

Reducing Pain and Inflammation Naturally - Part V: Improving Neuromusculoskeletal Health by Optimizing Immune Function and Reducing "Allergic" Reactions.

A Review of 16 Treatments and a 3-Step Clinical Approach

Alex Vasquez, DC, ND

Abstract: It is clear from experimental research and clinical experience that "allergic" reactions to foods and environmental toxicants can precipitate neuromusculoskeletal pain and inflammation. This is most obvious in patients with migraine headaches and inflammatory arthropathy such as "rheumatoid arthritis" – one of the most commonly overused diagnostic labels applied to patients with various types of idiopathic inflammatory arthropathy. Unfortunately, current treatments for the allergic diathesis have centered on either 1) symptom suppression, 2) identification and avoidance of the offending food/allergen, and/or 3) systemic immunosuppression with drugs. These approaches result in short-term and limited clinical improvement compared to what can be achieved with a more comprehensive approach that focuses on normalization of immune responsiveness. "Food allergies" are not the fault of the food; rather they are a manifestation of immune system hyper-responsiveness and dysfunction that must be treated comprehensively. This article focuses on techniques for reducing immune system hyper-responsiveness with the use of nutritional and botanical supplements, and the next article in this series (Part 6) will provide additional information on the optimization of gastrointestinal health by focusing on the eradication of immunodysregulatory microorganisms, particularly certain species of yeast, bacteria, amebas, and protozoa.

"Allergic disease is a manifestation of a fundamental distortion of the mechanism through which the individual adapts itself on a cellular level to a hostile environment."

Howard Rapaport, MD in *Journal of Asthma Research*¹

INTRODUCTION:

Allergic disorders are common and their incidence appears to be increasing. These conditions are complex, multifactorial, and range in severity from asymptomatic, to moderately problematic, to life-threatening. Different names and ICD-9 codes are applied to different types of immunodysfunction within the genre of "allergy"; however, the underlying problem—immune dysfunction—is almost never addressed directly. Rather, symptom suppression via lifelong medicalization is the mainstay of treatment—a quagmire that leaves patients under-treated and dependent on endless cycles of prescription drugs that never offer the opportunity for cure. Furthermore, some conditions traditionally thought of as "allergic" may more accurately be ascribed as "microbial", "metabolic" or "deficiency-induced" as will be exemplified in the sections that follow. While it is true that some patients will require some form of long-term treatment, clinicians should consider addressing and correcting the underlying immune dysfunction before resorting to symptom suppression (ie, antihistamines) and immunosuppression (ie, corticosteroid drugs). Until proven otherwise, "allergic" patients should be assumed to have one or more treatable causes of their allergic disorder before it is conceded that their allergies are "genetic" or "idiopathic" and therefore treatable only with drugs.

The allergic phenomenon is complex, interconnected, and multifaceted. It goes far beyond the dogma that IgE

binds with mast cells and results in the release of histamine, which then acts singly for the development of allergic manifestations.² The allergic response involves a wide range of cells including T-cells and epithelial cells, and the triggers and mediators of allergic pathophysiology extend beyond IgE and histamine to include corticotrophin-releasing hormone, IgG, cytokines, superoxide anion, IL-6, cyclooxygenase-2, lipoxygenase, NF-kappaB, and arachidonic acid metabolites, especially the leukotrienes. Evidence for the medical acceptance of the leukotriene theory of allergy is demonstrated by FDA approval and widespread use of montelukast, a leukotriene receptor type-1 blocker, marketed by the name of "Singulair" and FDA-approved for the treatment of asthma and allergic rhinitis.³ As we would expect, NF-kappaB is upregulated in allergic tissues, and therefore the clinical utilization of NF-kappaB inhibitors is justified, as recently reviewed in this Journal.⁴

Allergies do not cause themselves, nor is the putative offending agent to blame. In a patient allergic to strawberries, are the strawberries guilty? Does a patient with allergies have an antihistamine drug deficiency? A more likely cause of the problem lies in subtle perturbations affecting numerous immunoregulatory mechanisms, and these disturbances may include genetic, nutritional, metabolic, and microbial aberrations—most of which can be modulated by appropriate clinical intervention for the attainment of improved clinical outcomes.

OVERVIEW: THE ORIGINS OF ALLERGY AND THE REALITY OF ALLERGY-INDUCED PAIN

Allergy-induced arthritis affects a small but significant

portion of patients with joint pain and inflammation.⁵⁻¹¹ Impressively, some patients with rheumatoid arthritis can have their "disease" literally cured by food allergy elimination, only to have the disease recur when allergens are again consumed.¹² Given this evidence, it is inappropriate that food allergy is ignored by medical textbooks and that chemotherapeutic drugs such as methotrexate are advocated as the medical "treatment of choice" for patients who do not respond to non-steroidal anti-inflammatory drugs (NSAIDs).¹³ Advocated as "first line therapy" for the medical treatment of arthritis, NSAIDs are well-known to damage the intestinal mucosa (resulting in "leaky gut") and thereby allow increased absorption of food allergens which results in the exacerbation of allergic disease¹⁴—thus it is perfectly clear that medical treatment of arthritic patients with NSAIDs can lead to a worsening of their arthritis by amplifying the allergic reactions. Furthermore, it is also clear that NSAIDs promote joint destruction and bone necrosis.¹⁵⁻¹⁸ I have discussed this in great detail elsewhere in support of the position that chiropractic physicians must gain prescription rights for the sake of managing the overpharmaceuticalization of patients treated medically.¹⁹

Migraine headaches are another example of allergy-induced pain. While any migraneur may be allergic to any particular food, the most common offenders are wheat (78%), orange (65%), eggs (45%), tea and coffee (40% each), chocolate and milk (37% each), beef (35%), and corn, cane sugar, and yeast (33% each). It is not uncommon for patients to have to avoid up to 10 foods before attaining maximal improvement, and up to 85% of migraine patients can be cured of their headaches by the use of allergy avoidance alone.²⁰ While the allergen-avoidance approach to migraine treatment is highly efficacious and well documented in the biomedical research, patients and clinicians alike might wonder if a more convenient non-drug approach might be available that addresses the root of the problem. It is true that a dysfunctional immune system cannot react to an allergy-inducing food if the food is not eaten; however, the fact remains that the immune system is left in a state of dysfunction unless doctor and patient engage in the process of improving overall health. In contrast to a lifetime of allergen avoidance, improvement in immune function allows patients to consume a more normal diet and broader range of foods.

Patients with pain affecting the spine and peripheral joints may also respond to allergen avoidance or the immunomodulatory treatments described in this article. Doctors have an obligation to rule out common and serious diseases in patients with musculoskeletal pain, as I have described in extensive detail in my textbook *Integrative Orthopedics*.²¹ Following the exclusion of conditions such as hemochromatosis²², vitamin D deficiency²³, septic

arthritis, and other systemic and urgent orthopedic conditions²¹, both doctor and patient must engage in a process of therapeutic trial-and-error. This process is arduous and time-consuming unless the doctor uses a group of protocols such as those described herein which address the most common contributing factors to allergic problems. Here I describe a three-step process that has benefited many allergic patients in my clinical practice.

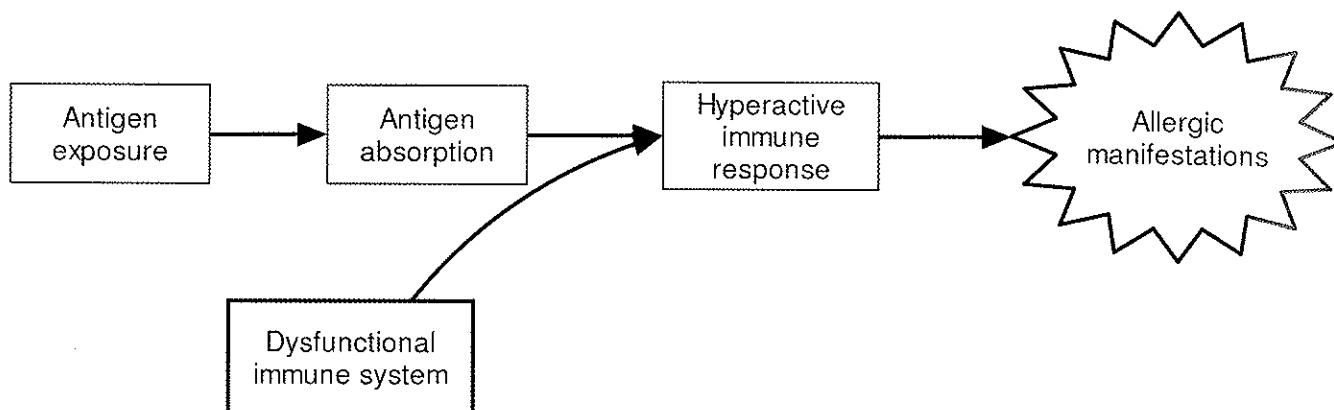
My clinical approach to improving immune function in patients with allergy begins with supplementation of vitamin E, CoQ-10, vitamin C, bioflavonoids, and fatty acids. We can also use honey, vitamin B-12, and glucosamine sulfate and purified chondroitin sulfate. In difficult cases, I look at hormones, particularly DHEA, progesterone, testosterone, and cortisol. I also look at diet and bowel health with respect to putrefaction and intestinal permeability. Although rarely powerful when used in isolation, these treatments when used in combinations tailored to the individual patient often result in an impressive reduction in allergic manifestations even when allergen avoidance is either not pursued or not feasible.

Step 1: From initial patient assessment to the first phase of treatment

In a patient with presumed "allergy" who is in otherwise good health, following a basic health assessment and exclusion of significant disease²¹, I begin by correcting problems that are common to patients with allergy. Minor improvements in allergy symptoms as a result of a low-cost low-risk interventions can be multiplied with a specified group of interventions; we aim for a modest improvement with several treatments rather than a "silver bullet" miracle cure with a single intervention. For example, 10% improvement in symptoms may be insignificant in itself; however a 10% improvement from six interventions results in a 60% improvement and enhances patient confidence long enough for other interventions and assessments to be implemented, if necessary. The goal with the first step of treatment is to correct the most common and most likely problems, namely fatty acid imbalances, micronutrient deficiencies, phytonutrient insufficiencies, and dysbiosis. Basic treatments on the first visit generally include the following, in addition to multivitamin/multimineral supplementation with additional vitamin D:

1. **Avoidance of suspected food allergens:** The most common allergens are wheat, cow's milk, and eggs; however any patient can be allergic to any food. Food allergy avoidance for 1 month helps achieve symptomatic relief and allows the gut to heal and the immune system to recalibrate.
2. **Consumption of the Paleo-Mediterranean Diet:** The diet should emphasize consumption of lean

Figure 1. Allergic inflammation is the result of antigen exposure to a dysfunctional immune system.
 From Vasquez A. *Integrative Orthopedics*. (OptimalHealthResearch.com): 2004



meats, fruits, vegetables, nuts, seeds, and berries to ensure a systemic anti-inflammatory effect and increased consumption of anti-inflammatory phytonutrients, especially flavonoids. High-glycemic foods are avoided as are “food additives” such as tartrazine, which is known to exacerbate allergic asthma. Details of this diet are provided on-line at OptimalHealthResearch.com/monograph05.

3. **Coenzyme Q-10:** CoQ-10 levels are low in approximately 40% of patients with allergies, according to a small study conducted by Folkers and Pfeiffer.²⁴ Asthmatics also have lower levels of CoQ-10 compared to healthy people.²⁵ In my experience, clinical improvement is commonly seen in allergic patients after supplementation with CoQ-10. I generally prescribe 100-200 mg per day of CoQ-10 for adults with allergy. Impressively, migraine headaches are known to be induced by consumption of allergenic foods²⁰, and migraine headaches can be powerfully prevented and alleviated with CoQ-10.²⁶
4. **Vitamin C:** Vitamin C reduces blood levels of histamine by increasing urinary excretion and metabolic breakdown of histamine. Cathcart hypothesized that high doses of vitamin C (i.e., bowel tolerance) may impair the adsorption of IgE with allergens and thus retard the allergic cascade from being initiated.²⁷ Either of these two mechanisms, perhaps in addition to other mechanisms, may explain the anti-allergy effects of ascorbic acid.²⁸ A recent clinical trial showed that 2 grams per day of ascorbic acid reduced blood histamine levels by 38%.²⁹ Supplemental vitamin C improves the health of intervertebral discs and alleviates pain and reduces the need for surgery in patients with lumbar disc herniations.³⁰

5. **Vitamin E:** Vitamin E has been shown to reduce IgE levels in humans and to reduce the manifestations of allergy-related disease.³¹ Vitamin E has been shown to relieve joint pain.³²
6. **Balanced fatty acid supplementation:** Balanced, combination fatty acid supplementation containing ALA, GLA, EPA, and DHA is the preferred method for fatty acid supplementation for reasons that I have detailed previously.^{21,33} The combination of fish oil and borage oil is known to reduce formation of leukotrienes, which are among the primary mediators of allergic reactions and joint inflammation.³⁴ Fish oil supplementation helps correct the fatty acid abnormalities seen in allergic patients³⁵ and reduces production of prostaglandin-D2, which increases the release of histamine from mast cells.³⁶
7. **Probiotics:** Supplementation with probiotics (beneficial strains of bacteria and yeast) appears to improve intestinal barrier function, promote microecological balance in the gastrointestinal tract, modulate immune function, and thus reduce manifestations of allergic disease.³⁷⁻³⁹

Step 2: Additional interventions for moderate or unresponsive allergies.

For patients who do not respond sufficiently to the first phase of treatment, the following interventions can be considered.

1. **Vitamin B-12:** Vitamin B-12 has been shown to reduce physiologic manifestations of allergy in ovalbumin-sensitized mice.⁴⁰ Since vitamin B-12 is safe, non-toxic, and bioavailable when administered orally in large doses to humans, I commonly prescribe 2,000-6,000 mcg per day for allergic patients. Although the benefit of vitamin B-12 in patients with sulfite-sensitive asthma is biochemically medi-

ated rather than immunologically mediated⁴¹, this research adds tangential support to the use of high-dose vitamin B-12 in selected patients with allergy (particularly asthma), at least for a short-term clinical trial. It is impressive to note that vitamin B-12 has anti-allergy effects, and that a recent clinical trial showed that high-dose vitamin B-12 supplementation was effective in alleviating back pain even in patients who were not vitamin B-12 deficient.⁴²

2. **Supplemental bioflavonoids/flavonoids:** Bioflavonoids stabilize mast cell membranes and thus reduce the liberation of histamine. Additionally, quercetin and catechin inhibit the action of histidine decarboxylase, which converts histidine into histamine. Many fruits, vegetables, and herbal teas are excellent sources of flavonoids such as quercetin, which can also be consumed in the form of tablets and capsules.
3. **Pancreatic and proteolytic enzymes:** Pancreatic enzymes have been shown to alleviate symptoms of food allergy in a controlled clinical trial.⁴³ Administration of enzyme preparations can alleviate intestinal and extra-intestinal manifestations of food allergy.⁴⁴ Proteolytic enzymes are safe and effective for the relief of musculoskeletal pain, as reviewed previously in this Journal.⁴⁵ When taken with food, pancreatic/proteolytic enzymes facilitate hydrolysis of proteins, fats, and carbohydrates and are then absorbed into the systemic circulation for an anti-inflammatory effect. Although individual enzymes may be used in isolation, enzyme therapy is generally delivered in the form of polyenzyme preparations containing pancreatin, bromelain, papain, amylase, lipase, trypsin and alpha-chymotrypsin.
4. **Honey:** Honey consumption has been shown to significantly reduce (-34%) serum IgE levels in humans.⁴⁶ The required dose is 1.2 g of honey per kg body weight. For a relatively large individual who weighs 220 lbs, the correct amount of honey to remain consistent with this study would be approximately 120 grams. Since one tablespoon of honey weighs 21 grams, the dose would be 5-6 tablespoons (one-third cup) of honey per day (for a person weighing 220 lbs). Since each tablespoon of honey contains 64 calories, six tablespoons of this powerful natural anti-inflammatory nutraceutical would add 384 calories to the daily diet. Honey should not be administered to infants because of the risk of botulism. Honey is a rich source of flavonoids, and many bee products contain caffeic

acid phenethyl ester, which is a potent inhibitor of NF-kappaB as I reviewed previously.^{4,21}

5. **NF-kappa B inhibitors:** The clinical significance of NF-kappaB and its phytonutritional modulation was reviewed recently in this Journal.⁴ Nutrients which can be used to downregulate inflammatory responses are vitamin D, curcumin (requires piperine for absorption), lipoic acid, green tea, rosemary, grape seed extract, propolis, and resveratrol.²¹

Step 3: Treatment for severe allergic disease

For some patients with severe allergies, we start with selected treatments from Step 2 or Step 3 on the first visit in addition to the treatments included in Step 1. Implementation can be customized based on history, examination, laboratory findings, and the doctor's experience and good judgment.

1. **Hormones:** Hormones such as DHEA, progesterone, testosterone, and cortisol tend to be lower in allergic/autoimmune individuals than in healthy controls.⁴⁷ I generally test with 24-hour urine samples before prescribing hormones, though I will empirically use progesterone in a woman or a 3-month trial of DHEA in a man with allergies if I find sufficient indications and no contraindications. Treatment is customized per patient based on clinical experience and lab tests.
2. **Calcium and magnesium butyrate:** Butyrate is a short-chain fatty acid which can be obtained from 1) a limited number of foods, namely butter, 2) intestinal fermentation of carbohydrates by probiotic bacteria, and 3) use of nutritional supplements. It is increasingly well-established that probiotic bacteria have immune-normalizing and "anti-allergy" effects, and this benefit is probably mediated at least in part by probiotic production of butyrate. The mechanisms of the anti-allergy effect of butyrate are manifold, and as a fatty acid butyrate activates peroxisome-proliferator activated receptor-alpha (PPAR-alpha) and thereby results in an immunomodulatory action and a suppressive effect on NF-kappaB.^{48,49} Butyrate is also a primary fuel for enterocytes and may improve enterocyte metabolism for the normalization of intestinal permeability. In the treatment of patients with inflammatory bowel disease, 4 grams per day of orally administered butyrate salts safely improves the action of mesalamine⁵⁰ as does topical application of butyrate in distal ulcerative colitis.⁵¹ As a normal dietary component and product of the gastrointestinal tract, supplemental calcium and magnesium salts of butyrate are safe and effective

for human consumption at doses of 1,000 – 4,500 mg butyrate per day for the alleviation of allergic diseases.^{52,53}

- 3. Purified Chondroitin Sulfate and Glucosamine Sulfate—underappreciated in the treatment of allergy:** Doctors and patients everywhere should know that chondroitin sulfate and glucosamine sulfate are safe and effective for the treatment of osteoarthritis.⁴⁵ There is also evidence that purified chondroitin sulfate is cardioprotective and that it helps to reduce the vessel occlusion characteristic of atherosclerosis.⁵⁴ Additionally, new experimental evidence shows that chondroitin sulfate and glucosamine sulfate can inhibit allergic reactions.⁵⁵ With this in mind, it is reasonable to speculate that many arthritic patients who respond to glucosamine and chondroitin may actually be responding to the anti-allergy benefits of chondroitin and glucosamine rather than or in addition to the “cartilage building” properties of these supplements. Furthermore, there is evidence that purified chondroitin sulfate can act as a “decoy” and reduce adhesion of harmful bacteria; the role of harmful gastrointestinal bacteria in the genesis and perpetuation of joint pain and inflammation will be discussed in the next article in this series. For now, it will suffice to say that occult gastrointestinal infections are a major contributor to the systemic pain and inflammation seen in conditions such as rheumatoid arthritis and ankylosing spondylitis.²¹
- 4. Eradication of harmful intestinal yeast, bacteria, and other “parasites”:** I have seen several patients become cured of their “allergies” once we eradicated the dysbiotic bacteria, yeast, amoebas, or other microorganisms from their gastrointestinal tract. Intestinal colonization with harmful bacteria/yeast/protozoa/amebas can cause mucosal injury and result in macromolecular absorption and thus promotes immune sensitization to dietary antigens; in these situations, correction of dysbiosis via eradication of harmful microorganisms can lead to an impressive reduction in food-associated allergic phenomena. Galland and Lee⁵⁶ reported that eradication of *Giardia lamblia* in patients with chronic digestive complaints lessened the severity of food intolerance/allergy in 54% of patients. The next article in this series will be completely dedicated to the topic of gastrointestinal flora assessment and modification, a supremely important topic.

CONCLUSIONS:

It is well established that musculoskeletal pain can result

from “allergic” reactions to foods, and occasionally to allergens in the surrounding environment. Rather than suppress the entire immune system with drugs, we can modulate and improve immune function with nutritional and botanical interventions. Specific nutrients that have been shown to alleviate pain and allergy/inflammation include vitamin B-12, purified chondroitin sulfate, glucosamine sulfate, balanced fatty acid supplementation, CoQ10, vitamin E, flavonoids, vitamin C, vitamin D, and pancreatic/peptolytic enzymes. The next article in this series will detail assessment and treatment of gastrointestinal dysbiosis, a commonly overlooked cause of musculoskeletal pain and inflammation.

ABOUT THE AUTHOR:

Dr. Alex Vasquez is a licensed naturopathic physician in Washington and Oregon, and licensed chiropractor in Texas, where he maintains a private practice and is a member of the research team at Biotics Research Corporation. As former Adjunct Professor of Orthopedics and Rheumatology for the Naturopathic Medicine Program at Bastyr University, he is the author of “Integrative Orthopedics: The Art of Creating Wellness While Managing Acute and Chronic Musculoskeletal Disorders” available from OptimalHealthResearch.com. Dr. Vasquez has published research in nearly every major medical journal in the world, including *The Lancet*, *Journal of the American Medical Association*, *British Medical Journal*, and *Arthritis & Rheumatism*.

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