef and chicken, corn, wheat and soy beans (Gaschen, 2011). Diagnosis may be confirmed with an elimination diet and response to re-challenge with the suspected allergen (Gaschen, 2011). Treatment for IBD/Food allergy usually revolves around avoidance of identified allergen. Immunosuppressant agents such as glucocorticoids and azathioprine may also be utilized to curb the inflammatory process (Silvia, 2008).

Case Description

Jake, a 5 month-old, entire male Bernese Mountain Dog weighing 25kg (55+ pound) presented with a three-month history of sloppy stools with mucous, a picky appetite and bilateral conjunctivitis. Chinese Herbal Medicine was used successfully to treat a young Bernese Mountain Dog with inflammatory symptoms in a number of different organ systems. This patient had clinical signs of conjunctivitis, otitis externa, possible balanoposthitis (evidenced by profuse preputial discharge) and diarrhea (large volume of stools with mucous). In Traditional Chinese Veterinary Medicine, the formulas used in this case; San Ren Tang and Si Miao San treat Damp Heat while providing Spleen support. The formulas were used consecutively not concurrently, San Ren Tang first, then Si Miao San. Herbs and chemical constituents of these formulas have been identified as having anti-inflammatory activity against various inflammatory mediators including nitrous oxide, tumour necrosis factor α and inter-leukin 6. Damp Heat, a pattern diagnosis in TCVM may provide an alternative explanation and treatment strategy for some cases of inflammatory bowel conditions including food allergy in the dog.
veterinarian for treatment of the conjunctivitis and was given Amacin® eye ointment (prednisolone, neomycin, sulfacetamide, polymyxin B sulfate). This initially improved the eyes. Two weeks later, the conjunctivitis returned and the owner was supplied Chloroint® (chloramphenicol, hydrocortisone acetate). This did not help so she then went back to Amacin® which also failed to improve the conjunctivitis.

Jake's energy was low, especially considering he was a puppy. He was a big drinker, did not tend to vomit, but ate grass and tended to struggle in the heat. He had a picky appetite such that the owner needed to encourage him to eat. His diet at presentation was Advance® Puppy Plus (growth large breed) and Tucker Time. Cheese and sardines was used to encourage him to eat. He usually defecated twice daily, sometimes stools were formed but tended to be quite sloppy with clear/white mucous. Tenesmus was not a prominent feature nor was the presence of blood. The stool odour was not particularly foul. Jake was on monthly Heartgard and had regular intestinal worming. Jake preferred a cooler environmental temperature and to sleep on hard floors. He liked to lie in cool damp sand in the garden. He did not appear to dream excessively and his coat and skin appeared to be in good condition.

Jake's lower eyelids were a little everted (ectropion) which may have contributed to development of conjunctivitis (the eyelids might need to be assessed once Jake has stopped growing in case surgery is required). The palpebral conjunctiva was very red and he had copious creamy discharge. On otoscopic examination, Jake had bilateral copious back-brown greasy discharge on the inner aspect of the pinnae and in the vertical and horizontal ear canals. The inside of his hind limbs were encrusted with creamy-yellow preputial discharge. Discharge was also evident at the end of his prepuce.

TCVM uses aspects of the patient's tongue and pulse to aid diagnosis and choose relevant therapy. In Jake's case, his tongue was pale pink to pink in colour, with excess moisture and a little frothy on the surface. His pulse was thin, moderately fast, soft and slippery. The paleness of his tongue was suggestive of deficiency and, put together with other symptoms, Spleen Qi deficiency was most likely. The moist tongue and slippery pulse were consistent with Damp.

Western Diagnosis
Jake had evidence of bilateral Otitis Externa (copious back-brown greasy discharge), bilateral Conjunctivitis (erythematous conjunctiva, copious, creamy discharge) and possible Balanoposthitis evidenced by profuse preputial discharge. The persistent diarrhoea (copious loose tools with clear mucous) and picky appetite may have been evidence of food intolerance, food allergy or some other inflammatory bowel disease (IBD). Other diagnostic possibilities for Jake's diarrhea include the presence of intestinal parasites e.g. giardia, cestodes or pathogenic bacteria e.g. salmonella, campylobacter. No fecal analysis or culture was performed on Jake's feces.

TCVM Diagnosis
From a TCVM perspective, many of Jake's symptoms were consistent with Damp and Damp Heat. This is reflected most in the presence and nature of Jake's secretions. In health, there should be minimal discharge from the ears, eyes and prepuce. Stools should be well formed without mucous. The presence of these sticky copious discharges is a sign of Damp. Properties of Dampness in the body mimic that found in the environment. So, Damp tends to be sticky and heavy, settles downwards and is hard to get rid of (Maciocia 1989). Discharges with yellow colouration (eg Jake's preputial and ocular discharges) are an indicator of excessive heat in TCVM. Accumulation of Damp in the body tissues slows the circulation of Qi and Blood, constraining their movement so excess energy is released as Heat. Damp and Heat readily combine to form Damp Heat.

Dampness forms as a result of improper transformation and transportation of fluids by the Spleen (Maciocia 1989). In TCVM, the Spleen processes foods and fluids taken into the body and is essentially the organ of digestion. The Stomach controls the ‘rotting and ripening’ of food, preparing it for the Spleen to process into usable substances and transports them throughout the body. Jake's Damp symptoms are suggestive of underlying Spleen pathology. His symptoms of poor energy, poor appetite, loose stools and grass eating, together with Damp symptoms, suggest an underlying pattern of Spleen Qi deficiency.

It is probable that this Damp/Damp Heat has entered the channels associated with the Liver and Gall Bladder, as this would explain the symptom
distribution. The Liver channel curves around the external genitalia (preputial discharge) and enters the ‘eye system’ (conjunctivitis) (Liangyue et al 1987). The Gall Bladder channel begins at the outer canthus of the eye (conjunctivitis), curves around and enters the ears (otitis), its internal channel exits the lower abdomen in the vicinity of the inguinal region (preputial discharge) (Liangyue et al 1987). It is possible the preputial discharge may have been associated with accumulation of Damp Heat in the Dai Mai; one of eight extraordinary meridians in the body. This channel encircles the waist (the only horizontal channel in the body). The points to access this channel fall within the Shao Yang (GB, SJ), so benefits of the herbal treatment selected, especially San Ren Tang (SRT), would probably have flowed into the Dai Mai. In Western medicine, the liver and Gall Bladder organs are closely related and interdependent both in terms of anatomy and function. This is true also in TCVM where the Liver and Gall Bladder are externally-internally related through their channels and organs. Appendix 1 shows a patho-physiological diagram highlighting Jake’s Patterns of Disharmony and symptoms.

TCVM Treatment and Results - Initial Formula: SRT at ¾ teaspoon bid

This formula was chosen due to signs of Damp in all three Jiaos, Spleen Qi Deficiency and Heat. In TCVM, the body is divided into three Jiaos that divide the body into three sections. The Upper Jiao is the upper part of the body (the area cranial to the diaphragm) and includes the Heart, Pericardium and Lungs. The Middle Jiao is equivalent to the middle abdomen and includes the Spleen, Stomach, Liver and Gall Bladder. The Lower Jiao includes the Small and Large Intestines and the Urinary Bladder (Maciocia 1989). SRT may be translated as Three Seed Decoction, named after the three seeds Yi Yi Ren (coix seed), Xing Ren (apricot kernel) and Bai Dou Kou (round cardamon) (Marsden 2010). Yi Yi Ren (Coix lachrymal jobi), Bai Dou Kou (Amomum kravanh), Xing Ren (Prunus armeniaca) are the chief herbs SRT. When used together, they can separate Dampness from the three Jiao and eliminate it. This allows Qi to move freely through the San Jiao (a passageway allowing communication within and between the three Jiao) and helps to alleviate symptoms (Yang 2010). Hou Po (Magnolia officinalis) aids in this process. It is an aromatic Damp-dispelling herb, it drains Damp and mobilizes Qi in the San Jiao. Ban Xia (Pinellia ternata) further dries Damp and resolves phlegm that may be obstructing the Middle Jiao. It redirects rebellious stomach Qi downwards, relieving any nausea (Yang 2010). Hua Shi (Talc), Tong Cao (Tetrapanax papyriferus) and Dan Zhu Ye (Lophatherum gracile) are a group of herbs that promote diuresis, helping to provide a means by which Damp is removed from the body (Yang 2010). They clear some Heat from the body and guide it out via urination.

Other Treatments

Dermotic® was dispensed (bid both ears) and the client was advised to clean Jake’s ears every other day with Epiotic®.

A diet of cooked chicken and pumpkin was suggested initially. Chicken is considered a warm meat in TCVM and this warm nature would support digestion. Pumpkin is considered to have Damp-draining properties which may be useful in resolving Jake’s diarrhea. Further, cooking the food lessens pressure on Jake’s digestion. Once his diarrhea resolves, other meats and vegetables may be included. A raw diet may be considered if digestive strength improves. I advocated the owner give Jake a good quality probiotic daily. Green tea could be used to bathe eyes as it is cooling and has antiseptic qualities (Marsden and Wynn 2003).

At each visit Jake received acupuncture directed at draining Damp Heat (eg SP9, BL25, LI4, LI11, ST37), supporting the Spleen (eg SP6, ST36 BL20, BL21), moving possibly stagnant Qi (eg LR3, GB34, BL18, BL19) and dredging the Shao Yang channels (to benefit the eyes and help relieve obstructions in the channels so that Damp and Heat could drain away) (eg GB41, GB43, SJ5). Many of these points have multiple uses, with an effect on channels and organs.

Follow-up Appointments

Over the next two visits, Jake’s energy and appetite improved. His owner no longer needed to tempt Jake to eat. His stools became well formed with no mucous, the preputial discharge ceased. The ears improved but he was also on Dermotic® with regular cleaning with Epiotic®. The changes occurred quickly, within the first two weeks of beginning SRT, Jake’s owner noticed improvement in energy and stools and the preputial discharge disappeared. If the owner experimented too much with different foods (eg raw foods), his stools would deteriorate. The amount of discharge from his eyes
had decreased a little but was still quite copious (creamy in colour) and the conjunctiva remained very red. Jake was still sensitive to heat and would lie in moist sand even though it was the middle of winter at the time of his revisits. As signs of inflammation were still evident in his eyes and he had continued heat sensitivity, SRT was replaced by Si Miao San (SMS).

Subsequent formula: SMS at 1 teaspoon bid

This formula is more cooling than SRT and has more anti-inflammatory action (Marsden 2010). It contains Yi Yi Ren (Coix lachrymal jobi) (drains Damp, supports the Spleen), Cang Zhu (Atractylodis lancea) (tonifies Spleen, drains Damp), Huang Bai (Phellodendron amurese) (clears heat, dries Damp) and Huai Niu Xi (Achyranthes bidentata) (moves Blood) (Marsden 2010).

Subsequent Follow-up Appointments

Over the next couple of visits, Jake's eyes improved markedly. By the second visit after beginning SMS, there was minimal conjunctival erythema and minimal discharge. Jake’s stools were well formed with no mucous. His appetite was good and he was eating well (brown rice, vegetables, raw mince and chicken necks). He was drinking less, coping better with heat and had good energy. His ears continued to have greasy discharge. Following this last follow-up, Jake was weaned off SMS and has continued to be symptom free. Appendix 2 provides consultation notes relating to Jake’s appointments.

Discussion

The first formula used in this case, SRT, is useful to drain Damp, resolve phlegm and clear a little heat and it helps to open up the San Jiao. This was important due to the distribution of lesions which appeared to show significant involvement of the Liver and Gall Bladder (eyes, genitals, ears). The Gall Bladder is exteriorly-interiorly related to the Liver. In turn, the Gall Bladder channel and San Jiao channel are related through the lesser Yang or Shao Yang. Points on one of these channels may be used to treat the other and vice versa. Movement of Qi and other vital substances in the San Jiao can be hindered by the accumulation of Damp and phlegm, so opening up this communication pathway proved useful in this case.

SRT was able to elicit quite a marked improvement, however conjunctivitis remained. At this stage, Long Dan Xie Gan Tang (LDXGT) may have proven useful as it drains Damp Heat from the Liver meridian (Marsden 2010). It is, however, a very cooling formula that may have adversely affected Jake's Spleen and led to diarrhea. At this time, Jake had a tendency to diarrhea with raw food. SMS was chosen as it is has a stronger anti-inflammatory, Heat clearing action than SRT and also supports the Spleen. LDXGT could then have been added with less risk of adverse effects, if necessary.

Both SRT and SMS contain Yi Yi Ren (Coix lacryma-jobi) otherwise known as Job's tears or coix seed (Chen & Chen 2004). Yi Yi Ren is a cool, sweet, bland herb. The bland flavour is associated with a Damp leeching effect and its sweetness supports the Spleen (Bensky 2004). From a TCVM view, it is a useful herb to include in this case. It also has significant anti-inflammatory effects. A recent study that isolated a flavonoid-rich fraction of Adlay bran (coix) found that in vitro it suppressed LPS (lipopolysaccharide)-stimulated IL-6 and TNF-α in a concentration dependent manner (Hong-Jhang Chen et al 2010). LPS is found in the outer membrane of gram negative bacteria, so is used as a stimulator for the stimulation of the inflammatory process. IL-6 and TNF-α are pro-inflammatory agents that can induce production of NO (Hong-Jhang Chen et al 2010). When produced in large amounts, NO perpetuates chronic and acute inflammation (Achike and Kwan 2003).

Hou Po (Magnolia officianalis), another herb in SRT, warms the Middle Jiao (ie Spleen) and drains Damp. Again it is useful in this case from a TCVM view and it contains a substance named honokiol with potent anti-inflammatory effects (Wu et al 2011). This study again used a model involving LPS-induced inflammation and found honokiol was able to inhibit inflammatory cytokines and mediators in human renal mesangial cells (Wu et al 2011). A study involving modified SMS (mSMS) where Huang Lian (Coptis chinensis) was used in place of Huai Niu Xi (Achyranthes bidentata), found mSMS inhibited inflammatory mediators such as IL-6, TNF-α and NO in LPS-stimulated mouse macrophages (Fan et al 2010).

From a Chinese Medicine perspective, SMS is used mainly to drain Damp Heat from the Lower and Middle Jiaos, nevertheless it was used successfully in this case to attain resolution of Jake’s symptoms, including conjunctivitis. Cang Zhu is aromatic, Damp drying in nature and is useful to dry Damp...
from the Spleen (Chen & Chen 2004). This means the Spleen's transformation/transportation function is improved and Damp is less likely to accumulate. Cang Zhu also benefits the eyes (Chen and Chen 2004). Huai Niu Xi is a Blood invigorating, stasis-removing herb and directs fire and Blood downwards, so this action may have helped the conjunctivitis (Chen and Chen 2004). Huang Bai's Damp Heat draining effect is focused mainly in the Lower Jiao, so it would be useful in draining Damp Heat from the intestines in particular (Chen and Chen 2004). Yi Yi Ren strengthens the Spleen and resolves Damp in the Middle Jiao, helping Cang Zhu to strengthen the Spleen (Chen and Chen 2004). From a TCVM view, the conjunctivitis improved in part because this formula drained Damp so the Spleen could function appropriately. It is possible SRT had helped open up the San Jiao and Gall Bladder meridians, allowing residual Damp Heat to drain from the body and improve the conjunctivitis. Research indicates SMS and SRT contain potent anti-inflammatory components so, from a conventional view, these herbs may have helped resolve the inflammatory processes occurring in this dog.

Jake was five months old on presentation and already had multiple issues in a number of different organ systems and poor energy. There was probably some congenital weakness associated with his Spleen. The highly processed diet Jake was consuming was further impacting the Spleen's function of transformation and transportation of food and fluids, contributing to his general malaise and Damp problems. The presence of Damp in the middle jiao although produced by the Spleen would also further weaken the Spleen, perpetuating his problem. Damp as a pathogenic factor tends to slow things down in the body releasing heat in the process, so Jake's Damp Heat issues had the potential to become much worse and much more entrenched.

In TCVM all food has inherent properties in terms of what it will do in the body post ingestion. Different foods have different flavours, thermal properties and effects on the bodies' Qi, Blood Yin and Yang. Different foods also enter different meridian pathways and direct their effects toward particular organs. Consequently diet can be used to treat and prevent disease; but the wrong foods may also cause and perpetuate disease. Dry dog food, may contain a high grain percentage relative to meat protein, which for carnivores can create Damp (Marsden, 2010). As far as TCVM is concerned the longer food is cooked the more heating it is once eaten. So this type of food is better avoided given Jake's Damp Heat tendencies. Jake did very well with some rice in his diet; in TCVM rice has Spleen Qi supporting qualities. Jake's inability to deal with raw food in his diet was again down to his Spleen's poor function; once this had been improved and the Damp drained from his body and Spleen then Jake was able to cope quite well on a diet that included raw meat and bones. Jake is now off Chinese herbs. Having a largely unprocessed diet with a significant raw component will not be a burden on his Spleen and hopefully over time help to strengthen it. Jake's current diet and his healthier body and Spleen should avoid production of excess Damp and Heat issues that plagued him at such a young age.

From a TCVM point of view Jake's loose stools with mucous is evidence of Damp/ Damp Heat in the intestines. Damp as a pathological factor causes tissues to be overly moist and swollen, with excessive secretions. Heat as a pathological factor causes tissues to be more erythematous. So Jake's intestines had we been able to see them may have appeared red, swollen and mucous secreting. Histologically the external layer of the gastro-intestinal tract (GIT) consists of a single layer of columnar intestinal epithelial cells connected by tight junctions, covered by a thick layer of mucous (Scott et al, 2010). The luminal border of the GIT and mucous contains enzymes, bile salts and extremes of pH that render antigens from food and bacteria less antigenic (Scott et al, 2010). One theory concerning the development of food allergy or IBD is that altered permeability of intestinal mucous allows greater than normal exposure of antigens (from food and bacteria) to intestinal lymphocytes leading to the release of proinflammatory mediators (Silvia, 2008). Continued altered permeability of the intestinal mucous/mucosa together with an intense inflammatory response will lead to chronic inflammation. An intestinal tract affected by Damp/Damp Heat will be inflamed with potentially reduced cellular cohesion; a thinner more liquid layer may replace the thick mucous barrier. This situation increases the exposure of the immune system to antigens in food and bacteria. The subsequent inflammatory response may result in the release of many inflammatory substances such as prostaglandins, leukotrienes, IL6, IL8 and TNF-α; potentially eliciting a
chronic inflammatory process (Silvia, 2008). Damp /Damp Heat involving the GIT may be an alternate explanation for the development of food allergies.

Western treatment for IBD/Food allergy usually revolves around a food trial involving novel protein and carbohydrate sources or commercial hypoallergenic diets with hydrolyzed proteins (Silvia, 2008). Immunosuppressant agents such as glucocorticoids and azathioprine may also be utilized to curb the inflammatory process (Silvia, 2008). Glucocorticoids (GC) from a TCVM point of view have a cooling and moistening effect on the body (Marsden, 2010). It’s cooling nature can therefore help with inflammatory conditions. The moistening aspect of Prednisolone may eventually exacerbate symptoms in an animal with Damp patterns.

Glucocorticoids (GCs) do have a profound anti-inflammatory effect in the body. Grossly they decrease redness, heat and pain through the inhibition of capillary dilatation, the migration of leukocytes and release of vasoactive amines (Madison, 2009). GCs have a global effect on the body, targeting all tissues. They promote gluconeogenesis, leading to hyperglycemia and promote insulin resistance (Madison, 2009). GCs promote insulin resistance through many mechanisms including the promotion of proteolysis, lipolysis, increased free fatty acid production and fat accumulation in the liver (Heather et al 2012). These processes can release substances that can reduce the sensitivity of body tissues to the action of insulin (Heather et al 2012). Studies in human obesity and insulin resistance have revealed associations between decreased insulin sensitivity and the chronic activation of proinflammatory pathways (Luca & Olefsky, 2007). Increased levels of inflammatory mediators TNF, IL6 and IL8 have been reported in various diabetic and insulin resistant states (Luca & Olefsky, 2007).

The formulas used in this case San Ren Tang and Si Miao San and their individual herbs have been shown to have substantial activity against many inflammatory mediators including Nitrous oxide (NO), Tumour Necrosis Factor α (TNF-α), and Interleukin 6 (IL-6); but they also help to ameliorate insulin resistance. A study involving modified SMS (again substituting Huang Lian (Coptis chinensis) in place of Huai Niu Xi (Achyranthes bidentata)) showed that mSMS improved insulin sensitivity in cultured human hepatocytes (Liu et at, 2011). Chinese herbal formulas such as SRT and SMS, when patterns agree are used for the treatment of Diabetes in animals and can decrease insulin resistance and allow for improved Diabetic control (Marsden 2010).

So in this case the use of an unprocessed diet and the two formulas has led to resolution of clinical signs without the need to rely on pharmacological agents such as Glucocorticoids (e.g. Prednisolone). GCs although useful in many situations do carry with them potential side effects at the cellular level such as increased insulin resistance and the potential for eliciting chronic inflammatory pathways. They can also have deleterious effects on the gastro-intestinal tract such as a risk of ulceration, vomiting and further diarrhea (Madison, 2009). The use of GCs down regulate the initial inflammatory process but it doesn’t address the underlying pathphysiology. By approaching this case from a TCVM point of view, resolving Damp Heat and tonifying the Spleen, the potential for treating the root of the problem as well as the signs is possible.

Jake’s age would have been a factor in his response to treatment. Being very young, TCVM patterns would be less entrenched so his progress was quite speedy. In general, Damp and Damp Heat-type issues often resolve more slowly as the pathologic Damp tends to be quite ‘sticky’ and difficult to shift.

Conclusion
The Chinese herbal formulas SRT and SMS were used to help resolve conjunctivitis, otitis externa, profuse preputial discharge and loose stools with mucous in a Bernese Mountain Dog. These formulas have traditionally been used for inflammatory conditions in Traditional Chinese Medicine. Constituents of these formulas in vitro and ex vivo have exhibited activity against key mediators of the inflammatory process.

References


Chen J and Chen T (2004). *Chinese Herbology and Pharmacology*, Art of Medicine Press Inc, City of
Industry, CA USA.


Appendix 1. Pathology Diagram Jake

Appendix 2. Consultation Notes

<table>
<thead>
<tr>
<th>Date</th>
<th>Tongue/Pulse/Findings</th>
<th>TCVM Diagnosis</th>
<th>Treatment Plan</th>
</tr>
</thead>
<tbody>
<tr>
<td>25/5/12</td>
<td>Tongue: Pale pink-pink, moist, froth on surface</td>
<td>Spleen Qi Xu (poor appetite, intolerant raw food, loose stools, low energy, grass eating)</td>
<td>San Ren Tang (3/4 tsp bid) Probiotic Diet - avoid processed – use cooked chicken and pumpkin initially, gradually introduce other meat and vegetables, cooked initially Green tea infusion to bathe eyes Epiotic to clean ears</td>
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<tr>
<td></td>
<td>Pulse: Moderately fast, thin, soft, slippery</td>
<td>Damp/Damp Heat (loose stools with clear/white mucous, intolerance of heat, copious creamy conjunctival and preputial discharge, bilateral yeast otitis)</td>
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</tr>
<tr>
<td></td>
<td>Bilateral conjunctivitis (creamy discharge)</td>
<td>Damp/Damp Heat in Liver/Gall Bladder channels (distribution of symptoms, preputial discharge, conjunctivitis, otitis)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Bilateral otitis externa</td>
<td>Liver Qi Stagnation</td>
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<td></td>
<td>Excessive preputial discharge (creamy-yellow discharge)</td>
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<td></td>
<td>Diarrhea (large volume, normal frequency with mucous)</td>
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<td></td>
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<td></td>
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<tr>
<td>15/6/12</td>
<td>Tongue: pink-dark pink, moist</td>
<td>See above</td>
<td>Maintain San Ren Tang Maintain Probiotic, Dermotic bid and Epiotic eod</td>
</tr>
<tr>
<td></td>
<td>Pulse: thin, slippery</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Well-formed stools no mucous</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Energy picked up</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Ears improved but still producing discharge</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Much less preputial discharge</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Still drinking a lot</td>
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<td></td>
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<tr>
<td></td>
<td>Eyes still red with copious discharge</td>
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<tr>
<td></td>
<td>Appetite still fussy</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Owner is finding it too hard to bathe eyes with Green tea infusion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Date</td>
<td>Tongue/Pulse/Findings</td>
<td>TCVM Diagnosis</td>
<td>Treatment Plan</td>
</tr>
<tr>
<td>--------</td>
<td>--------------------------------------------------------------------------------------</td>
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<td>---------------------------------------------------------------------------------</td>
</tr>
</tbody>
</table>
| 6/7/12 | Tongue: Pink, moist  
Pulse: Moderately fast, slippery, thin  
Stools firm, no mucous  
Ears much better, much less discharge  
No more preputial discharge  
Appetite and energy very much improved  
Has physically filled out a little  
Still drinking a lot  
Eyes still red with chunky creamy discharge | Spleen Qi Xu (improving)  
Damp/Damp Heat (improving)  
Damp/Damp Heat in Liver/Gall Bladder channels (conjunctivitis remaining)  
Liver Qi stagnation (improving) | San Ren Tang (3/4 tsp bid)  
Probiotic  
Diet - more varied with meat, vegetables and a small amount of rice  
Epiotic to clean ears |
| 10/8/12| Tongue: pink, moist  
Pulse: thin, slippery  
Well-formed stools now but had deteriorated with some mucous - the owner had been experimenting with raw food  
Eyes still quite red and discharging  
Ears fine  
No preputial discharge  
Still very sensitive to heat, will lay in moist sand even though winter  
35kg (77+pound) | See above | Change to Si Miao San (3/4-1 tsp bid)  
+/- Long Dan Xie Gan Tang  
Maintain Probiotic  
Diet - more varied with meat, vegetables and a small amount of rice |
| 20/9/12| Tongue: Pink, moist  
Pulse: Moderately fast, more tone, less slippery  
Owner has not actually LDXGT as was having some mucous in stools periodically due to several dietary indiscretions, so just on SMS  
Eyes very much improved, conjunctiva still a bit reddened but much less discharge  
Ears fine  
No preputial discharge  
Still prefers cool | Spleen Qi Xu (improving)  
Damp/Damp Heat (improving)  
Damp/Damp Heat in Liver/Gall Bladder channels (conjunctivitis remaining)  
Liver Qi Stagnation (improving) | Si Miao San (1 tsp bid)  
Probiotic  
Diet - more varied diet of meat, vegetables and a small amount of rice, begin more raw  
Epiotic to clean ears, if necessary |
| 2/11/12| Tongue: pink, moist  
Pulse: thin, slippery  
Stools consistently well formed, no mucous  
Eyes very much improved, much less conjunctival erythema and minimal redness  
Eating well (raw pet mince, chicken necks, brown rice vegetables)  
Drinking less  
Coping better with heat  
Good energy  
Ears good.  
Did not use LDXGT, just SMS  
Now 45kg (99+pound) | Spleen Qi Xu (improving)  
Damp/Damp Heat (improved)  
Damp/Damp Heat in Liver/Gall Bladder channels (conjunctivitis resolving)  
Liver Qi Stagnation (improved) | Gradually reduce Si Miao San and wean off  
If any recurrence of symptoms, can reintroduce Si Miao San  
Maintain current diet |
Case Report
Successful Treatment of Anxiety in a 10 year-old Weimeraner Using the Chinese Herbal Formula Xiao Yao San
Rowena Barrett, BSc BVMS

Abstract
The Chinese herbal formula Xiao Yao San (XYS) was used successfully to treat a 10 year-old Weimeraner with severe anxiety. The patient exhibited both significant physical symptoms and disturbed behaviour. XYS has been used traditionally in China for many disorders including depression, mental-emotional problems and anxiety. Herbs and individual chemical constituents in XYS have been shown to have an effect on brain neurochemicals and their related receptors.

Introduction
Anxiety is a very common problem in dogs. It underpins many behavioural disorders including: separation anxiety; phobias (eg noise, thunderstorm); panic and obsessive-compulsive disorders; elimination disorders related to fear and some aggression disorders (Hernandez 2011) (Frank 2007). Anxiety can be defined as ‘the anticipation of future danger or threat, real or imaginary’ (Frank 2007). It can be perfectly normal and transitory in response to a novel situation or, if excessive and frequent, as a sign of illness (Frank 2007). Signs of anxiety can be quite dramatic, including: inappropriate elimination; vomiting; diarrhea; excessive salivation; destruction of physical objects in the dog’s immediate environment; self-mutilation and excessive vocalization (Overall 2011) (Hernandez 2011). More subtle expressions of anxiety include: panting; puffing cheeks; yawning; licking lips; trembling; pacing and even becoming less active than normal (Frank 2007). Behavioural disorders in dogs may frequently lead to the surrendering of a pet by the owner or even euthanasia. Therefore, effective treatment is essential (Overall 2011).

Conventional veterinary treatment of anxiety disorders, eg separation anxiety, involves the use of behavior-modification programs in conjunction with medication to relieve stress (Overall 2011). Medications used include anxiolytic and antidepressant drugs that modulate neurotransmitter activity in the brain and nervous system (Overall 2006). The neurotransmitters affected by these medications include acetylcholine, noradrenaline, dopamine and particularly serotonin and gamma amino butyric acid (GABA) (Overall 2011). The drugs used in anxiety disorders are not without potential side effects. They include: tricyclic antidepressants (TCA), eg clomipramine (Clomicalm®); selective serotonin reuptake inhibitors (SSRI), eg Fluoxetine (Reconcile®); and Monoamine oxidase inhibitors (Overall, 2011). The side effects tend to be due to blockage of muscarinic acetylcholine receptors and manifest in alteration of gastrointestinal function and heart rate (Overall 2006).

Care needs to be taken using these drugs with other medications as there may be interactions (Overall 2006). They are metabolized via renal and hepatic pathways so care is required in animals with other pathologies. Drugs that lead to elevation in serotonin levels may also lower seizure thresholds. For many of these medications, it can take many weeks before a result is seen. There is variation in how effective a particular drug, or combination of drugs, is in a particular individual so it can take some time before an effective treatment is elicited (Overall 2011).

The Chinese herbal formula XYS has been used for over one thousand years in China (Qin et al 2011). Traditionally used to soothe the liver, relieve Qi stagnation, strengthen the Spleen and tonify Blood; its clinical applications vary from mental-emotional problems, depression and anxiety to gynecological, reproductive and liver disorders (Chen and Chen 2009). Interestingly from a mental-emotional perspective, many of the herbs and constituents of the herbs found in XYS have been found in vitro, and in some animal studies, to have an effect on brain neurochemicals and their related receptors. Individual herbs and chemical substances in XYS have been shown to have an affinity for serotonin (5HT), dopamine and GABA receptors in the brain as well as affecting other neurochemicals such as Brain derived neurotropic factor (BDNF) (Qin et al 2011) (Singhuber 2012).

Case Description
Matty, a 10 year-old male neuter Weimeraner, weighing 26kg (57+pound) presented with a history of anxiety. At the time of initial presentation, Matty was in foster care after being surrendered to a Weimeraner rescue organization. At his original home, he had been kept outside with another dog
that had a tendency to prevent him from accessing food. Matty displayed high levels of anxiety often, which included excessive barking, whining, jumping and spinning. This behaviour manifested in response to stimuli such as people walking past or a cat on the garden wall. On car journeys, he would whine and cry and circle repeatedly. Matty did not seem to get physically destructive (although he was confined when the carer was out) and was not aggressive. He did however howl when the carer was out, drawing complaints from the neighbors. Given the chance, he would escape and run away, something the carer describes as ‘strong desire to flee.’ He got on with the other two dogs in the household (apart from a few incidents with food) and was gentle with people once he calmed down.

At the time of consultation, Matty was on Reconcile® (fluoxetine hydrochloride and SSRI). This had led to polyuria/polydipsia and, according to the carer, seemed to make him distant and less tolerant. As soon as he reached the full dose of Reconcile® (1x32mg tablet sid), he developed hind limb ataxia and had a seizure. On presentation, the carer was weaning Matty off Reconcile®. Seizures are a rare but reported adverse reaction with the use of Reconcile® (Reconcile® data sheet).

Matty was underweight, very boney and poorly muscled, with the lack of muscling particularly noticeable in the head, shoulders and spine regions. He had gained 3kg in the 3 months he had been with the carer. His diet in the past three months had consisted of raw meat, vegetables and raw bones. Matty had a good appetite and was a big drinker. His stools were generally well formed but loose toward the end, with no blood or mucous. Sometimes he had softer motions but no constipation. The carer noted no vomiting, but Matty did tend to eat a lot of grass. He was insatiably coprophagia, eating his own and the other two dogs’ stools when given the chance. When he was not in a heightened state of anxiety his energy was low. He had otitis externa with copious black discharge and stiffness in the lower back. No ear or eye redness was present, nor any obvious temperature preference.

Traditional Chinese Veterinary Medicine (TCVM) uses aspects of the patient’s tongue and pulse to aid diagnosis and choose relevant therapy. Matty’s tongue was pale and lavender in colour with normal moisture. Paleness of the tongue is consistent with Spleen +/- Blood deficiency. Lavender colour reflects Liver Qi stagnation – the Blood is not flowing freely so the tongue has a purplish hue. Matty’s pulse was thin and wiry and moderate in rate. The wiriness reflects Qi stagnation and fits with the lavender tongue colour. The thin pulse is suggestive of deficiency, particularly of Blood. Appendix 1 highlights abnormal findings in Matty’s hematological and biochemistry results.

TCVM Diagnosis

From a TCVM perspective, Matty is exhibiting a number of interacting patterns, including: Spleen Qi deficiency (poor muscling, low energy, coprophagia, grass eating, a tendency for soft stools); Liver Qi stagnation (lavender tongue, wiry pulse, frantic anxious behavior); and Blood deficiency (low normal red and white blood cell count, very mild elevation AST/ALT, severe anxiety, pale lavender tongue, thin, wiry pulse). Together, these patterns led to symptoms of Liver-Spleen disharmony and manifest in his physical symptoms and anxiety. The Liver is responsible for ensuring the smooth flow of Qi throughout the body in all directions (Maciocia 1989). Being supplied with the right amount of free-flowing energy allows the body to function optimally. Harmonious flow of Qi is of vital importance in the Middle Jiao where digestion takes place. The Middle Jiao is equivalent to the middle abdomen and includes the Spleen, Stomach, Liver and Gall Bladder.

In TCVM, the Spleen is the source of nourishment for the body. It processes food and fluid and produces Gu Qi, or Food Qi, which in turn is the basis for the production of the body’s Qi and Blood (Maciocia 1989). The Spleen transports Gu Qi to where it is needed in the body and controls the muscles and four limbs, directing refined Qi to the muscles (Maciocia 1989). Matty exhibited signs of a weak Spleen manifesting as poor muscling, low energy, coprophagia (equivalent to eating predigested food), grass eating and a tendency for soft stools. A well-functioning Spleen is dependent on the Liver to ensure a smooth flow of Qi (Maciocia 1989). In Matty’s case, stagnant Liver Qi may well have impaired the Spleen’s function.

Matty exhibited signs of Blood deficiency indicated by various blood parameters (low normal red blood cell values and mild elevation in AST and ALT), a pale lavender tongue and thin, wiry pulse. In TCVM, Blood provides the material foundation for the mind and deficiency in Blood can mani-
fest as uneasiness or anxiety (Maciocia 1996). The Spleen as the source of Blood therefore plays a role in Blood-deficient signs.

If the Spleen is not processing fluids well, this may give rise to Damp, a useless form of fluid that obstructs tissues. Matty exhibits some mild evidence of Damp in the form of copious brown and greasy discharge in his ears.

The Liver is essentially the regulating and harmonizing organ of the body (Maciocia 1996). Not only does it ensure the smooth flow of Qi throughout the body, but also the smooth flow of emotions. Stagnant Liver Qi therefore has a significant negative impact on the emotional state of an individual. In order for the Liver to work well in regulating Qi and Blood, it requires a good supply of Qi and Blood, therefore pathology involving the Spleen will also impact the Liver. This is a self-propagating dynamic with Spleen weakness creating Liver weakness and Liver weakness creating Spleen weakness. Effective treatment needs to act at each of these links in the cycle. Getting these two organs back in harmony was the initial aim of Matty's treatment.

**TCVM Treatment and Results**

**Initial formula:** XYS at ½ tsp am, ¾ tsp pm

XYS was chosen as Matty was showing signs of Liver Spleen disharmony. This involves Liver Qi stagnation, Liver Blood deficiency and Spleen Qi deficiency. In Liver Spleen disharmony, each of the aforementioned patterns can impact on, or be influenced by, the others so it is important to treat each in a balanced way (Yang 2010). The broad function of this formula is to gently disperse stagnant Liver Qi, tonify Blood and tonify Spleen Qi. It also has some limited Damp-resolving capacity. XYS contains Chai Hu (Bupleurum chinense), Bo He (Mentha haplocalyx), Dang Gui (Angelica sinensis), Bai Shao (Peony lactiflora) Bai Zhu (Atractylodes macrocephala), Fu Ling (Poria cocos) and Gan Cao (Glycyrrhiza glabra) (Chen and Chen 2009).

**Diet**

The diet was good, having been changed from a largely dry food basis when Matty entered his current home, to include liver and vegetables such as dark greens (eg kale, spinach) and beetroot, all good Blood tonics. I advocated a fish oil supplement: 2–3 x 1000mg/d (a good Blood tonic). A spirulina/chlorella supplement was suggested as another good Blood tonic. In addition, a diet high in tryptophan amino acids (eg beef liver, tuna, turkey) may be of benefit as tryptophan is the precursor to serotonin (Marsden 2010).

The foster carer provided regular feedback on Matty’s progress. Within three weeks of beginning XYS, he had gained 2kg and was off Reconcile®, his behavior had become less frantic and would settle more quickly when upset. A permanent home was found for him at this time. He moved in with an elderly Weimeraner with minimal problems. Matty was maintained on XYS and continued to make progress in his new home. Within three weeks of being there, he was able to have some off lead walks and would return to the owner when called.

**First follow-up appointment**

This was arranged at Matty’s new home approximately three months after his initial presentation. He had been without XYS for three weeks. He had put on muscle and fat and was in danger of being called overweight (he was still on a raw meat and vegetable diet with raw bones). Matty’s head, once sunken and boney, was well muscled. He still ate quite a bit of grass, had the occasional vomit and was coprophagic. He only ate the other dog’s feces, not his own anymore.

His ears were fine and had little body odour. Ventrally, the area was irritated, had been licked and had a great deal of erythema and brown discoloration of skin and fur. Matty radiated heat from the vertex of his head and lateral limbs. His tongue was now pink to dark pink (pale lavender previously). His pulse was now strong, broad, moderately fast and slightly slippery (thin and wiry previously). Matty’s TCVM patterns had clearly changed. He was now showing more signs of Damp Heat (overweight, ventral erythema, discoloration and irritation, body heat radiation, strong, broad, moderately fast and slightly slippery pulse). The Liver Spleen disharmony appeared to have transitioned to primarily a Spleen pattern (vomiting, grass eating and coprophagy) with Damp Heat.

**Subsequent formula:**

**Si Miao San (SMS) at ¾-1 tsp bid**

SMS is a cooling, damp-draining formula with Spleen support. It contains Yi Yi Ren (Coix lachrymal jobi) (drains Damp, supports the Spleen), Cang
Zhu (Atractylodes lancea) (tonifies Spleen, drains Damp), Huang Bai (Phellodendron amurense) (clears heat, dries Damp) and Huai Niu Xi (Achyranthes bidentata) (moves Blood) (Marsden 2010).

Second Follow-up Appointment
This was arranged three months after Matty started SMS and he had finished the SMS supply two weeks previously. Matty was now 31kg (68+pound), looked in good body condition and was well muscled. He was no longer coprophagic, ate grass but not to excess, his stools were well formed and he no longer vomited. His skin was very much improved with no sign of erythema or irritation. Matty’s tongue was pink to dark pink. His pulse was of moderate rate, reasonable thickness and tone. His owner was happy with his behavior, although he still whined and circled in the car. Matty had also begun ‘Tracking’.

During October/November 2012, Matty gained his ‘Tracking Dog Excellent’ title. He regularly socializes without any issues at the Weimeraner Social Club.

Discussion
TCVM
From a Traditional Chinese Medicine perspective, Matty clearly showed symptoms of Spleen Qi deficiency, Liver Qi stagnation and Blood deficiency. His anxiety was a manifestation of disharmony between Liver and Spleen and the Blood deficiency. XYS addresses each of these patterns.

Chai Hu enters the Liver meridian, is ascending and dispersing in nature, moving stagnant Liver Qi (Yang 2010). Acrid Bo He also enters the Liver meridian providing some aid to Chai Hu in moving stagnant Liver Qi (Yang 2010). It’s cool nature helps disperse heat from the Liver channel built up due to Liver Qi stagnation (Marsden 2010). If Liver Qi is not flowing well and aiding the free flow of emotions, anxiety and irritability may emerge (Maciocia 1989).

Free flowing Liver Qi also promotes the transformation, transportation functions of the Spleen, therefore aiding digestion. Liver Qi ensures the smooth flow of Bile, which again supports digestion (Maciocia 1989). Stagnant Liver Qi therefore impacts on the Spleen’s normal functioning. Conversely, the Liver needs an adequate and reliable supply of Qi and Blood in order accomplish its role in maintaining the smooth flow of Qi in all directions; this supply is highly dependent on unimpeded Spleen function.

XYS contains Bai Zhu, Fu Ling and Gan Cao, being three of the four herbs found in Si Jun Zi Tang, the quintessential Spleen tonifying formula (Marsden 2010). Bai Zhu is sweet and warm, enters the Spleen meridian, strengthens the Spleen and tonifies Qi. It is has a Bitter aspect which drains any accumulated Damp from the Spleen (Bensky 2004). The blandness of Fu Ling helps to leech Damp, while its sweetness supports the Spleen (Bensky 2004). Further, Bai Zhu helps to calm the mind (Chen and Chen 2004). Gan Cao is a good harmonizing herb, sweet in nature, tonifies the Spleen and benefits Qi (Chen and Chen 2004).

As mentioned previously, Blood houses the mind. If Blood is deficient then a certain amount of anxiety may be evident. XYS contains Dang Gui and Bai Shao, herbs that tonify Blood and are often used together for this function (Yang 2010). Dang Gui is warm and acrid, tonifies and moves Blood. Bai Shao is cool, bitter and sour, it nourishes Blood and astringes Yin. Together, they tonify the Yang and Yin aspects of Blood (Yang 2010).

The final herb in XYS is Sheng Jiang. It is an acrid and slightly warm herb that enters the Spleen and Stomach, harmonizing and warming the Middle Jiao (Chen and Chen 2004).

It is probable in Matty’s case that Spleen Qi deficiency may have developed as a consequence of his poor diet and poor access to food in his original home. Once the Liver Spleen disharmony had improved, the underlying Spleen pattern was laid bare (weight gain, vomiting, coprophagy, slippery pulse). The initial Spleen Qi deficiency may have led to a deficiency in Liver Blood. Without an adequate Blood volume, Liver Qi would have stagnated giving the initial symptoms of Liver Spleen disharmony and anxiety. Emotional distress from living in an unsupportive environment may have contributed to the Liver Qi stagnation.

The final formula SMS supported the Spleen while draining Damp Heat. Both Yi Yi Ren and Cang Zhu drain and dry Damp while strengthening the Spleen (Chen and Chen 2004). Huang Bai drains Damp but also clears heat and Huai Niu Xi activates blood circulation (Chen and Chen 2004). In Matty’s case this formula was probably quite effective at removing Damp from the Middle Jiao, enabling...
the Spleen to function more effectively. SMS was able to improve Matty’s residual Spleen deficiency symptoms and Damp Heat signs. With the foster carer and new owner, Matty was in stable, emotionally nourishing environments. Together with a healthy diet, this would have contributed to his recovery.

Pharmacology

Serotonin, or 5-hydroxytryptamine (5-HT) is one of the key neurotransmitters involved in depression and anxiety disorders. It is found throughout the body including the central and peripheral nervous systems, gastrointestinal tract, cardiovascular and immune systems (Walstab et al 2010). Serotonin is believed to be responsible for general awareness, feelings of well-being and facilitation of appropriate social interactions (Gaughan 2006). It is believed low levels of serotonin can lead to anxiety related disorders (Fernandez and Gaspar 2012). There are many different subtypes of serotonin receptors (Overall 2011). 5HT-3 receptors are expressed in brain areas associated with anxiety and mood. Animal studies have led to the view that 5HT-3 antagonists have anxiolytic effects (Rajkumar 2010). 5HT-1 receptors appear to be the focus of many behavioral drugs used in animals (Overall 2011). Many individual constituents of XYS target the serotonin receptors (Qin et al 2011).

GABA is a major inhibitory neurotransmitter in the mammalian brain (Singhuber 2012). It has a role in regulating the level of awareness and anxiety in mammals. It is also involved in memory, learning and muscle tension (Gaughan 2006). GABA receptors are the target of benzodiazepine and barbiturate drugs (Gaughan 2006). Constituents of herbs in the XYS formula (eg Bai Zhu) may exert anti-anxiety effects by targeting these receptors (Singhuber 2012).

BDNF is a growth factor present in the brain believed to have an important role in neurogenesis, neuroplasticity and neuron resilience (Ball 2013). It has been implicated in the pathophysiology of depression and anxiety. During stress conditions in animal studies, BDNF may become dysregulated leading to neuronal atrophy and cellular loss (Ball 2013). Herbal components of XYS, such as the peony glycosides (from Bai Shao) have been shown to elevate BDNF and relieve depressive symptoms (Mao et al 2011).

A number of studies below indicate how XYS, and components of XYS, elicit anti-anxiety effects. A study involving Jia Wei Xiao Yao San (Xiao Yao San with two extra herbs, Zhi Zi and Mu Dan Pi), found it reduced anxiety behaviour in rats exposed to an enhanced, single prolonged-stress paradigm. This consisted of two hours constraint, a 20-minute forced swim, ether induced loss of consciousness and electric foot shock (Wang 2009).

Depressive-like behaviour induced in mice through repeated cortisone injections was relieved by treating the mice with total glycosides of peony (from Bai Shao) (Mao et al 2011). This treatment increased BDNF production in the frontal cortex and hippocampus and it was postulated the BDNF increase in this area relieved the depressive symptoms (Mao et al 2011).

A recent study identified a number of constituents of ginger (Sheng Jiang). It found the whole lipophilic component extracted from ginger partially activated 5HT 1a receptors (Nievergelt et al 2010). These are believed to be the dominant receptors responsible for anxiolysis. Further, they are believed to be involved in the mechanism of action of a number of antidepressant drugs, including fluoxetine, by signaling the neuron to slow serotonin transmission (Nievergelt et al 2010) (Gaughan 2006).

Chai Hu has been found to have an affinity for dopamine D2, 5HT-1a receptors and GABA receptors (Liao et al 1995). In a recent study involving rats, Chai Hu increased levels of BDNF and decreased immobility time during a forced-swim test (the immobility is believed to represent a ‘state of despair’ and model for depressive behaviour) (Seo et al 2012).

Constituents of Bai Zhu, Atractylenolide II and III, have been found to have a positive modulatory activity on the GABA receptor. GABA is the major inhibitory neurotransmitter in the mammalian brain and its activation is believed to have anxiolytic and sedative effects (Singhuber et al 2012).

Dang Gui has been found to have an affinity for GABA and 5HT1a receptors (Liao et al 1995). A study involving mice indicated the essential oil of Dang Gui had an anxiolytic effect and activation GABA receptors were believed to be partly involved (Chen et al 2004).

Constituents of Bai Zhu, Atractylenolide II and III, have been found to have a positive modulatory activity on the GABA receptor. GABA is the major inhibitory neurotransmitter in the mammalian brain and its activation is believed to have anxiolytic and sedative effects (Singhuber et al 2012).

Gan Cao (in the form of an ethanol extract of...
Glycyrrhiza glabra and its flavonoid Glabrol have been found to have a positive modulation effect on GABA(A)- benzodiazepam receptors. This may explain its neurological properties relating to its anxiolytic, antidepressant and anticonvulsant effects (Cho et al 2012).

Conclusion
XYS may be useful in the treatment of anxiety in dogs with the appropriate TCVM diagnosis. Many constituents of Xiao Yao San appear to exhibit centrally acting effects on the brain’s neurotransmitters and neuroreceptors.

References


### Appendix 1. Biochemistry and Hematology - Matty

<table>
<thead>
<tr>
<th>Test</th>
<th>Result 21/1/11</th>
<th>Reference range</th>
</tr>
</thead>
<tbody>
<tr>
<td>RBC</td>
<td>5.8</td>
<td>5.5-8.5 x 10 /L</td>
</tr>
<tr>
<td>WBC</td>
<td>5.9</td>
<td>6-17</td>
</tr>
<tr>
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<td>47-228 U/L</td>
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<tr>
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<td>Chol</td>
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<td>3.3-6.9 mmol/L</td>
</tr>
<tr>
<td>Total T4</td>
<td>20.8</td>
<td>17-37 pmol/L</td>
</tr>
</tbody>
</table>
Case Report
Acute Glaucoma: Treatment with Long Dan Xie Gan Tang

Roo Makosky, DVM CVA

Abstract
This report demonstrates the integrative use of the Chinese herbal formula Long Dan Xie Gan Tang to treat acute glaucoma in a middle-aged neutered Brittany spaniel. Despite slightly elevated intraocular pressure, the patient maintained long-term vision and good comfort on this formula alone. The formula’s anti-inflammatory and neuroprotective effects are the proposed methods of action in the treatment of glaucoma.

Introduction
Acute glaucoma in dogs often presents with a red and painful eye. It is most often initially unilateral, but can become a bilateral condition. Initial emergency management can be successful with the use of topical or injectable medication. Long-term management can be challenging and may involve multiple chronic topical or oral medications, laser ablation of the ciliary body, or eventual surgical enucleation. Many clients are unable to maintain long-term treatment obligations or the financial commitment of expensive medications or advanced surgery. They eventually opt for enucleation of the affected eye or eyes. A simple and affordable method to manage canine glaucoma, preserving both the globe and the vision, is desirable.

Signalment and History
Corey, an eight-year old, male neutered Brittany spaniel, was presented for acute glaucoma. He had been seen earlier in the day by another veterinarian for a suddenly red and painful right eye. There was no corneal erosion. Intra-ocular pressure (IOP) obtained by applanation tonometry (Tonopen) on the right eye was 63 mm Hg, while the left eye had a normal IOP of 15 mm Hg. The right eye was treated with Xalatan (latanoprost) topical drops twice over the next three hours and the pressure dropped to 35 mm Hg and stabilized. The dog’s comfort improved. The client declined further Western treatments, including referral, due to expense and was interested in alternative strategies, including Traditional Chinese Medicine as first line treatment.

Diagnosis
Corey was diagnosed with acute glaucoma, seizure disorder, aggression and dermatitis/otitis. From a Traditional Chinese Medicine perspective, he was diagnosed with Liver Yang rising and Damp Heat.

Treatment and Outcome
The client did not want to fill a prescription for eye medications because of their cost. She was advised about the severe nature of acute glaucoma and the potential for vision loss and pain necessitating surgery. She declined ophthalmology referral, so a definitive ophthalmologic cause of the glaucoma was never known. Corey was given another drop of Xalatan in the office and then started on Long Dan Xie Gan Tang (LDXGT) granules (Natural Path Herbs) at ½ tsp every 12 hours. The owner

Corey’s history included episodic aggression over the last six years. He was generally a friendly dog but would sometimes suddenly turn and attack, usually without apparent cause. When this occurred, it was difficult to get him to relax again. He has had sporadic seizures over the last three years and been treated with zonisamide. Corey has had elevated alkaline phosphatase and chronic otitis externa. The client had noted red and inflamed gums in the two days prior to glaucoma diagnosis and increased seizure activity over the last two weeks.
was also instructed to use a medicated bath for the skin and feet and topical medication was prescribed for the otitis. Zonisamide was continued as previously prescribed. The client was asked to come back once daily for the next week to be given additional daily doses of Xalatan from the hospital supply while the herb effects were building. At the end of Week 1, Corey’s eye was comfortable and clear, with no sign of corneal edema or uveitis. Retinal exam was normal. Right eye IOP was normal at 17mm Hg, compared to left eye IOP at 15mm Hg. Xalatan drops were discontinued at this point and the herbal formula alone was continued. At the end of Week 1, Corey’s eye was comfortable and clear, with no sign of corneal edema or uveitis. Retinal exam was normal. Right eye IOP was normal at 17mm Hg, compared to left eye IOP at 15mm Hg. Xalatan drops were discontinued at this point and the herbal formula alone was continued. At the end of Week 2, right eye IOP had risen to 28mm Hg, but Corey was comfortable, the eye was still visual and its exam was generally unchanged. The client had used the topical ear medication and shampoo only once. Despite this, the dermatitis on the feet and the groin was resolving. The ears still had an odor, but there was no moisture and minimal debris. The tongue was dark pink, but not red. Pulses were full, but not as wiry.

At the end of Week 4, Corey’s skin and ears were essentially normal, the right eye was comfortable and visual. Right eye IOP was still slightly elevated at 28mm Hg. There had not been any seizures or episodes of aggression during this time. His tongue was a light pink and pulses were much softer, almost slippery. He had developed diarrhea and because of this, he was started on Si Miao San (SMS) for Spleen support at ¼ tsp bid in addition to LDXGT. After eight weeks, Corey’s gingivitis had resolved as well. He had had only a single mild episode of aggression that he seemed to come out of relatively quickly. He had not had any seizures. Right eye pressure maintained at 28mm Hg and the left eye continued to have an IOP of 15mm Hg. At this point, I felt the initial presenting Liver Yang rising had resolved and elected to discontinue LDXGT and SMS and replace them with Xiao Yao San to soothe Liver Qi and support Spleen function. I felt the latter was an underlying deficiency and cause in the generation of Damp and Damp Heat. The formula LDXGT has overall properties to clear Heat and drain Damp, especially from the Liver channel (Fougere 2010, Chen and Chen 2009). Fire in the Liver channel tends to travel upwards, creating hot, painful eyes and ears, while Damp Heat in the Liver channel goes downward to the genital area, creating turbid urine, dysuria, or discharges (Chen and Chen 2009). LDXGT’s pharmacologic effects are antibacterial and anti-inflammatory, anti-allergic, immunostimulant and cardiovascular (hypotensive). These all reflect its characteristic taste of bitter and cold (Chen and Chen 2009). At least 51 different flavonoids have been found in the formula (Wang et al 2008) and these are likely to be largely responsible for its actions. According to the compilation of research by Chen and Chen (2009), LDXGT has been studied for hypertension, hepatitis, gastritis, hyperthyroidism, migraines, headaches, and a variety of other conditions.

### Discussion

Glaucoma is characterized by ‘too much energy in the head’ due to Liver Yang rising (Wynn and Marsden 2003). This syndrome has components of Heat, that can include the signs of irritability, vomiting and ocular pain. Deep red tongue and wiry pulses confirm the diagnosis. Underlying Liver Damp Heat or Yin deficiency exist concurrently. The syndrome is treated with LDXGT (Fougere 2010), also known as Gentian Drain the Liver.

It might be expected that the chronically high IOP in Corey’s right eye would cause poor vision or blindness due to eventual neuropathy of the optic nerve. This case and the research presented in this paper suggest that preservation of microcirculation to the optic nerve may be more important than specific reduction of intraocular pressure in preserving vision and reducing pain in the management of glaucoma. In a rabbit study examining the effects of the herb Salvia, it was found that administration of Salvia resulted in less optic nerve and capillary pathology despite similar IOPs compared to saline administration (Zhu and Cai 1993). Early glaucoma has been shown to have decreased antioxidant systems in the aqueous and lacrimal fluids and that increases in retinal glutathione protects the blood supply to the optic nerve (Head 1999, Head 2001). These studies confirm the need to preserve optic nerve blood supply and an antioxidant-rich local environment.

The formula LDXGT has overall properties to clear Heat and drain Damp, especially from the Liver channel (Fougere 2010, Chen and Chen 2009). Fire in the Liver channel tends to travel upwards, creating hot, painful eyes and ears, while Damp Heat in the Liver channel goes downward to the genital area, creating turbid urine, dysuria, or discharges (Chen and Chen 2009). LDXGT’s pharmacologic effects are antibacterial and anti-inflammatory, anti-allergic, immunostimulant and cardiovascular (hypotensive). These all reflect its characteristic taste of bitter and cold (Chen and Chen 2009). At least 51 different flavonoids have been found in the formula (Wang et al 2008) and these are likely to be largely responsible for its actions. According to the compilation of research by Chen and Chen (2009), LDXGT has been studied for hypertension, hepatitis, gastritis, hyperthyroidism, migraines, headaches, and a variety of other conditions.
shingles, pelvic inflammatory disease, polycystic ovarian syndrome and others characterized by heat intolerance, agitation, restlessness, and inflammation. LDXGT can be used for any acute eye disorder (Fougere 2010), but especially acute glaucoma with eye pain, irritability and vomiting (Wynn and Marsden 2003).

Its anti-inflammatory and immune-mediating properties were demonstrated in a mouse model of systemic lupus erythematosus (SLE). Lee and Chang (2010) showed that mice who received LDXGT had more T-helper cells, fewer inflammatory leukokines, fewer immune complex deposits and increased renal glutathione levels. Glutathione further protected the mice from effects of inflammatory mediators. The authors felt the formula limited the progression of SLE syndrome in these mice. LDXGT formula is composed of ten individual herbs, each with known pharmacologic properties and traditional medicine functions (Table 2). In this formula, the properties of individual herbs contribute especially to the formula’s cooling and anti-inflammatory effects. Gentian root (Long Dan Cao), for which the formula is named, is bitter and cooling. It enters the Liver, Gall Bladder, and Stomach channels. It has properties of clearing Damp Heat in the Liver and Gall Bladder and sedating rising Liver fire (Chen and Chen 2004), thus making it a very appropriate herb to use in Corey’s case. Gentianine (a gentian component) was shown to suppress production of the inflammatory mediators tumor necrosis factor and interleukin-6 in rats given bacterial lipopolysaccharide, a potent inducer of inflammation (Kwak et al 2005). In another rheumatoid rat model study, the authors found administration of gentian resulted in reduction of inflammation and inflammatory prostaglandins to a level comparable to that of prednisone (Yu et al 2004). Gentian species have been investigated for their neuroprotective properties. In a study of experimentally induced epilepsy in mice, the gentian treated mice showed improved seizure control due to effects at the GABA channels or sodium-dependent ion channels (Mustafa et al 2011). Further, gentian has been found to inhibit monoamine oxidase B which contributes to age-related neurodegeneration (Mazzio et al 2012).

Scutellaria, another prominent herb in the formula, has also been found to have significant anti-inflammatory and neuroprotective effects. It too is bitter and cooling. Its actions are to clear Heat and drain Damp, sedate fire, eliminate toxins and cool Blood (Chen and Chen 2004). The herb was found to have significant anti-inflammatory and antioxidant properties in both a free-radical scavenging model and a biologic yeast model (Zhang et al 2011). Scutellaria herb is also neuroprotective and was found to reduce hemorrhage, edema and blood-brain barrier permeability after injury to the blood-brain barrier in rats (Shin et al 2012). At least two of Scutellaria’s major components, baicalin and woginin, have been implicated in neuroprotective effects by reducing blood-brain barrier permeability after oxygen and glucose deprivation (Zhu 2012) and reducing pathogenic inflammatory responses in neurodegenerative disease (Lee et al 2003).

Research is available on the other herbal ingredients in LDXGT, as well as much more on the previously discussed herbs, detailing their anti-oxidant, anti-inflammatory, and neuroprotective nature. Unfortunately, much of this research is unavailable to this author as it is often published in Chinese, Korean or Russian.

Conclusion
Acute glaucoma is symptomatic of too much Yang energy rising to the head. In Corey’s case, there were seizures and aggression, aiding in confirmation of diagnosis. The client was satisfied with improvement in the condition of the dog’s eye and the added benefit of reduction of seizures and aggression. The client declined any Western treatment other than initial emergency management. Although Corey’s eye was visual, IOP remained slightly high.

In human tertiary-care clinics, 11% of glaucoma patients were found to use some form of complementary medicine, most without telling their physicians (Wan et al 2012). This number is likely to be larger if primary-care clinics were sampled. It is likely a sampling of our veterinary patients would yield similar, if not even higher numbers. Therefore, it behooves us as scientists and clinicians to become familiar with the effects of these plant medications. With further research, LDXGT may become part of an affordable and effective management strategy in the treatment of acute and chronic glaucoma in the dog.
### Table 1: Traditional Chinese Veterinary Medicine Etiology of Symptoms

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Etiology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Red and painful eye</td>
<td>Liver Yang rising, Heat, Qi stagnation</td>
</tr>
<tr>
<td>Aggression</td>
<td>Liver disorder, Yang rising, Phlegm obstruction, Qi stagnation</td>
</tr>
<tr>
<td>Seizures</td>
<td>Yang rising, Phlegm obstruction</td>
</tr>
<tr>
<td>Otitis, pungent</td>
<td>Heat, Damp</td>
</tr>
<tr>
<td>Pododermatitis</td>
<td>Heat, Damp, Liver-Blood deficiency</td>
</tr>
<tr>
<td>Gingivitis</td>
<td>Heat, Upper Burner</td>
</tr>
<tr>
<td>Intermittent vomiting</td>
<td>Stomach/Spleen deficiency, Qi obstruction</td>
</tr>
<tr>
<td>Increased ALP (alkaline phosphatase)</td>
<td>Damp Heat</td>
</tr>
<tr>
<td>Preputial discharge</td>
<td>Damp, Liver channel</td>
</tr>
<tr>
<td>Tongue red</td>
<td>Heat</td>
</tr>
<tr>
<td>Pulse wirey, forceful, strong, fast</td>
<td>Heat, Qi stagnation</td>
</tr>
<tr>
<td>Diarrhea after LDXGT</td>
<td>Spleen deficiency, Damp</td>
</tr>
<tr>
<td>Deep sleep</td>
<td>Damp</td>
</tr>
<tr>
<td>Agitated/nervous</td>
<td>Liver deficiency, Yin deficiency</td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>Heat, Damp, Liver</td>
</tr>
<tr>
<td>Pinnal erythema</td>
<td>Heat</td>
</tr>
<tr>
<td>Increased thirst</td>
<td>Yin deficiency, Heat</td>
</tr>
<tr>
<td>Dry diet</td>
<td>Spleen deficiency, Heat</td>
</tr>
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</table>

(Chen and Chen 2009, Marsden 2008)

### Table 2: Herbal Components of LDXGT

<table>
<thead>
<tr>
<th>Herbal Component</th>
<th>Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rehmannia root</td>
<td>Sheng Di Huang (Cools Blood, protects and replenishes Yin)</td>
</tr>
<tr>
<td>Angelica root</td>
<td>Dang Gui Shen (Prevents Qi and Blood stasis,)</td>
</tr>
<tr>
<td>Gentian root</td>
<td>Long Dan Cao (Clear Heat from Liver, dry Damp)</td>
</tr>
<tr>
<td>Alisma tuber</td>
<td>Ze Xie (Drain Damp from Triple Burner and Upper Burner, cool Upper Burner)</td>
</tr>
<tr>
<td>Poria</td>
<td>Fu Shen (Drain damp, cools upper burner)</td>
</tr>
<tr>
<td>Bupleurum</td>
<td>Chai Hu (Prevents Qi and Blood stasis, soothes Liver Qi, guides formula to Liver, Triple Burner and Gall Bladder)</td>
</tr>
<tr>
<td>Plantain seed</td>
<td>Che Qian Zi (Drain Damp, cool Upper Burner)</td>
</tr>
<tr>
<td>Licorice root</td>
<td>Gan Cao (Harmonizes formula)</td>
</tr>
<tr>
<td>Scutellaria root</td>
<td>Huang Qin (Drain Liver Heat, dry Damp)</td>
</tr>
<tr>
<td>Gardenia fruit</td>
<td>Zhi Zi (Drain Liver Heat, dry Damp, guides to Triple Burner and Gall Bladder)</td>
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(Chen and Chen 2009, Marsden 2008)
References


Vitality, Mitochondria, Real Healing and Integrative Veterinary Medicine
Richard Palmquist, DVM

Vitality and Energy in Medicine
From the beginning of medical history, humankind observed that illness changed a patient’s characteristics and led to development of signs and symptoms. One of the first things a clinician observes on examination is patient ‘vitality’. This word was first used in 1592 and is defined as:

1) (a) the peculiarity distinguishing the living from the nonliving;
   (b) capacity to live and develop; physical or mental vigor especially when highly developed

2) (a) power of enduring;
   (b) lively and animated character [1].

Monitoring vitality is part of the re-evaluation process and leads to various prognoses as patients move through treatment programs.

We know energy is a variable. Living organisms consist of energy, seek it out and alter it to achieve homeostasis – vital for their continued existence. Biological sciences are dedicated to understanding that process and the energies involved.

Many complementary and alternative veterinary medicine (CAVM) modalities refer to fundamental energy, or energies that are manifested in living organisms [2]. Difficulties in delineating, demonstrating and defining these terms can generate disagreement and professional travail. Terms like Qi from Chinese medicine, Vital Force in homeopathy and Innate Intelligence in chiropractic all refer to poorly definable factors and phenomena that practitioners perceive and balance, or attempt to manipulate or influence [3,4].

Terminology, understanding and paradigms
As our ability to understand various forms and behaviors of energy increases, our ability to integrate therapies also increases. Only a few years ago, the idea that cells emit photons and could be affected by light elicited scoffs. We now know this is accurate and routinely use lasers and other photo-therapies in our work to help patients. As we study how the body transmits and uses photons, we see a field in its infancy. Research will help to better delineate the usefulness of photons and our ability to use them to monitor therapeutic responses [5,6,7]. It is possible that some medical interventions may affect photon production or transmission and there may be a new category of therapy in the future [8]. A growing evidence base is necessary for precise terminology and to improve our ability to communicate.

Medicine functions within paradigms. These belief systems evolve based upon what we can perceive and conceive of our world [9]. Words and definitions develop depending upon our ability to perceive and conceptually describe energy forms. Ultimately, in reductionist medicine, we seek a Thing that exists in present time, so we can observe and document its behavior and relationship to other Things. For example, for many years the idea ‘exogenous pathogens’ existed. On discovering bacteria, germ theory gained momentum as investigators were able to fulfill Koch’s postulates for each pathogen. This led to discovering ways to fight bacterial infection and the creation of drugs to fight bacterial infections. Discovery of the cell membrane’s molecular nature and its receptors that communicated with the nucleus, opened the door to therapies affecting receptor function.

As we perceive new things, our paradigms shift to align known information with new knowledge. When evidence rises to a level of wider acceptance, rapid changes in paradigms occur.

Words developed in all fields are mental tools to tell the story to those who have yet to see or use the Thing. The very new realization that energy is a Some-Thing, tangible and when subdivided to its source appears to come from No-Thing [9], may explain why there is difficulty understanding energy medicine. Its root is No-Thing, not nothing – conceptual but real. It is yet to be categorized and understood.

The idea that No-thing exists and can change characteristics simply by having someone view it is mind boggling. How do we describe No-thing and its qualities? Physics works on that every day. Chinese medicine simply calls it Qi and continues to assist patients and study its effects on living systems. 3,000 years later, we are beginning to see
how these old, more descriptive terms connect to our knowledge of cell and tissue function.

Intuition, Science and Investigation
It is important to note that a century ago we had no idea how cells generated energy. As investigators developed better methods to examine cells, they discovered organelles and gradually delineated their proposed functions. We learned about glycolysis, the Kreb’s cycle and electron transport. Enzymes transfixed our attention as did gene activation and transcription. Discovery of the chemical structure of DNA revolutionized genetics and arose from pioneering genius applied intuitively and analytically over a long time [10]. DNA’s structure was ‘figured out’ on paper before investigation confirmed it. New observations led to hypotheses and further investigations, gradually knowledge increased and what was believed to be impossible was shown to be normal [11]. We are beginning to understand how energy medicines like acupuncture and homeopathy work by affecting all cellular structures.

A paradigm shift in energy medicine?
Where our ability to perceive aligns with our interest, there are scientific frontiers. Currently there is a massive increase in medical understanding due to the importance of mitochondria and cellular cross talk in energy production and cellular regulation. Discovered over a century ago, mitochondria are theorized to be symbiotic bacteria that moved into the cell to exchange improved energy production for a safe environment. Perhaps mitochondria had different origins and impacts on cellular development. Such discussion is more philosophical than useful for our patients. Mitochondria have their own separate bacterial DNA inherited from the maternal line. It was thought they produced energy only, but it is becoming evident they are intimately involved in bioregulation, having direct effects on the cell’s genomic expression. For a review of this subject see [12,13,14].

Historically, pioneering clinicians in CAVM and CAM actively sought out agents for their ability to improve patient vitality. As they experimented with these agents to improve patient conditions, especially those failing conventional therapies, animal guardians reported improved vitality. This manifested as a brighter appearance, improved activity and mobility, better appetite, improved digestion, stool or bowel habits, etc. The descriptions outline improved energy status of the organism.

Following improved vitality, pioneering clinicians led patients to recovery and observed differences between suppressive therapies and ones that stimulated and collaborated with the patient’s unique bioregulatory efforts. With further research, investigators realized that therapeutic nutrition and herbs were often antioxidant in their properties [15]. Tonic herbs such as red ginseng were shown to protect mitochondria [16]. In fact, a whole theory of healing and aging arose stating that aging was the effect of reactive oxygen species and subsequent injury to the cell. A branch of CAVM, orthomolecular medicine, used massive doses of vitamins and antioxidants to attempt cure and prevention of various diseases. In these advancing paradigms we learned about enzymes, their induction, production and the process regulating these.

As DNA discoveries gave understanding of gene regulation, we learnt that gene expression could be activated by environmental factors from food to pharmaceuticals [17]. The new genomics age saw us value not just Some-Things, but their relationships and interactions.

New discoveries fuel theories that show degradation and degeneration of mitochondria precede chronic inflammation and degeneration. There are abundant chronic diseases with mitochondrial elements and we can address and improve those negative factors [18, 19].

After years of discovery and paradigm shifts, clinicians still begin by observing patient vitality, monitoring it and other parameters that reflect improved homeostatic control. Vitality can be directly observed and is the difference between animated and inanimate matter. Our clients prefer their animals to be animated for as long as possible.

Most professionals practice ‘first do no harm’. If we discover that many drugs harm mitochondria,
then we must evaluate our propensity to use such drugs. For example, a pediatric patient has a low grade fever of unknown origin and we know that nonsteroidal anti-inflammatory drugs (NSAIDs) or antibiotics can harm mitochondria and thereby the patient’s ability to generate and use energy. We should seek better ways to address the condition or be open to healing with, for example, herbs, antihomotoxic or homeopathic agents.

In a recent Veterinary Information Network rounds, veterinary pharmacologist Lester Mandelker, challenged the class to find information on mitochondrial health and damage and to choose if they wanted to continue approaching chronic disease using agents that suppressed symptoms, while damaging the body. Alternatively, they could find and apply treatment options that address the fundamental conditions leading to mitochondrial degeneration, thereby treating the root of diseases [20, 21]. This is the challenge we face as medical practitioners. It is what attracts many of us to CAVM and integrative veterinary care. I believe that veterinarians are good people and that selecting therapies to support the patient will win out.

Listed below are factors relating to mitochondria and chronic disease. As you examine them, consider both research to document the effect of CAVM modalities on mitochondria and current directions in integrative veterinary medicine:

- Each liver cell in a human has between 1,000 and 2,000 mitochondria.

- Mitochondria self-replicate. Once the population is diminished it may be a long time before it repairs itself. Delayed repair may compromise immunity and cell regulation.

- Many toxins create damage the structure, number and regulatory ability of mitochondria. Environmental contamination with cadmium leads to renal damage through mitochondrial compromise. Insecticides and other toxins damage mitochondria as do viruses, fungi, bacteria and radiation. These agents are linked to development of autoimmunity [22, 23].

- Drugs toxic to mitochondria include: antibotics, NSAIDs, analgesics, anesthetics (bupivacaine, lidocaine, propofol), antiarrythmics, antipsychotics, antidepressants, barbiturates, statins, chemotherapics (mitomycin c, profiromycin, doxorubicin), mood stabilizers and antivirals [24].

- Stress and negative emotion may affect mitochondria through cortisone excess and negative feedback between other endocrine organs.

- While chronic inflammation predisposes to chronic diseases like diabetes and cancer, we may be able to assist patients with simple actions like nutrition heeding caloric intake, exercise and stress management [25].

- Some drugs seem to preserve or protect mitochondrial function: doxycycline, minocycline, low-dose cyclosporin, dexamethasone and mxelitine are a few examples [21, 26].

- Synergistic effects may lead low doses of substances to have strong regulatory effects at the level of mitochondria and patient DNA. Current testing of single agents for toxicity may not be sufficient to detect these combined toxic reactions. Similarly, low doses of multiple agents may be shown to be protective. Further research is indicated.

- Food, herbs and supplements including vitamins, cofactors, minerals and phytochemicals are some of the largest known protectors of mitochondrial function. Afflicted with the severe degenerative condition, multiple sclerosis, a medical doctor researched the mitochondrial connection and developed a high vegetable diet that lead to her recovery from wheel chair to normal function [27].

- Normal metabolism and food excesses lead to the generation of endogenous toxins that damage mitochondria. Calorie excess generates fat and adipose tissue is the largest endocrine gland in the body. If adipose goes out of regulation, major degenerative processes begin.

- Mitochondria code for apoptosis of cancer cells but cancer cells also use mitochondria to maintain the tumor. There is much to learn before we can better influence tumors, but we are reminded that simple things like exercise and good diet are amongst the most powerful tools to build health.
We are grateful for the support from pioneering clinicians vested in learning more about CAVM. To quote Leonardo DaVinci, ‘a wise person seeks knowledge’. Through our collaboration we become wiser and more effective in helping people and animals live better, longer and more productive lives.

References


Zoopharmacognosy at Work
Cynthia Lankenau

I want to share a case of a horse self-healing with access to weeds.

Knight had been diagnosed with Lyme disease and was treated by a conventional veterinarian. I saw him when he was in liver failure from that treatment. He responded very well to several Chinese formulas.

It was the first case of Lyme disease I’d seen and it didn’t occur to me he might relapse. He did the next spring and the owners refused to put further money into treatment. Rather frustrated, I said that since deer do not get Lyme disease, the owners should put Knight on the large pasture they had. They did and in a month they were riding him again.

I was amazed and spent a day watching Knight. The following was his ‘formula’:

- He dug up and ate the whole yellow dock plant, Rumex crispus. This clears damp heat, reduces liver congestion and removes accumulations.
- He grazed massive amounts of dandelion, Taraxacum officinale. This treats all fire conditions, detoxifies liver and gallbladder as well as being a remedy for hepatitis.
- Red clover, Trifolium pratense. This has an antibiotic effect, clears damp heat and toxins and enriches Yin.
- Black raspberry leaves, Rubus ideaus. This has a hemostatic effect and is an astringent (Culpeper said “it is profitable against the bitings of serpents”).
- A few mustard heads, Sinapsis arvensis. This alleviates body and point pain.
- Wild carrot, Queen Anne’s Lace, Daucus carota. This is diuretic and stimulant, and treats liver disorders and jaundice.
- Violet, Viola papilionacea. This has antipuretic effects and is alterative, cooling the heat of fevers.
- Plantain, Plantago spp. These clear heat and toxins.
- Goldenrod, Solidago virgaurea. This treats fever and jaundice.
- Spruce tree buds, Abies sp. These aid calcium reabsorption and enhance bone healing.

Knight liked to stand on patches of skunk cabbage, Symlocarpus foetidus (with a slightly narcotic and antispasmodic effect) as well as pearly everlasting, Gnaphalium obtusifolium (which Native Americans used on horses’ feet for speed).

Knight often ‘smelt the flowers’ and likely gained positive flower essence effects. Flowers included milkweed, used to aid coping with normal demands and responsibilities.

I have never needed to treat Knight again. As long as he is on pasture, he is his owners’ soundest horse.
Research Updates


Retained placenta remains a therapeutic challenge in cattle. Certain traditional medicines are believed to be able to alleviate retained placenta condition and improve overall fertility in cows. The aim of the present study was to evaluate the efficacy of an herbal tincture for treatment of retained placenta. The herbal tincture was extracted from a combination of Herba Leonuri, Angelicae Sinensis Radix, Flos Carthami, Myrrha and Rhizoma Cyperi. 48 cows diagnosed with retained placenta were randomly divided into one of two treatment: group A receiving herbal tincture orally, and group B receiving oxytetracycline infusion into the uterus. A control group of 86 cows, with no clinically visible pathological conditions following birth, were included in the control group. Retained placenta was expelled within 72h following initial treatment in 19 cows in group A, yet no cows in group B were recorded to expel the placenta in the same time. The median number of days to first service (70.0 vs. 102.5 days; P<0.05) and median number of days open (76.0 vs. 134.0 days; P<0.01) were lower in group A than in group B. Percentage of cows pregnant within 100 days postpartum was the highest for animals in group A compared to controls (61.5% vs. 39.5%, P<0.05), and for animals in group B (61.5% vs. 22.7%; P<0.01). Herbal tincture used in the present study might facilitate expulsion of retained placenta and improve subsequent fertility, thus could present effective treatment option for retained placenta in cows.


Sheng Hua Tang is a classical herbal formula known to be beneficial in alleviating postpartum diseases and facilitating a return to normal reproductive function. The formula consists of Radix Angelicae sinensis, Ligustici rhizoma, Semen persicae, Zingiberis rhizoma, and Radix glycyrrhizae. This study investigated whether the administration of Sheng Hua Tang within 2 to 4 hours after delivery was effective as a preventive treatment for reducing the risk of retained placenta in Holstein dairy cows. A total of 357 cows, each of which had delivered its calf spontaneously, were randomly allocated to one of two groups. In the treatment group, the cows (n = 175) received Sheng Hua Tang with an oral dose of 0.36 g crude herb per kg body weight once daily for three consecutive days. The controls (n = 182) received no treatment. The placental retention proportion was 4.0% and 17.0% within 12 hours after delivery in the treated and control animals, respectively (P < 0.01). There were decreases in the calving-to-first-service interval (73.2 ± 25.1 vs. 81.9 ± 32.8 days; P < 0.01), calving-to-conception interval (93.4 ± 38.8 vs. 114.6 ± 42.9 days; P < 0.01), and service per conception (1.5 ± 0.8 vs. 1.9 ± 1.0 days; P < 0.01) in the treatment group compared with the control group. The first artificial insemination conception proportion was higher in the treatment group than in the control group (60.4% vs. 41.1%; P = 0.01). Moreover, the between-group difference in the proportion of cows that were pregnant within 180 days postpartum approached statistical significance (88.2% vs. 80.6%; P = 0.07). Sheng Hua Tang showed beneficial effects in reducing the incidence of retained placenta and improving subsequent reproductive performance in cows. This preventive treatment strategy would be effective in improving the management of puerperal health. The potential benefits of Sheng Hua Tang warrant further investigation to determine whether this preventive treatment strategy can be endorsed as a general preventive approach in postpartum cows.


Acupuncture is a commonly used therapy for treating functional diarrhea (FD), although there is limited knowledge on the mechanism. The objectives of this study were explore possible mechanisms through an investigation of the differences in brain activities elicited by acupuncture between FD patients and healthy controls (HC). Eighteen FD patients and eighteen HC received 10 sessions of acupuncture treatment
at ST25 acupoints. Functional magnetic resonance imaging (fMRI) scans were, respectively, performed before and after acupuncture. The defecation frequency, Bristol stool form scale (SBFS), and MOS 36-item Short Healthy Survey (SF-36) were employed to evaluate the clinical efficacy. After acupuncture, the FD patients showed a significant decrease in defecation frequency and BSFS score. The regional homogeneity (ReHo) map showed a decrease in the paracentral lobule and postcentral gyrus, and an increase in the angular gyrus, insula, anterior cingulate cortex (ACC), and precuneus in the FD group. Moreover, the changes in ReHo values in the ACC were correlated with the reduction in defecation frequency. Decreasing functional connectivity among the ACC, insula, thalamus, and orbital frontal cortex only existed in the FD group. Conclusively, acupuncture alleviated defecation frequency and improved stool formation in FD patients. The efficacy might result from the regulation of the homeostasis afferent processing network.


Hawthorn (Crataegus oxyacantha) is a widely used Chinese herb for treatment of gastrointestinal ailments and heart problems. In North America, the role of treatment for heart problems dates back to 1800. Currently, evidence is accumulating from various in vivo and in vitro studies that hawthorn extracts exert a wide range of cardiovascular pharmacological properties, including antioxidant activity, positive inotropic effect, anti-inflammatory effect, antiacardiac remodeling effect, antiplatelet aggregation effect, vasodilating effect, endothelial protective effect, reduction of smooth muscle cell migration and proliferation, protective effect against ischemia/reperfusion injury, antiarrhythmic effect, lipid-lowering effect and decrease of arterial blood pressure effect. On the other hand, reviews of placebo-controlled trials have reported both subjective and objective improvement in patients with mild forms of heart failure (NYHA I-III), hypertension, and hyperlipidemia. This paper discussed the underlying pharmacology mechanisms in potential cardioprotective effects and elucidated the clinical applications of Crataegus and its various extracts.
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