

Can Chinese Herb-based Medicines Heal the Immune System and Cure Allergies?

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Abstract

This chapter explores the science and practice of adapting traditional Chinese medicine (TCM) to treat the modern epidemic of allergic diseases such as eczema, asthma, and food allergies and correct imbalances in the immune system. These diseases have burgeoned with the changes associated with Western models of economic development, diet, and treating disease. They have resisted pharmaceutical cures. The TCM formulary has a long track record of treating conditions in the skin, airways, and digestion. In our research and my practice, we use derivatives of the classical formulas to treat all the organ systems involved in a disease rather than single systems and symptoms. Contemporary science gives us the ability to refine the medicines to increase potency, and make them more compatible with patient behavior. We chose this path because patients are suffering, and depriving children of their childhoods.

1. Introduction

Allergic diseases are a significant health problem in “Westernized” countries. They are a tremendous burden on quality of life for both patients and their families, and health care expenditures for the society as a whole. Food allergy in particular has no definitive treatment. For many years, the rise of allergic disease has been widely attributed to the “hygiene hypothesis” which contends that hygiene and other byproducts of modern life have deprived our immune systems of their natural enemies such as parasites and microbes, and have turned on normally harmless proteins in food. But a more varied set of explanations has emerged.

One researcher traces the beginnings of epidemic levels of sinus allergies and asthma to the creation of afternoon children’s television programming, which shifted afterschool activity indoors.ⁱ More recently, depletion of the protective microbiome through overuse of antibiotics and Caesarian section has come under scrutiny.ⁱⁱ So have changes in gene expression—not the DNA itself but switching the genes on and off—which can be induced by environmental factors and stress. These epigenetic changes can be passed to offspring and may account for the accumulation of allergic tendencies from one generation to the next. While the specific etiology of individual cases of allergic

disease is difficult to pin down, what we do know is there is an imbalance of innate immunity, which is governed by one set of T helper cells, known as Th1 and acquired immunity, Th2. The medical challenge is to reset that balance.

The term “atopic march” describes the progression of allergic disease from early infancy, in the form of eczema, through sinus allergies and asthma, to food allergies. These are diseases of the tissue that faces the external environment where the immune system is potent—the skin, the airways, and the digestive tract.

The accustomed medical approach is to control the response through medication and curtailing exposure. Certainly these are valid and important. But medications have problems of their own. For example, corticosteroids, which are used in various formulations to control inflamed skin, sinuses, lungs and the esophagus depress innate immunity, can damage tissue, and can produce both depression and anxiety. Limiting exposure particularly to food allergens is difficult because sensitization happens early, usually to the most common foods in the customary diet, such as peanuts, milk, and eggs, which are often eaten alone or are additives to prepared foods.

Traditional Chinese medicine has been used effectively to treat diseases of the gut, airways, and skin for thousands of years. Western science allows us to study the underlying mechanisms of disease and treatment. TCM practitioners know that their medicines work, but the science allows us to understand how and why they work, and how to make them more effective.

2. Dual Approach to Research and Clinical Efficacy

After years of discussion, in 2000, the FDA recognized the importance of the movement towards alternative medicine by issuing the Guidance for Industry Botanical Drug Products, which states that active constituents in a botanical drug might not need to be identified when studying an investigational new drug if this is shown to be infeasible. Instead, the FDA will rely on other tests, including chromatographic fingerprints, chemical assays of characteristic markers, and biological assays, to ensure the quality, potency, and consistency.

In this changing landscape, we began to explore the possibility of applying the lessons of thousands of years of Chinese medicine to a modern global epidemic.

We have been pursuing this research on two tracks. One is the protocol for pharmaceutical development in full accord with our regulators. We have two certified investigational drugs, one for food allergies and one for asthma.

I also use medicines in current treatment for a range of co-morbid allergic diseases in weekend private practice, mostly with children, where we not only see very encouraging results and gain insights that can be used to refine and adjust the medicines. These patients and their parents feel poorly served by standard of care from their allopathic physicians. We also conduct “practice-based research” on a smaller scale and at less cost than full clinical trials.

It is important to recognize that these drugs work with one another. While we have registered investigational drugs for food allergies and asthma, in practice the different medicines are administered in combination to treat the co-morbid conditions. They also are delivered in different forms, some by mouth and others via the skin, to enhance absorption.

3. Eczema

Eczema, which is often used synonymously with the term atopic dermatitis, has gained new prominence in discussions of allergic disease. It has long been considered the first sign of allergic tendencies in small children, but we are only beginning to understand how central a role it plays in the atopic march. Healthy skin is a barrier to infection and irritants. An imperfect barrier, inflamed and dry, allows these things to penetrate. This imperfect barrier has been attributed to a filaggrin mutation. The peanut-allergy epidemic has led to a new prominent line of research that attributes sensitization to peanuts not to ingestion but to infant exposure to peanut protein in the home. As discussed above, the first line of pharmaceutical defense is to reduce inflammation, but while the immediate inflammation may be reduced, persistent use of topical steroids can weaken the skin further and in infants especially weaken innate immunity to infection. Another necessary treatment is the application of emollients, but these may contain potentially allergenic ingredients that may sensitize patients. While not life threatening, as measured by various quality of life scales, eczema is even worse day-to-day than other asthma or serious food allergies.

The peanut allergy epidemic, which has attracted so much attention to allergic disease, has led to a possible role of the skin as the starting point for allergic sensitization. British researchers have found that peanut residue is stubborn and biologically active in homes where lots of peanut products are consumed. Eczematous skin is vulnerable to these residues, which can penetrate in sufficient quantities to start an immune response.

Starting with medicines to treat open wounds and burns suffered in combat dating from the bellicose Tang Dynasty (618-906), we developed a protocol of an internal remedy and two external remedies to treat the skin. We have used these to treat dozens of patients, and studied 14 of them retrospectively who began with recalcitrant eczema. They were aged six months to 52 years with various co-morbid asthma, environmental allergies, and food allergies. Half had been treated intermittently with oral corticosteroids before starting TCM, including five who had taken oral steroids in the previous three months. Three had taken immune suppressants usually used by organ transplant patients to combat rejections. All patients reported topical steroids on-and-off, including half in the three months prior to presentation. Median quality of life as measured by the SCORAD Index (0-103), was 89. ⁱⁱⁱ

The internal remedy is *Erka Shizheng Herbal Tea*, in practice called *Shi Zhen* tea, an extract of nine herbs. The external ones are a bath additive containing eight individually extracted herbs, an herbal cream containing two herbs, and a paste made from herbs used in our food allergy herbal formula.

Three months after therapy began, oral steroid use fell 25%. Topical steroid use went down 21% after three months. The reduction in both oral and topical steroid use after 3 months was 29%. Antihistamines, which all patients used, including 11 out of 14 at the onset of TCM, was reduced 32% after three months.

Eleven of 14 patients experienced at least a 50% improvement in quality of life during the first 1-3 months of therapy. At the end of the study period, 12 of 14 patients reported sustained improvement in quality of life with 10 of 14 reporting >80% improvement.

Going forward, we are creating a practice network of physicians to treat patients for recalcitrant eczema. Using these medicines requires no special training in TCM. In this way, we hope to not only relieve current suffering, but also to slow the progress of the rest of the atopic march.

4. Asthma

According to the World Allergy Organization 2011 White Book, some 300 million people suffer from asthma worldwide, contributing to the deaths of 250,000 people annually. In the United States, 9.3% of children and 8% of adults have asthma. Economic costs to the United States approach \$60 billion each year in treatment, 10.5 million missed days of school, and 14.2 million missed days of work. About nine people die from asthma every day, well over 3,000 each year. Poorly controlled asthma can have very serious consequences for food allergy patients with no previous history of respiratory reactions. There is also the danger of "airway remodeling" causing airway smooth muscles (ASMs) to lose their elasticity, among other problems.

Inhaled corticosteroids (ICS) have been the dominant treatment for controlling asthmatic inflammation, and they, like powerful systemic steroids, have some serious side effects. Moreover, there are other conditions that have asthma-like symptoms that don't respond to steroids although they are treated with them. There is no broad-based treatment for all asthmatic phenotypes.

We faced hurdles in creating a TCM anti-asthma drug. Many TCM drugs have relied on Ma Huang, or ephedra, which is frowned on by Western regulators because it can be used to make methamphetamine. We used a 14-herb combination to create an investigational drug we called MSSM-002 which showed promise but because it had so many ingredients we studied the components and arrived at a three-herb version we call ASHMI (anti-asthma herbal medical intervention). This combination of *Ling-Zhi* (*Ganoderma lucidum*), *Ku-Shen* (*Radix Sophora flavescens*), and *Gan-Cao* (*Radix Glycyrrhiza uralensis*), suppressed airway hyper-responsiveness and the collection of certain white blood cells in the airways, called eosinophils, which are drawn to inflammation, as effectively as the original. This research has been going on for 10 years as part of an NIH protocol.^{iv}

We have now done a series of clinical studies in China in cooperation with my former fellows. We have seen that the drug is safe and as effective at suppressing asthmatic inflammation as systemic steroids but with no cytotoxicity and suppression of innate immunity. Moreover, in murine models we have seen evidence that it can help control neutrophilic asthma, which is dominated by another white blood cell—the neutrophil—and doesn't respond to inhaled steroids.

ASHMI inhibits the production of several inflammatory cytokines all at once. Standard pharmacological research focuses on these one at a time, in the form of monoclonal antibodies.

Finally, whereas steroids suppress innate immunity while controlling inflammation, they also are associated with mood disorders, resulting in higher rates of anxiety and depression for asthmatics in treatment than among their peer groups. This is considered especially problematic for children and teenagers. These effects can be measured in the peripheral blood. ASHMI doesn't produce these effects.

5. Food Allergies

Food allergies seem to have come from nowhere, although they have really always been with us, as literature from Greek and Chinese medicine tells us. They have grown as a public health issue over the past two decades, with most cases in commodity foods—milk, eggs, peanuts, tree nuts, wheat, and soy—which are not only common but are often incorporated in processed foods. Symptoms range from uncomfortable itching of oral allergies, which are like pollen allergies, to alarming pruritis and hives, to vomiting, to catastrophic and occasionally fatal anaphylaxis, in which two or more organ systems react.

I began studying the potential for treating food allergies with TCM when I noticed a connection between the symptoms of food and the symptoms of infection by intestinal parasites. This made sense because the proteins in peanut resemble proteins in helminths. One feature of this approach is that it addresses food allergies as a digestive problem as well as an immune problem.

I chose a nine-herb formula Wu Mei Wan (WMW). It was classically prescribed “for colic, vomiting, chronic diarrhea or dysentery, and collapse (also translated as syncope) caused by parasitic worms.” We added two more ingredients particularly effective at immobilizing worms. This formula, which we called Food Allergy Herbal Formula-1 effectively cured anaphylactic peanut allergy in a murine model. Before we could adapt it to human use, we had to remove two alkaloids and came up with Food Allergy Herbal Formula-2, which also cured peanut allergy in mice.^v

We have now been through two human trials—Phase 1 for safety, which we passed with no serious adverse events or toxicity. The Phase 2 had an equivocal result, although there were encouraging signs in the peripheral blood. The study was too brief—six months compared to the equivalent of two years for the mouse studies. And the dosing was too arduous. Subjects aged 12-48 years were expected to take 10 pills at each of three meals a day—30 in all. At least 44% of them were non-compliant.^{vi}

This gives urgency to our efforts to apply Western chemistry to the herbal medicines. Using butanol, we have reduced the therapeutic dose by 80%, which the NIH has approved for another trial of 26-months duration. We have also experimented with another solvent that appears to be even more efficient at separating the active ingredients.

As with our eczema and asthma medicines, we use supplement versions of the food allergy herbal formulas in practice, with very good results, including documented, published cases of patients with frequent severe food anaphylaxis experiencing no additional exacerbations.

We also use our medications adjunctively with the desensitizing techniques oral immunotherapy (OIT) and sublingual immunotherapy (SLIT), which involve ingestion of increasing amounts of the allergen, often provoking adverse effects, particularly gastric distress. We are also working with researchers to explore various combinations because allergies are heterogeneous diseases for which no single therapy will ever be sufficient.

6. Other Research

My colleague Dr. Scott Sicherer has said that where Western science tends to focus on the effects of one molecule on another molecule, TCM allows us to study multiple molecules on multiple other molecules. That is the basis for use of our food allergy herbal formula with Crohn's disease, for which the current standard of care involves regular infusion of an expensive monoclonal antibody. We observed that in addition to inhibiting allergic antibodies, our food allergy formula inhibited production of tumor necrosis factor alpha (TNF- α). High levels of TNF- α are also associated with Crohn's disease. Two studies have shown that FAHF-2 two is very promising for modulating the inflammatory cytokines associated with Crohn's.^{vii}

A pediatric nephrologist at Mount Sinai has been exploring the use of a Chinese herb she found in our data base to try to mitigate rejection of transplanted kidneys in her patients, who currently must rely on powerful immune suppressants, and her work has been published in a major journal.^{viii}

We have a unique resource—the combination of a busy practice and a world-class lab team. We are using this combination in practice-based research operating under IRB rules to learn as we go. We have a bio-marker study to determine whether our patients are achieving tolerance to their allergens using individualized treatments. The initial phase was funded by parents of patients, who are also paying for treatment.

7. Altering the heritability of allergies

Food allergy parents particularly wonder what they did wrong, why their children were born allergic. In addition to trying to halt the atopic march, we are working to create an oral vaccine that would protect children from inheriting allergic tendencies, starting with peanut. It will employ as an adjuvant non-toxic cholera toxin B (CTB), which has been used safely by pregnant women and infants for 30 years in an oral cholera vaccine, delivered by a probiotic bacillus subtilis (BS) spore with the allergen and adjuvant bound to the surface. It also induces antigen-specific clinical tolerance in autoimmune disorders when co-administered with antigen by induction of IL-10 and Tregs.

This study doesn't strictly fall under the umbrella of TCM. However, our exploration of the immune system in studying the actions of herbal medicines gives us hope that this approach will work.

We also are trying to understand what it is about food processing and preparation that elicits a violent immune response through the study of advance glycation end products.

Much of this research is being done through collaboration with other scientists around the world.

Discussion

Australian allergist Dr. Susan Prescott has expressed optimism that the allergy epidemic, which has overtaken us in a matter of decades, it might be reversed over a similar period. "In theory, the very fact that modern diseases have increased means they must be modifiable. The same factors that are promoting the disease could also be actively harnessed to reduce the risk of disease."

However, while excellent work is being conducted, much of it is being done on the same timetables and piecemeal fashion that have left us with no more ability to cure allergies than we had a century ago, and at high cost. While it would be very difficult to unwind all the environmental, dietary, medical, and behavioral changes that have contributed to the epidemic, greater understanding of the physiology is giving us clues to how to roll back the effects. Traditional Chinese medicine, which has so many centuries of treating complex, multi-organ, infectious and inflammatory disease, gives a platform to build on.

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ⁱⁱ Susan L. Prescott, MD, PhD "Early-life environmental determinants of allergic diseases and the wider pandemic of inflammatory noncommunicable diseases" *Journal of Allergy and Clinical Immunology* January 2013 Volume 131, Issue 1, Pages 23–30

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^v Kamal D. Srivastava, MPhil, Jacob D. Kattan, BS, Zhong Mei Zou, PhD, Jing Hua Li, MD, Libang Zhang, MD, Sylvan Wallenstein, PhD, Joseph Goldfarb, PhD, Hugh A. Sampson, MD, and Xiu-Min Li, MD "The Chinese herbal medicine formula FAHF-2 completely blocks anaphylactic reactions in a murine model of peanut allergy" *Journal of Allergy and Clinical Immunology* January 2005 171-178

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