

Review

Management of Equine Allergic Airway Disease: A Review of Conventional and Complementary Therapies

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ABSTRACT

Respiratory allergies in horses are a common health problem and can vary from mild discomfort easily managed with husbandry changes to severe, performance-limiting effects with animals unable to participate in their routine training programs. Classic allergies are primarily Type 1 hypersensitivity reactions, in which the body produces immunoglobulin E (IgE) against normally innocuous environmental molecules. Other changes seen with Type 1 reactions include T-cell dysregulation, hyper-reactive responses of various organs (usually lungs and skin), and changes in the secretion of various cell-to-cell mediators. Allergies are generally suspected via history and clinical signs, but advanced tools such as upper airway endoscopy or bronchioalveolar lavage may be needed for confirmation. The key to allergy treatment is environmental changes, but this takes time and may be impossible based on a horse's lifestyle. Conventional medications to treat allergies have focused on anti-inflammatory and bronchodilator administration, which provide rapid relief, while the environment is modified if possible. Integrating traditional Chinese veterinary medicine (TCVM) provides an additional approach to medical treatment that may reduce the need and/or dose of conventional medications, particularly during long-term disease management. It offers a variety of modalities such as acupuncture, Chinese herbal medicine, and food therapy that can be targeted to patient need and temperament. Significant improvement in quality of life may be seen with the individualized patient management that integrating TCVM treatment provides. This paper reviews immune mediated mechanisms associated with allergic respiratory disease and explores both conventional and TCVM based treatment protocols used to treat affected horses.

Keywords: acupuncture, allergies, asthma, Chinese herbal medicine, cough, dyspnea, equine, TCVM, Wind

ABBREVIATIONS: AP: acupuncture; CHM: Chinese herbal medicine; CS: corticosteroids; EAP: electro-acupuncture; IgA: immunoglobulin A; IgE: immunoglobulin E; IgG: immunoglobulin G; RAO: recurrent airway obstruction; TCVM: traditional Chinese veterinary medicine; Th1: T helper cell 1; Th2: T helper cell 2; TNF α : tumor necrosis factor- α

One of the most common non-infectious respiratory conditions in equine medicine is a patient with allergies. These patients often present, due to not only their own discomfort, but the disturbance that it creates in the animal owner's life caused by perceived distress, coughing, sneezing or performance limitations. Horses have a unique place in the human-animal bond through connections formed as they cross the spectrum from pets to performance animals. When they are considered pets, it may be the perceived discomfort that prompts owners to seek treatment. If a horse is managed as a competition animal, performance limitations may be the main concern.

Allergens, the causative agents of allergic disease, can interact with a horse's immune system through 3 main areas: respiratory tract, skin and gastrointestinal tract. These locations are areas of contact between the environment and an animal's immune system. In particular, the act of

inhalation constantly creates exposure of the respiratory tract to allergens. While all feedstuffs can be sources of allergens, stored feeds such as dried hay, which harbor dust, mites or other allergens, are some of the worst offenders.

In this review, allergies will primarily refer to recurrent airway obstruction (RAO) or non-infectious inflammatory airway disease, also known as asthma or heaves. The pathophysiology of this chronic airway condition, as well as optimal management through the integration of both conventional and complementary therapies, will be discussed.

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PATHOPHYSIOLOGY

Hypersensitivity Reactions

Allergen exposure is handled by specific immune cellular pathways. If these reactions are at a subclinical or non-pathologic level, the horse mounts a normal immune response to agents in the environment. When the response becomes excessive, it is termed hypersensitivity and has traditionally been categorized as Type I-IV reactions.^{1,2} New research is prompting further description of allergies based on time to clinical sign emergence.¹ Type I allergic reactions (classic immediate hypersensitivity) occur when a horse produces immunoglobulin E (IgE) antibodies against molecules that are normally considered innocuous (allergens). Type II (cytotoxic) allergic reactions result when allergens are associated with cells or receptors leading to the release of immunoglobulin G (IgG). Type III hypersensitivity responses (immune complex deposition) also depend on IgG [less so immunoglobulin A (IgA)] and other circulating molecules, to form complexes with the antigens under specific conditions and deposit in tissues. Type IV allergic reactions (delayed hypersensitivity) are cell-mediated responses.^{1,2}

In horses, the most common type of allergic reactions are Type I. These hypersensitivity reactions, seen most frequently in atopy or asthma, result from increased IgE production against allergens, T-cell dysregulation, hyper-reactive responses of various organs (usually the lungs and skin), and changes in the secretion of various cell-to-cell mediators.³ When an antigen is presented and encounters its specific antibody, a series of inflammatory mediators are released including, but not limited to, interleukin-8, interferon- γ , and histamine. An imbalance between Th (T helper)1 and Th2 cells play a role in the ongoing inflammatory and allergic response seen in asthma in humans.⁴ Cellular changes cause increased activation of lymphocytes, mast cells and other inflammatory cells.⁵ These changes lead to a cascade of intra and intercellular signaling which result in the clinical signs. Two of the most important responding cells are eosinophils and mast cells. These cells contain molecules such as histamine that activate the signaling cascade leading to respiratory inflammation. The clinical signs are seen relatively soon after the insult, usually less than 6 hours, but sometimes are delayed up to 24 hours.¹ Contrasting evidence exists as to the correlation between atopy and chronic obstructive pulmonary disease, also known as RAO and now, asthma.³

Inflammatory Airway Disease

Horses developing the asthma-like condition of RAO typically respond to antigen exposure (i.e. dusty hay/straw) by developing airway bronchoconstriction, pulmonary neutrophilia and excessive mucous production.^{6,7} Type I hypersensitivity (IgE mediated) to aeroallergens with activation of inflammatory cells, modulation of transcription factors that regulate cytokines [i.e. nuclear factor kappa B (NF-kB)] and release of inflammatory mediators has been the hallmark of RAO

inflammatory airway disease. Some authors also suggest that Type III hypersensitivity reactions play a role in the airway inflammation due to the presence of neutrophilic bronchitis associated with antigen-antibody complex formation and subsequent complement cascade activation.⁶ A principal lesion in RAO-affected horses is bronchiolitis characterized by peribronchiolar accumulation of lymphocytes and intraluminal accumulation of neutrophils. A Type III hypersensitivity explains in part the neutrophilic inflammation in RAO-affected horses.⁶ Both Type I and III hypersensitivity are associated with increased expression of Th1-Th2 cytokines, chemokines, adhesion molecules and release of reactive oxygen species (ROS). Additionally, the regulation of inflammatory gene expression in affected horses is dependent on the binding of transcription factors such as NF-kB, AP-1 (activator protein-1) and CREB (cyclic AMP response element binding protein) to the promoter region of target genes.⁶ It is apparent from research on the mechanisms of RAO that the disease syndrome is a multifaceted and dynamic process.⁶

CLINICAL SIGNS AND DIAGNOSIS

Inflammatory Airway Disease

In horses with severe allergic respiratory disease, signs of respiratory distress may be seen at rest and include flaring of the nostrils, inappetence, and an increased abdominal component creating muscular hypertrophy (i.e. “heave line”) when breathing. At the opposite end of the spectrum, mild respiratory disease may only be noted as a decrease in performance or occasional cough. Diagnosis is established by the findings of airway inflammation in the absence of an infectious agent.⁸ While inflammatory airway disease may be suspected based on the clinical signs, additional testing is indicated to determine the best method of treatment. Testing can include blood sampling, rebreathing exam, airway endoscopy, ultrasonography, thoracic radiography and airway sampling. Confirmation of inflammatory airway disease is based on endoscopy, with a visualized tracheobronchial mucus score over 2-3/5 (depending on horse’s career) or a bronchoalveolar lavage cytology showing mild increases in mast cells, eosinophils, and/or neutrophils (Table 1).⁸ Bronchoalveolar lavage cytology cell differentials are also critical for determining the best medications to use as part of the treatment plan.⁸ Different types of cells are present with different specific allergies, for example mast cell versus neutrophilic inflammation.⁸

Table 1: Confirmatory diagnostic tests and results for horses with inflammatory airway disease

Test	Result
Tracheobronchial Endoscopy	Mucus score greater than 2-3 (out of 5) ⁸
Bronchoalveolar Lavage	Mild increases in mast cells, eosinophils, and/or neutrophils ⁷

Traditional Chinese Veterinary Medicine

When using traditional Chinese veterinary medicine (TCVM) as part of a diagnostic protocol to complement conventional assessment of equine respiratory disease, a practitioner usually integrates results from the conventional diagnostics with Eastern perspectives to evaluate the disease-causing imbalances within the patient’s body. This approach facilitates the goals of Eastern medicine, which is to return a patient to a balanced, healthy state.⁹ In TCVM, the diagnostic system (*Bian Zheng*) or TCVM Pattern diagnosis is determined by clinical history (e.g. patient’s personality, lifestyle, diet, environment, temperature preference) and the TCVM clinical exam (e.g. *Shen*, tongue and pulse characteristics). From the Pattern diagnostics, appropriate TCVM treatment modalities [e.g. acupuncture (AP), Chinese herbal medicine (CHM), diet modification] are then selected.

Respiratory disease, from a TCVM perspective, is associated with the Metal element which contains the *Zang-fu* organs: Lung and Large Intestine. The Lung dominates *Qi* and respiration, regulates the water pathway and controls the body surface. It has a propensity to become dry/hot and is vulnerable to attack by pathogens (environmental, infectious) which can be carried deep into the Lung by the Wind.^{9,10} The TCVM Patterns are divided into Excess and Deficiency conditions. Excess patterns include: Invasion of Lung by Wind-Cold, Wind-Heat or Dry-Heat. The Deficiency conditions include: Lung *Qi* Deficiency, Lung *Yin* Deficiency, Lung *Qi-Yin* Deficiency or Lung *Qi*/Kidney *Qi* Deficiency (Figure 1).⁹

Allergies are usually associated with Wind and/or Heat and commonly present as part of an Excess condition. Horses with respiratory allergies typically have Wind-Heat invade the Lungs. This leads to Lung Heat, with drying out of fluids causing a dry cough, and impaired normal movement of *Qi* and Blood leading to dyspnea. The Heat-toxins often include environmental pathogens/allergens (e.g. dry-dusty environment, mold spores in hay).¹⁰

Over time, as the body’s *Qi* and Blood are consumed, the condition slowly evolves into a Deficiency pattern. In particular, Lung *Qi* is consumed leading to weakness, asthma and spontaneous sweating. For Lung *Qi* to descend into the body for normal respiration, it must be grasped by Kidney *Qi*. If either is deficient, breathing difficulties will occur. Geriatric animals commonly present with both Lung and Kidney *Qi* deficiencies. At this stage, whole body *Qi* may be depleted, since the Source-*Qi* (Kidney *Jing*) cannot help support the body *Qi*. Additionally, deficient Spleen *Qi* fails to transport and transform fluid/dampness, leading to production of Phlegm which accumulates in the Lung. This may turn into Heat/Fire impairing Lung *Yin*, and lead to dyspnea.

The clinical TCVM exam will reflect the pattern to be treated. For example, Cold or Deficient patterns cause the tongue to be wet and pale or dusky purple, while Excess Patterns have a pinker dry tongue that may be small. The pulses also reflect the pattern (often fast and shallow due to Excess pattern) although in chronic conditions may be deep and difficult to feel due to deficiencies.

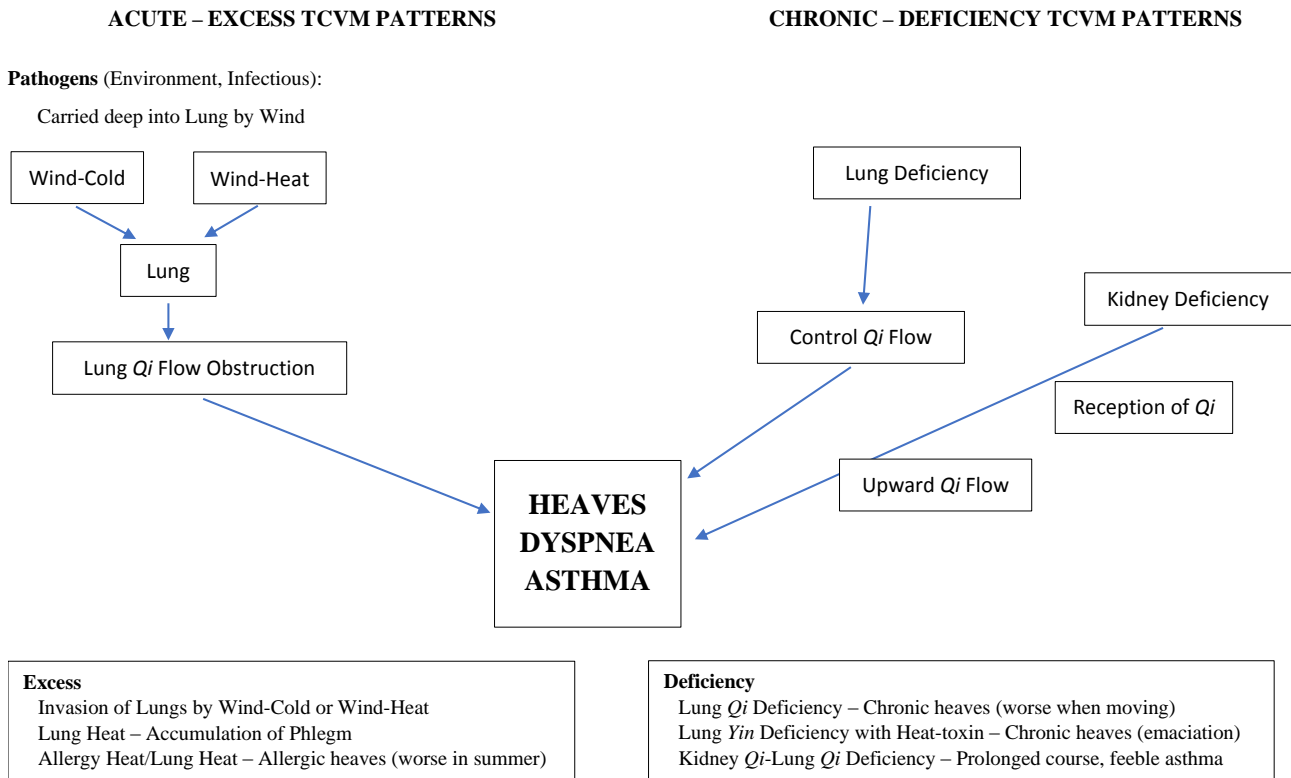


Figure 1: The TCVM pathophysiology of the conventional diagnosis of “Heaves, Asthma”. Allergies are usually associated with Wind and/or Heat and commonly present as part of an Excess condition (left side). The Heat-toxins often include environmental pathogens/allergens (dry-dusty environment, mold spores in hay). Over time, as the body’s *Qi* and Blood are consumed, the condition slowly evolves into a Deficiency Pattern (middle/right side).

TREATMENT – CONVENTIONAL THERAPY

Environmental

Conventional medical treatment for allergies has been centered around removing the allergen (or the patient from the allergen) and decreasing the inflammatory response. Removal of the allergen can be achieved by halting its administration, physically removing the animal from the area or decontaminating the animal by bathing. While effective in the short term, this is not always a reasonable solution for a patient that must live in one region of the country or where certain plants cannot be completely eradicated. If, however, the allergen can be removed, this is the most successful method of preventing and minimizing the allergic reaction.

Anti-inflammatory Therapeutics

In cases where the allergen cannot be removed, treatment is aimed at reducing the inflammatory response through long-term medication therapy. The most commonly used pharmaceuticals include antihistamines and corticosteroids (CS) with less common therapies including desensitization regimens, mast cell stabilizers and bronchodilators (Table 2).⁸ Corticosteroids, whether inhaled or systemic, are the mainstay of respiratory allergy therapy. Dexamethasone is commonly used and has been shown to improve lung function and decrease mucus accumulation.^{8,11} Prednisolone (not prednisone due to poor oral absorption) is also a commonly used steroid.⁸ One advantage of administering glucocorticoids via an inhaled route is the relative reduced dosage compared to systemic use. Dexamethasone, however, significantly suppresses the hypothalamic-pituitary-adrenal axis regardless of route of administration, so other inhaled glucocorticoids such as beclomethasone, fluticasone or ciclesonide may be indicated for long-term therapy (Table 2).^{12,13}

Table 2: Conventional medications with doses used to treat equine respiratory allergies⁸

Drug	Dose
Systemic Corticosteroids	
Dexamethasone	0.04 mg/kg IV or IM q24h then tapered
Prednisolone	1.1-2.2 mg/kg PO q24h then tapered
Inhaled Corticosteroids	
Beclomethasone	1-8 µg/kg q12
Fluticasone	1-6 µk/kg q12
Ciclesonide	2744 µg q12h for 1200# horse initially, then decreased
Bronchodilators	
Clenbuterol	0.8-3.2 µg/kg PO q12h
Pentoxifylline	35 mg/kg PO q12h
Theophylline	5-10 mg/kg PO q12h
Albuterol	1-2 µg/kg q1-3h via inhaler
Ipratropium bromide	Dose varies based on nebulizer/inhaler used, given q8-12h
Mast Cell Stabilizer	
Cromolyn sodium	Dose and frequency vary based on nebulizer used

Ancillary Therapy

Ongoing ancillary therapy for respiratory allergies includes bronchodilators, again either oral or inhaled, mast cell stabilizers and changes in diet fatty acid levels.¹⁴ Bronchodilators are not effective or appropriate as sole therapy due to the risk of increased allergens reaching the (now dilated) lower airways and downregulation of cell receptors for certain drugs after thirty days of treatment.^{11,15} Common bronchodilators include clenbuterol, pentoxifylline, theophylline, albuterol or ipratropium bromide (Table 2).⁸ Interestingly, concurrent administration of glucocorticoids and the most common bronchodilator (clenbuterol, a β₂-adrenergic agonist) prevents downregulation of the β₂-adrenergic receptor on lymphocytes.¹²

The administration of a mast cell stabilizer (cromolyn sodium), can improve clinical signs for specific types of respiratory allergies based on respiratory cytology findings.⁸ Fatty acids have been shown to be anti-inflammatory in some studies; however, further research is ongoing to determine which fatty acids, at what rate, and in what ratio, should be administered for the best improvement.⁵ Various studies have shown flaxseed and commercial fatty acid supplements containing omega-3 fatty acids provide clinical improvement in horses with respiratory allergies.^{5,8}

TREATMENT – TCVM THERAPY

Conventional therapy requires long-term medication, as treatment is merely suppressing the immune response, not correcting the root cause. The use of various TCVM modalities as an adjunctive treatment is intended to decrease dosage requirements of pharmaceuticals as well as improve quality of life for horses suffering from chronic allergic respiratory disease. Common TCVM therapies used as an adjunct to conventional therapy include AP (dry needle, electro-acupuncture, aqua-acupuncture), CHM and food therapy.

Acupuncture – Evidence-based Studies

Humans suffering from asthma undergoing AP treatment have shown improved pulmonary function parameters and enhanced quality of life.⁷ Peripherally applied electro-acupuncture (EAP) causes measurable changes in the level of various neuropeptides responsible for intracranial signaling of sensation and can modify immune system function.^{16,17} Rhinitis, one of the main clinical signs associated with allergic respiratory disease in humans, has been effectively treated with AP.¹⁸ For bronchial asthma, acupuncture is considered by the World Health Organization as more effective than antihistamine drugs, with a success rate of 60-70%.¹⁸ There are a large number of studies in humans, including multiple double-blinded studies evaluating the response to AP or EAP demonstrating improvement in clinical signs and quality of life with varying responses in cellular or humoral measurable outcomes.¹⁹ Carlsson et al. designed an allergic disease model in humans using a standard dose of an allergen followed by measurement of the perceived level of discomfort.²⁰ It was theorized that benefit from AP was associated with dampening of the allergic

response through modulation of C fiber activation, as well as portions of the cerebral cortex.

Through review of current research in animal models, several possible mechanisms for improvement of equine inflammatory respiratory disease by AP have been proposed.⁷ These include improved mucociliary action of the airway epithelium, reduced airway and pulmonary tissue inflammation, cholinergic anti-inflammatory effects, alteration of immune responses, modulation of the autonomic nervous system, and alteration in the peripheral sensory input from inflamed pulmonary tissue.⁷ Although studies investigating AP treatment of inflammatory respiratory disease in horses have been rare, Tangjitjaroen et al. explored differences in the level of the pro-inflammatory cytokine, tumor necrosis factor- α (TNF- α) between sham-treated and EAP-treated horses.¹⁷ The group demonstrated that healthy horses treated with EAP had decreased levels of TNF- α in whole blood as compared to the sham-treated horses. Other studies have stressed the need for multiple AP sessions in horses to see significant improvement and that AP/EAP treatment in animal models with respiratory allergies can modify mucociliary transport, act as an analgesic, and reduce inflammatory cell infiltrates in the lungs.²¹⁻²⁴

Acupuncture – Therapy

The selection of AP points to treat respiratory allergies using TCVM theory is compounded by the various patterns that can accompany the clinical signs (Table 3). In general, treatment is aimed at eliminating whichever pathogen (usually Wind) has created imbalances (i.e. Excess), supporting the *Zang-fu* organs and Channels necessary for healing, and improving *Qi*-Blood flow. Respiratory allergies can be associated with Lung *Qi* Deficiency, Lung *Yin* Deficiency, a combination of the two, or Lung *Qi*/Kidney *Qi* Deficiency. Treatment patterns are targeted at tonifying Lung either primarily or by supporting the mother-child relationship (supporting Spleen to tonify Lung).⁹ Lung *Qi* tonic points in the horse include CV-6, CV-17, LU-9, BL-13 and *Bai-hui*. *Yin* tonic points include KID-3, KID-6, BL-13, SP-6, SP-9, and SP-10 (Tables 3 and 4). Horses diagnosed with Lung and Kidney *Qi* Deficiency must have both Meridians strengthened by using a selection of the following points: BL-13, BL-23, BL-42, LU-1, LU-9, KID-7, *Shen-shu*, *Shen-peng*, *Shen-jiao*, *Fei-men* and *Fei-pan*.⁹

With chronic conditions, Lung and Kidney *Qi* become exhausted leading to a Deficient state. In these cases, treatment should be targeted at tonifying each as needed. For generalized respiratory support, *Ding-chuan* is an excellent classical point as its indications include stopping dyspnea and asthma. In a human study, bilateral AP of LU-1, LU-9, LI-18, ST-36, GB-12, BL-13, BL-20 and BL-23 reduced dyspnea in patients with chronic obstructive pulmonary disease.²⁵ These acupoints are often used in horses as well.

Of interest is the use of Back-*shu* points associated with the Lung (BL-13, BL-42) for both humans and horses. Back-*shu* points have been shown to stimulate associated portions of the dorsal horn of the spinal cord where somatic and visceral-associated afferent fibers of

their specific organ converge. This convergence, via the somaticovisceral reflex, allows organ modulation.²⁶ That is, AP stimulation of BL-13 and BL-42 allows for modulation of the lungs.

The AP technique utilized in a patient will depend on the pattern, personality of the horse, and practitioner comfort level. Treatment for respiratory allergies caused by Lung Heat is aimed at clearing the Heat and tonifying the Lung. Hemo-acupuncture has been shown to be the most effective method for clearing excess Heat.²¹ In addition to the previously mentioned acupoints, hemo-acupuncture of *Er-jian* and *Wei-jian* will help clear Heat, if patient compliance allows (Tables 3 and 4). Electro-acupuncture may also be helpful to drain excess Heat and move Blood and *Qi*. When using EAP, low frequency/high intensity energy (5-20 Hz oscillating frequency) should be used for the maximum cumulative effect and to help Deficient conditions.²⁷ The intensity should be adjusted based on the tolerance of the individual patient.

The addition of gold implants to the AP therapy protocol in canine and feline patients has been used in the treatment of asthma with successful results. When implanted into tissues, gold releases positively charged ions which then destroy inflammatory cells around the bead itself.²⁷ This therapy could be applied to large animal cases. Moxibustion is commonly used to improve *Qi*-Blood flow for chronic musculoskeletal conditions. Depending on the diagnosed pattern, moxibustion may be helpful in allergy cases with chronic Deficiency and/or Damp. Caution should be used in these animals due to risk of aggravating the clinical signs from inhaled particles.

Chinese Herbal Medicine – Evidence-based Studies

Human medical research has evaluated the role of CHM in the treatment of respiratory allergies. Comparison of herbal medications with corticosteroids has shown equal improvement in clinical signs, with 1 study demonstrating a significant reduction in total IgE level in the herbal treatment group when compared to steroid therapy.²⁸ The use of CHM in humans has been shown to be persistent and effective for refractory asthmatics and imbalance. Additionally, herbal therapy has been shown to improve imbalance in Th1 and Th2 responses, thought to play a role in the chronicity of allergies.²⁸

Pharmacologically active compounds responsible for the major medicinal benefits of plants contained in herbal medicines are in the form of secondary metabolites. Synthesis of these require unique biochemical pathways that are distinctive to each group of plants. They include alkaloids, terpenoids, glucosides, phenolic compounds, phenazines, polyketides, fatty-acids and non-ribosomal peptides.²⁸ There are 23 Chinese herbs that are predominately used for treating equine chronic respiratory disease. Although veterinary studies, in general are few, there has been a variety of pharmaceutical, animal model and human clinical studies evaluating the wide variety of pharmacologically active compounds in these plants. The reader is referred to a review of these metabolites and their biological activities.²⁸

Table 3: Traditional Chinese veterinary medicine (TCVM) diagnostic patterns for equine allergic respiratory disease with treatment protocols for acupuncture and Chinese herbal medicine¹⁰

TCVM Pattern Diagnosis	Clinical Signs	Acupuncture	Chinese Herbal Medicine
Lung Heat	Allergic heaves (worse in summer); cool seeking; dry cough; tongue (red-dry); pulse (strong-fast)	GB-20, LU-5/10/11, BL-10/13, GV-14, LI-4/11, CV-17/22, ST-40, <i>Ding-chuan</i> ; Hemo-AP at <i>Er-jian/Wei-jian</i>	Schisandra 5 ^a
Lung Heat with <i>Yin</i> Deficiency	Chronic heaves/asthma; emaciation; cool seeking; dry cough; tongue (red-dry); pulse (thready-fast)	LU-7/9, SP-6/9, KID-3, BL-13/42, CV-22, <i>Ding-chuan</i> , <i>Fei-men</i> , <i>Fei-pan</i>	<i>Bai He Gu Jin Tang</i> (Lily Combination ^a)
Lung <i>Qi</i> Deficiency	Chronic heaves/asthma; weak voice; fatigue; dyspnea worse when moving; tongue (pale-wet); pulse (deep-weak)	BL-13/42, LU-7/9, CV-6/17/22, SP-6/9, ST-36/40, <i>Ding-chuan</i> , <i>Qi-hai-shu</i> , <i>Fei-men</i> , <i>Fei-pan</i>	<i>Bu Fei San</i> ^a
Kidney and Lung <i>Qi</i> Deficiency	Prolonged course of asthma; feeble with weak respiration; exercise intolerance; dyspnea	<i>Shen-shu</i> , <i>Shen-peng</i> , <i>Shen-jiao</i> , BL-13/23/26, CV-4/6/17/22, ST-36, LU-7/9, KID-3/10, <i>Ding-chuan</i>	<i>Ren Shen Ge Jie San</i> (Breathe Easier B ^a)

Hemo-AP = hemo-acupuncture

Table 4: Summary of acupuncture points used for respiratory allergies; acupoints used with greatest frequency are in **BOLD**^{9,10}

Acupuncture Point	Main Goal	Ancillary Goal(s)	Additional Notes
CV-6	<i>Qi</i> tonic		
CV-17	<i>Qi</i> tonic		
CV-22	Stops asthma	Stops cough	
GV-14	Clears Lung Heat	Regulates immune functions	
LU-1	Clears cough	Stops asthma; opens the Lung Channel	Alarm point for Lung
LU-7	Clears cough and heaves	Master point for the head and neck	<i>Luo</i> -connecting point for the LU Channel
LU-9	<i>Yuan</i> -source point	Tonifies Lung <i>Qi</i>	Helpful for chronic cough
KID-3	<i>Yuan</i> -source point	Tonifies Kidney	
KID-6	<i>Yin</i> tonic point		
SP-6	Tonifies <i>Qi</i> and Blood; nourishes <i>Yin</i>	Strengthens Spleen to generate Blood	
SP-9	Nourishes <i>Yin</i>	Generates Blood	
SP-10	Cools Blood	Nourishes Blood and clears Heat	
BL-12/41	Influential point for Wind and trachea	Affects Wind-Heat; stops itching	Classical name is <i>Feng-men</i>
BL-13/42	Tonifies <i>Qi</i>	Disperses cough; resolves asthma	Lung Back- <i>shu</i> associate point Also known as <i>Fei-shu</i>
BL-23/52	Back- <i>shu</i> point for Kidney		Kidney Association point
SI-14	Tonifies <i>Qi</i> and Lung		Classical name is <i>Fei-men</i>
Fei-pan	Tonifies <i>Qi</i> and Lung		
Fei-men	Clears upper airway disease	Clears skin itching	
<i>Bai-hui</i>	<i>Qi</i> tonification	Helps resolve Wind	
<i>Shen-shu</i>	Tonifies Kidney	Tonifies <i>Qi</i> or <i>Yang</i>	
<i>Shen-peng</i>	Tonifies Kidney	Tonifies <i>Qi</i> or <i>Yang</i>	
<i>Shen-jiao</i>	Tonifies Kidney	Tonifies <i>Qi</i> or <i>Yang</i>	
Ding-chuan	Stops dyspnea and asthma		Helpful for chronic lung problems
<i>Er-jian</i>	Clears Heat		
<i>Wei-jian</i>	Clears Heat		

Chinese Herbal Medicine – Therapy

Inflammatory airway disease in horses usually requires life-long medications. Chinese herbal medicine provides an alternative long-term therapy that avoids some of the major adverse effects such as immunosuppression from corticosteroids and altered endogenous adrenocorticoid production.¹² Four commonly used CHM formulas for

treatment of chronic respiratory disease in horses include Schisandra 5^a, Lily Combination^a, *Bu Fei San*^a, and Breathe Easier B^a.²⁹ The herbs in these preparations have been evaluated for individual therapeutic action and shown to have many attributes common to traditional medical pharmacologics. The clinical effects seen are

those as an expectorant, anti-spasmodic, antitussive, antihistamine, anti-inflammatory and anti-oxidative.²⁹ Additionally, white blood cell changes and inflammatory cytokine modulation demonstrate immunomodulatory agent behavior.^{26,29}

The TCVM indications for use of Schisandra 5^a include heaves associated with Heat or Wind-Heat, Heat-associated allergy, general allergies, and chronic cough due to Lung Heat with *Yin* Deficiency. There are 5 biologically active herbs contained within this formula with various experimentally documented activities (Table 5).³⁰ *Chai Hu* (Bupleurum), for example, contains a major active phytochemical, saikosaponin, which has demonstrated anti-bronchoconstriction, attenuation of histamine release, and inhibition of inflammatory cytokines (e.g. prostaglandin E2, thromboxane B2).^{31,32} *Wu Wei Zi* (Schisandra), for which the formula is named, contains pharmacologically active compounds that possess immune modulatory and anti-inflammatory activities. For example, extracts have reduced in vitro expressions of TNF- α , IL-4 in IgE-induced RBL-2H3 cells.³³

Lily Combination^a (modified *Bai He Gu Jin Tang*) is effective in the treatment of Lung/Kidney *Yin* Deficiency, especially dry cough without phlegm while conventional use includes dry cough from bronchiolitis/bronchitis and RAO. These horses have a red tongue (without coating) with a fast-thin pulse. This herbal formula focuses on moistening the airways (Table 6).³⁰ Out of several biologically active chemical compounds isolated from *Bai He* (Lily bulb), berberine is of particular interest. It is an isoquinoline alkaloid that has both immunomodulatory activities (e.g. down regulation of inflammatory cytokines, improved Th1 and Th2 cytokine regulation) as well as increases mucin release to provide an expectorant effect.^{34,35} *Jie Geng* (Platycodon), one of the main herbs in this formula, has been shown to reduce pulmonary fibrosis by inhibiting expression of transforming growth factor- β (TGF- β) mRNA with an efficacy similar to methylprednisolone.³⁶

Bu Fei San^a (modified *Bu Fei Tang*) is indicated for Lung *Qi* Deficiency that presents as chronic heaves that worsens with exercise. Characteristic clinical signs include fatigue, shortness of breath, chronic cough or asthma, pale-wet tongue and deep-weak pulse. One of the constituent herbs, *Huang Qi*, goes to the root of the illness by tonifying *Qi* (Table 7).³⁰ In asthmatic humans, *Huang Qi* supplementation has demonstrated the capability to reverse the Th2 cytokine predominate status of these patients.³⁷ In an ovalbumin induced asthma model, supplementation of a polysaccharide extract from the herb prevents eosinophil

infiltration into the airways and inhibits lymphocyte proliferation and interleukin-2 (IL-2) production.³⁸ It has also shown the ability to reduce airway hyper-responsiveness to methacholine challenge.³⁹ The extract of *Bai Guo*, another important herb in this formula, has demonstrated the ability to significantly decrease the pulmonary infiltration of eosinophils and lymphocytes in asthmatic humans.⁴⁰ The extract also possesses a pulmonary protective effect by reducing oxidative injury manifested by improvement in histological changes.⁴¹

Breathe Easier B^a (modified *Ge Jie San*) should be used in animals with Kidney and Lung *Qi* Deficiency associated with RAO. This presents in animals as chronic dyspnea/asthma/cough, exercise intolerance, and musculoskeletal changes with a pale-swollen tongue and weak-deep pulse. Many of the herbs in this formula enter into the Lung Channel to eliminate Phlegm to stop cough and asthma.³⁰ One of the prominent herbs in this formula, *Zhe Bei Mu* (Zhejiang Fritillary), contains important phytochemical compounds, one of which (verticinone) possesses antitussive effects that are associated with modulation via opioid and non-opioid mechanisms (Table 8).⁴² One other herbal formula that has shown preliminary promise is *Zhi Sou San*^a (modified formula of classical antecedent, *Zhi Sou San*).²⁶ In a clinical trial in which *Zhi Sou San* was used to treat chronic coughing in 50 horses, clinical signs resolved in 90% of the horses.⁴³

Food Therapy

Traditional Chinese veterinary medicine aims to treat the entire patient and includes dietary modifications to clear Heat and Wind while supporting *Qi*, Blood and *Yin*. Depending on the specific pattern, the diet may be changed to provide foods that are cooling and help support *Yin* (green vegetables, alfalfa, watermelon, peppermint and barley). Cooling foods will help to reduce ongoing Heat allowing moisture to return to the tissues (Blood) and improve the flow of *Qi*.^{9,44} As horses are herbivores, and may be fussy eaters, this may have to occur through trial and error supplementation. The removal of certain foods may be of significantly more benefit. Any foods that are suspected allergens can be removed, then slowly added back into the diet once the allergies are under control. Foods that cause Heat in Excess conditions (leading to dryness) should also be removed. These include oats, millet, apple, citrus, apricot and ginger.^{9,44} It is important when evaluating diet to include evaluation of commercial processed grains and supplements, as owners may be unaware of what is in each specific mixture.

Table 5: Ingredients of the Chinese herbal medicine, Schisandra 5^a, and their actions

<i>Pin Yin</i> Name	Common Name	Actions ³⁰
<i>Chai Hu</i>	Bupleurum	Clears Wind-Heat, detoxifies, soothes Liver <i>Qi</i>
<i>Fang Feng</i>	Siler	Clears Wind-Cold, detoxifies, opens body surfaces
<i>Wu Mei</i>	Japanese Apricot	Astringently consolidates Lung to stop asthma
<i>Wu Wei Zi</i>	Schisandra	Nourishes Lung <i>Yin</i> , consolidates Lung
<i>Gan Cao</i>	Chinese Licorice	Harmonizes

Table 6: Ingredients of the Chinese herbal medicine, Lily Combination^a (modified *Bai He Gu Jin Tang*), and their actions

<i>Pin Yin Name</i>	<i>Common Name</i>	<i>Actions</i> ³⁰
<i>Sheng Di Huang</i>	Rhemannia	Cools Blood and nourishes <i>Yin</i>
<i>Shu Di Huang</i>	Rhemannia	Nourishes Kidney <i>Yin</i> and <i>Jing</i>
<i>Bai He</i>	Brown's Lily	Moistens the Lung and stops cough
<i>Mai Men Dong</i>	Ophiopogon	Nourishes <i>Yin</i>
<i>Bai Shao Yao</i>	Chinese Peony	Nourishes Liver <i>Yin</i>
<i>Dang Gui</i>	Dong Quai	Nourishes Blood
<i>Jie Geng</i>	Platycodon	Opens Lung and stops cough
<i>Zhe Bei Mu</i>	Zhejiang Fritillary	Moistens the Lung and stops cough
<i>Gan Cao</i>	Chinese Licorice	Harmonizes
<i>Xuan Shen</i>	Scrophularia	Cools Blood and Nourishes <i>Yin</i>

Table 7: Ingredients of the Chinese herbal medicine, *Bu Fei San*^a (modified *Bu Fei Tang*), and their actions

<i>Pin Yin Name</i>	<i>Common Name</i>	<i>Actions</i> ³⁰
<i>Huang Qi</i>	Astragalus	Tonifies Lung <i>Qi</i>
<i>Bai Guo</i>	Ginko	Astringently consolidates Lung, stops asthma/cough
<i>Dang Shen</i>	Codonopsis	Tonifies <i>Qi</i>
<i>Jie Geng</i>	Platycodon	Opens the Lung, transforms Phlegm
<i>Wu Wei Zi</i>	Schisandra	Astringently consolidates the Lung
<i>Zi Su Zi</i>	Perilla	Clears Wind-Heat, stops cough
<i>Zi Wan</i>	Tartarian Aster	Moistens Lung, stops cough/asthma
<i>Gan Cao</i>	Chinese Licorice	Harmonizes

Table 8: Ingredients of the Chinese herbal medicine, Breathe Easier B^a (modified *Ge Jie San*), and their actions

<i>Pin Yin Name</i>	<i>Common Name</i>	<i>Actions</i> ³⁰
<i>Bai He</i>	Brown's Lily	Moistens the Lung and tonifies Lung <i>Yin</i>
<i>Dang Shen</i>	Codonopsis	Tonifies <i>Qi</i>
<i>Jie Geng</i>	Platycodon	Opens the Lung and eliminates Phlegm
<i>Mai Men Dong</i>	Ophiopogon	Nourishes Lung <i>Yin</i>
<i>Qian Hu</i>	Peucedanum	Transforms Phlegm, stops asthma
<i>Rou Gui</i>	Cassia	Warms Kidney and dispels Cold
<i>Wu Wei Zi</i>	Schisandra	Consolidates and nourishes Lung <i>Yin</i>
<i>Zing Ren</i>	Apricot	Stops cough and asthma
<i>Zhe Bei Mu</i>	Zhejiang Fritillary	Eliminates Phlegm and clears Lung Heat
<i>Zi Su Zi</i>	Perilla	Descends <i>Qi</i> to stop asthma, stops cough

INTEGRATIVE MEDICAL TREATMENT

Combined Conventional and Complementary Therapy

In clinical practice, a combined treatment approach will often lead to the most favorable outcome. An example of this is the addition of AP to surgical anesthesia in human medicine which reduces consumption of anesthetics and analgesics, while augmenting perioperative pain relief.^{27,45} Conventional pharmaceutical-based therapy is often poorly welcomed by owners and patients due to the need for long-term administration and possible side effects. Conversely, the rapid initial response from pharmaceuticals is appreciated as it produces immediate relief for their dyspneic animal. Traditional Chinese veterinary medicine treatment allows the practitioner to

avoid long-term conventional medications but is usually associated with slower initial improvement and requires multiple sessions. A combined approach, in which conventional medications are administered for the acute clinical signs (respiratory distress and severe cough) and replaced with TCVM for ongoing maintenance provides the best of both worlds. While the negative effects of glucocorticoids on TCVM response have been published, the rapid improvement in clinical signs with conventional therapies cannot be ignored.²⁶ The combination of both therapeutic modalities can often result in an improved outcome for patients and increased compliance by owners.

In human medicine, studies have shown that AP does not change the histamine response in the airways but is effective in the long-term management of corticosteroid-dependent bronchial asthma.¹⁸ This implies that while AP may not regulate the acute response, it does modulate the long-term inflammatory response which suggests it would be an excellent tool in the management of respiratory allergies in horses. Some of the herbs in the combinations previously discussed have been shown to affect histamine release; however, it takes time for full effect.^{31,32} If sufficient, a single dose of a short acting CS to provide initial relief while the environment is adjusted is beneficial. The long-term administration of dexamethasone, a glucocorticoid, is contraindicated in some equine patients due to the risks of immunosuppression and the anecdotal risk of laminitis.¹² Replacement of chronic glucocorticoid administration with AP and/or herbal medications in the treatment of allergies can help improve a patient's quality of life while reducing these risks.

While TCVM may require more frequent patient assessments, it can be correlated to the specific animal and their main presenting complaints. Just as traditional clinical signs can change in response to therapy, TCVM patterns can change as clinical signs resolve. For this reason, especially when using combination protocols, it is recommended to reassess the patient and target the AP for whatever pattern is present at that moment. What may initially present as an Excess pattern (i.e. Wind-Heat) could become a Deficient pattern once the Heat is resolved, warranting different AP points and herbal formulation. In addition, horses with allergies are sensitive to environmental changes, and therapy may need to be modified with season, exercise, stabling or feeding changes. Collaboration of both the TCVM and non-TCVM trained veterinarians is optimal, particularly in complex cases, and serves the patient's best interests.

Integrated Medical Protocol – Case Example

Patient:

A 9-year-old Thoroughbred stallion with a 3-year history of chronic respiratory disease, previously diagnosed as RAO, is presented for clinical evaluation. He wheezes during the summers and his respiratory clinical signs have been worsening over time. He is a pleasure riding horse (45 minutes twice a week) and loves to compete in competitive trail riding. He is the dominant horse in a herd of 4 and has had no other medical complaints since birth.

Diagnosis:

Begin with a conventional examination followed by (or combined with) a TCVM examination which establishes a TCVM Pattern diagnosis. Key components to both examinations include information on the patient's history of illness, environment, previous treatments and owner goals.

➤ Physical Exam: Loud wheezes are audible outside the stall. The horse appears strong and sweats normally. Abnormalities of the exam include dry, cracked front hooves; red and dry eyes; warm ears; hot air on

expiration; obvious enlargement of the abdominal muscles on the lateral abdomen ("heaves line"); thick malodorous urine and increased drinking. No cough noted. TCVM: red-dry tongue, thready-weak and rapid pulse, no sensitivity of the Back-*shu* points or any Alarm points. TCVM diagnosis: Lung Heat with *Yin* Deficiency. Conventional suspected diagnosis: RAO ("allergies").

➤ Conventional Diagnostics: These should be done after the initial Conventional + TCVM clinical examinations as some tests may need to be done while sedated. The most common diagnostic tests indicated in these patients are airway endoscopy or bronchioalveolar lavage.

Treatment:

Use the clinical examination, historical, and advanced testing information to create 2 treatment protocols to run concurrently: a conventional plan and a complementary therapy plan.

➤ Conventional Plan: Determine what rescue pharmaceuticals are needed and the anticipated duration of therapy. Medical management includes initiating prednisolone at 1.5 mg/kg PO q24h for 3 days, then decrease by 25% per 3 days totaling 2 weeks of therapy. Given the severity of the clinical signs, medium duration therapy is selected to rapidly improve the patient's comfort.

➤ Complementary Plan: Treatment will include the initial AP treatment as well as CHM to address the TCVM Pattern (Lung Heat with *Yin* Deficiency).

- Dry needle at: LU-11, LI-1, LI-4, LU-5, GV-14. EAP (20 Hz oscillating frequency for 15 min) at: *Ding-chuan* bilateral and BL-13 bilateral. Aquapuncture with vitamin B12, 5 ml per acupoint at: LU-5, LI-11, GV-14 (address TCVM Pattern, Tables 3 and 4).
- Chinese herbal medicines: 1) Schisandra 5^a, 15 grams, twice daily for 2 months (clear Heat); 2) Lilly Combination^a, 15 grams, twice daily for 3 months (Nourish Lung *Yin*)
- Food therapy: Remove grains containing oats, if possible; change treats to watermelon or peppermint.
- Management recommendations: Environmental changes such as wet the hay to reduce dust and increase turnout if excessively stalled. Exercise restrictions (if indicated).

Maintenance:

Determine a recheck schedule. The recheck exam should be targeted for a time point where the acute clinical signs have been improved by the rescue pharmaceuticals and a second AP treatment is indicated. At the recheck appointment a longer term management plan can be established as well as the patient reviewed for improvement and/or changes in the TCVM Pattern. Patients will often significantly improve within the first week of treatment; as such, recheck examinations are often scheduled for 5-7 days after the initial evaluation.

Recheck the case example patient in approximately 1 week and determine if changes in the AP plan are needed. If clinical signs are not under control within 1 week, consider adding inhalation therapy. Continue combined therapy until clinical signs are under control, then discontinue medications and continue AP and CHM therapy for an additional 2-3 months.

Case Outcome:

The stallion was breathing more comfortably 1-2 weeks after the initial AP treatment and daily herbal medications. At 6 weeks, the horse was almost normal. The horse's RAO was successfully managed by instituting the same treatment plan each summer over the next 6 years.¹⁰

SUMMARY

Using a combination of Eastern and Western medicine to treat horses with allergies can help improve their quality of life and decrease the need for medications with negative side effects. Horse owners new to Chinese medicine may have some reluctance to use it initially for medical conditions, therefore, combination therapy allows a gentle introduction to TCVM. Combination therapy can also improve the owner's compliance and satisfaction, especially as educated owners are becoming more wary of long-term CS administration. Short-term conventional medications combined with TCVM will lead to more comfortable horses and, by extension, their owners. Successful patient response depends on correct identification of the disease or pattern, rapid control of the clinical signs, and long-term TCVM treatment combined with environmental changes.

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FOOTNOTES

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REFERENCES

- Mealey R, Long M. Mechanisms of Disease and Immunity. Equine Internal Medicine 4th Ed, Reed S, Bayly W, Sellon D (eds). New York, NY: Elsevier 2018:3-78.
- Felippe M. The Immune System. Equine Clinical Immunology, Felipe M (ed). Ames, IA: Wiley-Blackwell 2016:1-10.
- Lorch G, Hillier A, Kwochka K et al. Results of intradermal tests in horses without atopy and horses with chronic obstructive pulmonary disease. Am J Vet Res 2001; 62(3):389-397.
- Nurwati I, Muthmainah M, Huda K. Acupuncture for asthma: Its potential significance in clinical practice. Med Acupunct 2020; 32(5):272-279.
- Scott D, Miller W. Skin Immune System and Allergic Skin Diseases. Equine Dermatology 2nd Ed. Scott D, Miller W (eds). Maryland Heights, MO: Saunders 2011:263-313.
- Moran G, Folch H. Recurrent airway obstruction in horses - an allergic inflammation: A review. Vet Med 2011; 56(1):1-13.
- Tangjitjaroen W, Xie H, Colahan P. Possible mechanisms of acupuncture for the treatment of chronic inflammatory disorders of the equine lower airway. Am J Trad Chin Vet Med 2009; 4(2):37-47. doi: 10.59565/001c.83749
- Couët L, Cardwell M, Gerber V et al. Inflammatory airway disease of horses—revised consensus statement. J Vet Intern Med 2016; 30(2):503-515.
- Xie H, Preast V, Siahpolo H. Zang-Fu Physiology. Traditional Chinese Veterinary Medicine Fundamental Principles 2nd Ed, Xie H, Preast V (eds). Reddick, FL: Chi Institute Press 2013: 265, 85-110.
- Xie H. Acupuncture for Internal Medicine. Xie's Veterinary Acupuncture, Xie H, Preast V (eds). Ames, IA: Blackwell 2007: 267-308. Case example used with author permission.
- Leguillette R. Treatment and management of mild/moderate and severe equine asthma. In Proceedings from the 67th American Association of Equine Practitioners. San Antonio, TX: AAEP 2021; 67:469-478.
- Mainguy-Seers S, Lavoie J. Glucocorticoid treatment in horses with asthma: A narrative review. J Vet Intern Med 2021; 35(4):2045-2057.
- Pirie R, Mueller H, Engel O et al. Inhaled ciclesonide is efficacious and well tolerated in the treatment of severe equine asthma in a large prospective European clinical trial. Equine Vet J 2021; 53(6):1094-1104.
- White S. A diagnostic approach to the pruritic horse. Equine Vet Educ 2015; 27(3):156-166.
- Plumb D. Clenbuterol. Plumb's Veterinary Drug Handbook. <https://app.plumbs.com/drug-monograph>. Updated February 2022. Accessed May 15, 2023.
- Han J. Acupuncture: neuropeptide release produced by electrical stimulation of different frequencies. Trends Neurosci 2003; 26(1):17-22.
- Tangjitjaroen W, Rice B, Xie H, et al. Effects of electroacupuncture on pulmonary function and immune response in horses. In Proceedings from the 56th American Association of Equine Practitioners. AAEP: Baltimore, MD 2010: 413-422.
- World Health Organization and Thomson Gale (Firm). Acupuncture: Review and Analysis of Reports on Controlled Clinical Trials. World Health Organization 2002:20.
- Zijlstra F, Van Den Berg-de Lange I, Huygen F et al. Anti-inflammatory actions of acupuncture. Mediators Inflamm 2003; 12(2):59-69.
- Carlsson C, Wallengren J. Therapeutic and experimental therapeutic studies on acupuncture and itch: Review of the literature. J Eur Acad Dermatol Venereol 2010; 24(9):1013-1016.
- Xie H, Holyoak R. Ways to improve acupuncture outcomes in equine practice. Am J Trad Chin Vet Med 2020; 15(2):53-60. doi: 10.59565/001c.83750
- Wilson D, Berney C, Peroni D et al. The effects of a single acupuncture treatment in horses with severe recurrent airway obstruction. Equine Vet J 2004; 36(6):489-94.
- Baek Y, Choi D, Yang H et al. Analgesic effect of electroacupuncture on inflammatory pain in the rat model of collagen-induced arthritis: Mediation by cholinergic and serotonergic receptors. Brain Res 2005; 1057(1-2):181-185.
- Carneiro E, Carneiro C, de Castro M et al. Effect of electroacupuncture on bronchial asthma induced by ovalbumin in rats. J Altern Complement Med 2005; 11(1):127-134.
- Feng J, Wang X, Li X et al. Acupuncture for chronic obstructive pulmonary disease (COPD): A multicenter, randomized, sham-controlled trial. Medicine 2016; 95(40):e4879.
- Shmalberg J, Xie H. Acupuncture and Chinese herbal medicine for treating horses. Compend Cont Educ Vet 2011; 33(5):E1-E11.
- Pellegrini D, Muller T, Fontequé J et al. Equine acupuncture methods and applications: A review. Equine Vet Educ 2020; 32(5):268-277.
- Li X, Brown L. Efficacy and mechanisms of action of traditional Chinese medicines for treating asthma and allergy. J Allergy Clin Immunol 2009; 123(2):297-306.
- Tangjitjaroen W, Xie H, Colahan P. The therapeutic actions of traditional Chinese herbal medicine used for the treatment of equine respiratory diseases. Am J Trad Chin Vet Med 2009; 4(1):7-21. doi: 10.59565/001c.83751

30. Ma A. Clinical Manual of Chinese Veterinary Herbal Medicine 5th ed. Gainesville, FL: Ancient Art Press 2020:333-334, 62-65, 65-66, 334-336.
31. Park K, Park J, Koh D et al. Effect of saikosaponin-A, a triterpenoid glucoside, isolated from *Bupleurum falcatum* on experimental allergic asthma. *Phytother Res* 2002; 16(4):359-363.
32. Bermejo B, Martinez M, Silvan S et al. In vivo and in vitro anti-inflammatory activity of saikosaponins. *Life Sci* 1998; 63(13): 1147-1156.
33. Lee B, Bae E, Trinh H et al. Inhibitory effect of schisandra on passive cutaneous anaphylaxis reaction and scratching behaviors in mice. *Biol Pharm Bull* 2007; 30(6):1153-1156.
34. Lee C, Lee J, Seok J et al. Effects of baicalein, berberine, curcumin and hesperidin on mucin release from airway goblet cells. *Planta Med* 2000; 69 (6):523-526.
35. Colavita A, Reinach A, Peters S. Contributing factors to the pathobiology of asthma. The Th1/Th2 paradigm. *Clin Chest Med* 2000; 21(2) :263-277, viii.
36. Liu Q et al. Study on effect and mechanism of platycodin D on treating experimental pulmonary fibrosis in rats. *Chin Arch Trad Chin Med* 2012; 30(9):2057-9. [Chinese]
37. Wang G, Liu C, Wang Z, et al. Effects of *Astragalus membranaceus* in promoting T-helper cell type 1 polarization and interferon-gamma production by up-regulating T-bet expression in patients with asthma. *Chin J Integr Med* 2006; 12(4):262-267.
38. Xue J, Xu Y, Zhang Z, et al. The effect of astragalopolysaccharide on the lymphocyte proliferation and airway inflammation in sensitized mice. *J Tongji Med Univ* 1999; 19(1):20-22, 30.
39. Wang H, Chang B, Wang B. [The effect of herbal medicine including *astragalus membranaceus*, *codonopsis pilosula* and *glycyrrhiza* on airway responsiveness]. *Zhonghua Jie He He Hu Xi Za Zhi* 1998; 21:287-288. [Chinese]
40. Tang Y, Xu Y, Xiong S et al. The effect of Ginkgo Biloba extract on the expression of PKC α in the inflammatory cells and the level of IL-5 in induced sputum of asthmatic patients. *J Huazhong Univ Sci Technolog Med Sci* 2007; 27(4): 375-380.
41. Liu K, Wu W, He W et al. Ginkgo biloba extract (EGb 761) attenuates lung injury induced by intestinal ischemia/reperfusion in rats: Roles of oxidative stress and nitric oxide. *World J Gastroenterol* 2007; 13(2):299-305.
42. Xu F, Chen C, Zhang Y et al. Synthesis and antitussive evaluation of verticinone-cholic acid salt, a novel and potential cough therapeutic agent. *Acta Pharmacol Sin* 2007; 28(10):1591-1596.
43. Li D, Zhao Y. Effect of Zhi Sou San on chronic cough in large animals [Chinese]. *J Trad Chin Vet Med* 2007; 21(1):22. [Chinese]
44. Basko I. Food therapy to reduce the stress of summer climate changes. *Am J Trad Chin Vet Med* 2009; 4(1):77-83. [doi: 10.59565/001c.83752](https://doi.org/10.59565/001c.83752)
45. Lu Z, Dong H, Wang Q et al. Perioperative acupuncture modulation: More than anesthesia. *Br J Anaesth* 2015; 115(2):183-193.