

## Allergies

### Finding Relief for a Common Condition

Updated: 01/18/2006

Allergies are extremely common. Seasonal allergies (commonly called hay fever) alone affect at least 35.9 million Americans and account for approximately 16.7 million office visits to healthcare professionals each year (Natahn RA et al 1997). In children younger than 11 years old, allergic dermatitis (inflammation of the skin) is the most common skin condition. Allergies can affect people of all ages, although they tend to develop in childhood or adolescence. The leading risk factor for allergies is exposure to an allergen, even though there is a genetic component to allergies, and newer studies have linked them to obesity in women (Vieira VJ et al 2005).

Allergies occur because of an exaggerated immune response to a substance called an allergen. To be effective, the immune system must operate within a narrow balance; a lack of immune response leads to easy infection, while an overactive immune system can lead to autoimmune diseases (in which the body attacks itself) or allergies (in which the body overreacts to otherwise harmless substances).

Common inhaled allergens include pollen, animal dander, dust, mold, and insect parts (AAAAI 2005). Ingested allergens include medications (penicillin, for example) and foods such as milk, eggs, peanuts, tree nuts, shellfish, fish, wheat, and soy. People can also be allergic to plants, nickel, copper, and latex (Kasper DL et al 2005).

Symptoms of allergies include the following (NIH 2005a):

- runny nose
- tearing, burning, or itching eyes
- red eyes (conjunctivitis)
- swollen eyes
- itching (nose, mouth, throat, skin, or any other area)
- wheezing
- coughing
- difficulty breathing
- hives
- skin rashes
- stomach cramps
- vomiting
- diarrhea
- headache

The most severe form of allergic reaction is called anaphylaxis. This is a serious condition that results in respiratory distress and swelling of the larynx, often followed by vascular collapse or shock (Kasper DL et al 2005). It often appears within minutes of exposure to a specific allergen and should be treated rapidly because death can occur within minutes or hours after the first symptoms appear. Many people prone to anaphylaxis carry self-injecting epinephrine pens in case of emergencies.

Relieving allergy symptoms represents a large and extremely lucrative business for drug companies. Medicines frequently prescribed or sold over the counter for allergy relief include antihistamines, decongestants, and corticosteroids. While these medicines work, they may have significant side effects. Antihistamines, for example, can cause drowsiness, dry mouth, blurred vision, constipation, and many other unwanted effects (NIH 2005a). Oral corticosteroids taken for more than three or four weeks are associated with significant side effects, including a weakened immune system and many other unwanted consequences (NIH 2005b).

Fortunately, it is possible, by use of nutritional therapy, to reduce allergy symptoms through more natural methods. Additionally, antioxidants such as vitamin E, vitamin C, glutathione, and coenzyme Q10 (CoQ10) defend the body against oxidative molecules that are formed during the allergy response. Each of these will be discussed in detail.

### **FOOD ALLERGIES: ENHANCING NATURAL BACTERIA**

The symptoms seen with food allergies are often the same as allergic symptoms not related to foods. Other conditions are sometimes also associated with food allergies, such as migraine, chronic ear infections, arthritis, and inflammatory bowel disease

(Gaby A 1998). About 2 percent of adults in the United States have food allergies (Moneret-Vautrin DA et al 2005). Food allergies are sometimes associated with anaphylaxis, and can also cause low-grade gastrointestinal upset.

The health of the gastrointestinal system plays a pivotal role in food allergies. The gastrointestinal system acts as a semipermeable barrier, allowing only usable molecules into the bloodstream after food has been broken down. However, when the intestinal wall has been weakened by infection or inflammation (possibly caused by allergic reactions), the barrier function is compromised, allowing large molecules to pass through the intestinal wall and into the bloodstream (Moneret-Vautrin DA et al 2005). Allergic sensitization can occur as the immune system responds to these abnormally large molecules, causing digestive complaints such as upset stomach or diarrhea, or symptoms such as joint pain and headaches (Moneret-Vautrin DA et al 2005).

To avoid these kinds of allergic reactions, researchers have examined ways to reduce permeability in the intestinal wall. One promising method is to enhance the population of beneficial bacteria in the gut with probiotic bacteria. The human digestive tract relies in part on colonies of healthy bacteria to aid digestion. There is evidence that a healthy population of intestinal bacteria can help reduce intestinal permeability (Vinderola CG et al 2004; Gun F et al 2005).

Probiotic bacteria include Lactobacilli, Bifidobacteria, and Saccharomyces boulardii (Casas IA et al 2000; Peltó L et al 1998; Goldin BR 1998; Cross ML et al 2001). Also, fructooligosaccharides should be included to encourage the growth of beneficial bacteria (Bouhnik Y et al 1999). Freeze-dried beneficial bacteria and fructooligosaccharides are sold as dietary supplements.

### ***What Makes an Allergy Attack***

In most allergy cases, the body is first sensitized to a foreign protein (allergen), causing the production of an antibody called immunoglobulin E (IgE). The newly produced IgE antibody circulates in the bloodstream, where it attaches to another kind of white blood cell called a basophil. In addition, IgE binds to mast cells, a type of white blood cell located in the skin and the mucosal lining.

The next time the allergen is recognized, the IgE antibody provokes the release of chemicals that cause a typical allergy attack. These chemicals include histamine, prostaglandins, and leukotrienes. Histamine in particular is an important target for allergy medications. Produced by mast cells, histamine causes localized swelling and inflammation. Many conventional treatments block the action of histamine. Certain nutrients have been shown to depress the activity of mast cells.

Besides the release of histamine, activated mast cells cause inflammation in other ways. During the inflammatory response to an allergen, pro-inflammatory chemicals are released from mast cells. In response to the pro-inflammatory chemicals, leukocytes (white blood cells) are attracted. The result of this cascade is inflamed tissue and increased production of white blood cells—a runny nose and increased mucus secretion in the lungs.

### ***Testing and Conventional Treatment for Allergies***

Many types of testing are available to detect allergies, including the following:

- **Scratch or prick skin test:** This is the most commonly used allergy test. During this test, small amounts of allergens are introduced on or into the skin. Redness, itching, and a raised wheal appear within 20 minutes if there is a positive reaction to an antigen (NIH 2005b). This test can identify specific allergens or classes of allergens. Because it involves introduction of possible allergens, it does carry some risks, including the rare but serious occurrence of a life-threatening anaphylactic reaction.
- **Radioallergosorbent test (RAST):** This test evaluates IgE levels and activity in serum. Like the skin test, the RAST provides allergen-specific information. Because it is performed in the lab on serum only, there are no risks associated with this test.
- **Differential leukocyte count:** The white blood cell count and differential is part of the complete blood count. The total number and types of white blood cells are measured. They generally include neutrophils, lymphocytes, monocytes, basophils, eosinophils, and bands. Eosinophils are often elevated with allergic reactions (Fischbach F 1996). This test is nonspecific and provides no information about specific allergenic substances.
- **Enzyme linked immunosorbent assay (ELISA):** The ELISA is very sensitive and can measure various immunoglobulins. It is very useful because of its ability to detect both immediate and delayed hypersensitivity reactions (Bacarese-Hamilton T et al 2005). It provides an indirect determination of what materials a person may be allergic to. Like RAST, it carries no direct risk to the patient.
- **Elimination-challenge diet:** The elimination-challenge diet is useful for detecting food allergies. This diet involves eating only hypoallergenic foods for several weeks. The elimination diet is followed by a systematic reintroduction of possible triggers. Symptoms should be closely monitored (Rolnick-Werninghaus C et al 2005).

Once an allergen has been identified, traditional therapy relies on avoidance of the allergen whenever possible and a diverse group of pharmaceuticals. The most common pharmaceuticals include the following:

**Antihistamines.** This group of pharmaceuticals is used to treat symptoms caused by histamine, such as watery and itchy eyes,

hives, sneezing, and smooth muscle constriction in the lungs, which produces wheezing and aggravates asthma and obstructive pulmonary disease. Antihistamines are contraindicated for patients with high blood pressure or narrow angle glaucoma and can cause drowsiness.

**Decongestants.** These drugs cause small arterioles to constrict and decrease fluid and mucous secretion. Decongestants may be oral medications, nasal sprays, or eye drops. Active ingredients include pseudoephedrine, desoxyephedrine, oxymetazoline, and phenylephrine. Over-the-counter decongestants are frequently sold in combination products with antihistamines. Side effects may include increased blood pressure and drowsiness.

**Corticosteroids.** Steroids are taken orally or topically, inhaled into the lungs or taken in nasal sprays. They decrease inflammation. Side effects can be serious if corticosteroids are taken orally over a long period of time.

**Leukotriene antagonists.** Leukotrienes are generated in mast cells and other white blood cells and contribute to the allergic response. Leukotriene antagonists are designed to inhibit leukotriene formation.

**Cromolyn sodium.** Cromolyn is used as a nasal spray for rhinitis and inhaled for asthma and bronchospasm. It works by stabilizing mast cell membranes, preventing them from releasing histamine.

**Beta-agonists.** These are drugs that selectively inhibit beta-1- and beta-2-adrenergic receptors, causing smooth muscle relaxation and bronchodilation. Albuterol and epinephrine are included in this category.

**Immunotherapy.** During immunotherapy, allergy shots are given to gradually desensitize the immune response. Treatment may be continued for three or more years, although there is a risk of side effects because of allergic reaction to the shot itself.

### ***What You Have Learned So Far...***

- Allergies are extremely common among both children and adults. Common allergens include environmental substances like pollen, food, and medications.
- An allergic reaction is caused by a hyperactive immune response to a foreign protein (allergen). Allergic responses can be triggered by antibodies that are produced in response to the allergen. The most common allergenic antibody is immunoglobulin E (IgE).
- During an allergy attack, the activated antibodies stimulate other types of immune cells, including mast cells, to release pro-inflammatory chemicals (e.g. histamine, leukotriene) that cause the symptoms associated with allergies. These symptoms can range from mild to serious, including life-threatening anaphylactic shock, which requires immediate medical treatment.
- Drugs commonly used to treat allergies include antihistamines, decongestants, and corticosteroids. While these drugs work, they are associated with significant side effects in some cases.
- Natural therapies for allergies are available and work along the same biological pathways as pharmaceutical treatments.

## **FIGHTING ALLERGIES THE NATURAL WAY**

People who wish to avoid pharmaceuticals or who cannot use allergy medications will find that several nutritional therapies help reduce the symptoms of allergies.

**Perilla frutescens and rosmarinic acid.** Perilla contains many active ingredients, such as rosmarinic acid and luteolin. Oral supplementation with perilla leaves or extracts of rosmarinic acid has been shown to suppress allergic reactions (Takano H et al 2004). Rosmarinic acid relieves allergy symptoms by preventing the activation of immune responder cells and by inducing apoptosis, or cell death, in already activated immune responder cells (Hur YG et al 2004). Natural flavonoids like rosmarinic acid kill off excess allergy-activated immune cells while leaving the vast bulk of responder cells to fight off bacteria and other foreign invaders. Rosmarinic acid has been demonstrated to kill allergy-activated T cells and neutrophils without affecting the T cells or neutrophils in their resting state (Sanbongi C et al 2003). Perilla leaf extract and rosmarinic acid were found to be nearly equally effective at inhibiting the allergic response when given orally. A follow-up study confirmed that oral administration of perilla leaf extract inhibits production of tumor necrosis factor-alpha and attenuates the allergic response and inflammation in mice (Ueda H et al 2002). Other studies have shown the following:

- Rosmarinic acid inhibited interleukin-2 (IL-2) promoter activation of T cells (Won J et al 2003).
- Rosmarinic acid had potent immunosuppressive effects and inhibited both the activation and proliferation of T cells (Yun SY et al 2003).
- Researchers demonstrated that daily treatment with rosmarinic acid in perilla leaf extract given orally to mice prevented allergic asthma caused by dust mite allergen. The study concluded that oral administration of perilla-derived rosmarinic acid

may treat allergic asthma effectively by limiting cytokines and allergy-specific antibodies (Sanbongi C et al 2004).

- Another study demonstrated that perilla leaf extract enriched with rosmarinic acid is effective among humans suffering from seasonal allergic symptoms (Takano H et al 2004). In this study, rosmarinic acid particularly inhibited the eye-related symptoms associated with seasonal allergies.

Like rosmarinic acid, luteolin is a natural plant flavonoid that may have potent antiallergic properties. It is found along with rosmarinic acid in various species of the perilla plant but at lower concentrations. In one study, luteolin was shown to be the most potent inhibitor of interleukin-4 (IL-4) production in certain immune cells. Okayama University researchers found that luteolin was the most potent inhibitor of histamine release from immune mast cells (Inoue T et al 2002). Oral administration of perilla leaf extract inhibited inflammation, allergic response, and tumor necrosis factor in mice (Ueda H et al 2002). Also, luteolin was documented to inhibit interleukin-5 (IL-5), which promotes the growth and survival of eosinophils, one particular type of leukocyte that is activated during allergies (Park KY et al 1999).

**Quercetin.** Quercetin, a flavonoid found in red wine and green tea, has been studied for its ability to reduce the symptoms of allergies. Studies have shown:

- Subjects with nasal allergies treated with a nasal spray that included quercetin, along with extract of *Artemisia abrotanum* L, experienced rapid and significant relief of nasal symptoms that was comparable to antihistamine preparations (Remberg P et al 2004).
- Among patients with IgE-mediated nasal allergies, quercetin was found to be a safe therapy that could be used as a primary therapy or in conjunction with conventional pharmaceuticals (Thornhill SM et al 2000).
- In an in-vitro study, quercetin was investigated for its ability to inhibit histamine release in IgE-mediated allergic responses (Kiamata M et al 2000).

Evidence suggests that quercetin inhibits the ability of neutrophils to promote histamine release (Wang YC et al 1990).

**Fish oil.** Fish oils contain the omega-3 fatty acids docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA). EPA and DHA exert anti-inflammatory and antithrombotic effects (Calder PC 2005) because omega-3 fatty acids compete with arachidonic acid, which serves as a substrate for conversion into pro-inflammatory eicosanoids (Leaf A 2002; Connor WE 2001; Calder PC 2001). Studies suggest that fish oils reduce the production of cytokines such as interleukin-1, IL-2, and tumor necrosis factor, which are all involved in the allergic response. Additionally, fish oil can suppress B- and T-lymphocyte synthesis and decrease delayed-type hypersensitivity skin reactions. In one study, an ointment containing DHA and EPA produced satisfactory results in 64 patients with refractory dermatitis (Watanabe T et al 1999).

**GLA.** Gamma-linolenic acid (GLA) is an omega-6 (n-6) fatty acid found in borage seed oil, evening primrose oil, and black currant seed oil. GLA serves as a substrate for prostaglandins, including the anti-inflammatory prostaglandin-1, and as a precursor in the synthesis of EPA.

**Green tea (*Camellia sinensis*).** Green tea contains several active constituents, such as flavonoids, polyphenols, catechins, and caffeine. Catechins such as epigallocatechin, epigallocatechin gallate (EGCG), and epicatechin gallate are potent antioxidants. By studying mast cells that release histamine, researchers found that a methylated form of EGCG blocks the IgE receptor, which is involved in the allergic response (Tachibana H et al 2004; Fujimura Y et al 2004).

**Stinging nettle (*Urtica dioica*).** Stinging nettle leaf contains carotenoids, vitamin C, vitamin E, calcium, potassium, and flavonoids such as quercetin and rutin. This herb has anti-inflammatory effects (Riehemann K et al 1999). Historically, nettle has been used as a laxative and diuretic. Nettle may be beneficial for the treatment of allergic rhinitis, possibly because of the quercetin content (Blumenthal M 1998).

**N-acetylcysteine (NAC).** NAC has a powerful effect on raising glutathione levels in the body. Glutathione is a naturally occurring antioxidant that protects cells from the damage inflicted by free radicals. It prevents oxidative cell damage and is involved with immune system function. Glutathione depletion is linked to many chronic diseases. Studies suggest that it may be poorly absorbed and that supplementation with precursors may be more effective in raising glutathione levels (Witschi A et al 1992).

NAC has been shown to increase lung function by decreasing inflammation in experimental asthma models (Blesa S et al 2003). Additionally, NAC has been found to enhance T cell function. One in vitro study showed that NAC increased levels of IL-4 (Monick MM et al 2003). IL-4 enhances the ability of T cells to regulate pro-inflammatory cells, which further suggests that NAC can help reduce inflammation.

**Vitamin C.** Vitamin C (ascorbic acid) is found in many fruits and vegetables, especially citrus fruit. It appears that vitamin C increases the function of many immune cells, including T cells, phagocytes (which destroy invader cells), and others. As an antioxidant, ascorbic acid can protect cells from reactive oxygen species known to cause tissue damage and disease. Vitamin C

has antihistamine properties (Johnston CS et al 1996) that can help relieve allergy symptoms.

Studies have demonstrated that 2 g of vitamin C improves pulmonary function one hour after ingestion, compared with a placebo (Bucca C et al 1990). Another study found a fivefold increase in bronchial hyperreactivity among those with the lowest intake of vitamin C (Soutar A et al 1997).

**Vitamin E.** Vitamin E is a fat-soluble vitamin that acts as a free-radical scavenger. It protects cell membranes and prevents damage to membrane-associated enzymes. Research suggests that vitamin E inhibits the activation of neutrophils, chemicals that, in asthmatics, result in the synthesis of leukotrienes (Centanni S et al 2001). Studies indicate lower levels of antioxidants such as vitamin E increase the risk of allergies threefold (Hijazi N et al 2000).

**CoQ10.** CoQ10 is essential for energy production in the mitochondria of cells. It is also a potent antioxidant. Studies have shown that people with allergies may lack CoQ10 (Ye CQ et al 1988; Gazdik F et al 2002).

**Magnesium.** Magnesium is utilized by every cell in the body and participates in energy metabolism and protein synthesis. The body vigilantly protects blood magnesium levels, in part because at least 350 enzymatic processes depend on magnesium status for activation. As magnesium levels decline, the incidence of allergies and asthma increases, and magnesium has been used in the acute treatment of asthma attacks (Langsjoen P et al 1994; Hijazi N et al 2000). Magnesium directly depresses smooth muscle activity, which may help relieve the bronchoconstriction seen in asthma (Swain R et al 1999).

## HORMONE MODULATION

The correlation between immune response and hormonal status has been documented. For example, research shows that DHEA levels have an impact on immune-cell function (Bauer ME 2005; Tabata N et al 1997; Kos-Kudla B et al 2001). Also, the imbalance of adrenal hormones under stressful conditions may weaken the immune response (Elenkov IJ et al 2005). See the chapters on “Female Hormone Restoration” or “Male Hormone Restoration” for more details.

## LIFE EXTENSION FOUNDATION RECOMMENDATIONS

Whenever possible, the best therapy for an allergic problem is to avoid the offending substance or substances. For food allergies, this means avoiding the allergen and being vigilant about reading food labels. Nuts in particular are found in many foods in which people might not expect them.

For environmental allergies, the environment should be kept as free of known and potential allergens as possible. Allergy-proof and mite-proof covers should be used on all pillows, mattresses, and box springs in the sleeping area, and all bedding should be washed weekly in very hot (135°F) water. Removal of carpet and other dust collectors in the sleeping area may also help cut down exposure to insect droppings and tiny pieces of insects. Mold exposure can be avoided by eliminating moisture-laden growth areas, and any new growth must be removed promptly. Mold-inhibiting substances are available and should be used freely on mold-prone surfaces. Pets should be kept out of the sleeping area, and cats and dogs should be bathed frequently to reduce the amount of surface allergens on their bodies. HEPA air filters at home and work may decrease allergens. Avoiding cigarette smoke is also important. Always introduce new foods and medications gradually to assess whether an allergic reaction may develop.

In addition, numerous nutrients have been shown to reduce allergy symptoms by affecting the biochemical pathways that are activated during allergic outbreaks. People with allergies may want to consider the following supplements:

- **Rosmarinic Acid Extract**—100 to 200 mg (with 4 to 8 mg of luteolin) in the morning
- **EPA/DHA**—700 to 2100 mg of EPA and 500 to 1500 mg of DHA daily with food
- **GLA**—285 to 1425 mg daily
- **Vitamin C**—1 to 3 g daily in divided doses
- **Vitamin E**—400 to 800 IU daily
- **NAC**—600 to 1800 mg daily (along with vitamin C)
- **Green tea extract**—725 mg daily
- **Nettle leaf extract**—100 to 200 mg daily
- **CoQ10**—30 to 100 mg daily
- **Magnesium**—150 to 300 mg daily

To enhance digestive tract function:

- Probiotics (beneficial bacteria) or fructooligosaccharides, as directed on label

For modulation of hormones:

- **DHEA**—a suggested starting dose is 15 to 75 mg. Blood testing should be performed.
- **Pregnenolone and other hormones**—blood testing is recommended. For more information on hormone blood testing, call Life Extension at 1-800-544-4440.

## ALLERGY SAFETY CAVEATS

An aggressive program of dietary supplementation should not be launched without the supervision of a qualified physician. Several of the nutrients suggested in this protocol may have adverse effects. These include:

### Coenzyme Q10

- See your doctor and monitor your blood glucose level frequently if you take CoQ10 and have diabetes. Several clinical reports suggest that taking CoQ10 may improve glycemic control and the function of beta cells in people who have type 2 diabetes.
- Statin drugs (such as lovastatin, simvastatin, and pravastatin) are known to decrease CoQ10 levels.

## **DHEA**

- Do not take DHEA if you could be pregnant, are breastfeeding, or could have prostate, breast, uterine, or ovarian cancer.

## **EPA/DHA**

- Consult your doctor before taking EPA/DHA if you take warfarin (Coumadin). Taking EPA/DHA with warfarin may increase the risk of bleeding.
- Discontinue using EPA/DHA 2 weeks before any surgical procedure.

## **GLA**

- Consult your doctor before taking GLA if you take warfarin (Coumadin). Taking GLA with warfarin may increase the risk of bleeding.
- Discontinue using GLA 2 weeks before any surgical procedure.
- GLA can cause gastrointestinal symptoms such as nausea and diarrhea.

## **Green Tea**

- Consult your doctor before taking green tea extract if you take aspirin or warfarin (Coumadin). Taking green tea extract and aspirin or warfarin can increase the risk of bleeding.
- Discontinue using green tea extract 2 weeks before any surgical procedure. Green tea extract may decrease platelet aggregation.
- Green tea extract contains caffeine, which may produce a variety of symptoms including restlessness, nausea, headache, muscle tension, sleep disturbances, and rapid heartbeat.

## **Magnesium**

- Do not take magnesium if you have kidney failure or myasthenia gravis.

## **NAC**

- NAC clearance is reduced in people who have chronic liver disease.
- Do not take NAC if you have a history of kidney stones (particularly cystine stones).
- NAC can produce a false-positive result in the nitroprusside test for ketone bodies used to detect diabetes.
- Consult your doctor before taking NAC if you have a history of peptic ulcer disease. Mucolytic agents may disrupt the gastric mucosal barrier.
- NAC can cause headache (especially when used along with nitrates) and gastrointestinal symptoms such as nausea and diarrhea.

## **Vitamin C**

- Do not take vitamin C if you have a history of kidney stones or of kidney insufficiency (defined as having a serum creatine level greater than 2 milligrams per deciliter and/or a creatinine clearance less than 30 milliliters per minute).
- Consult your doctor before taking large amounts of vitamin C if you have hemochromatosis, thalassemia, sideroblastic anemia, sickle cell anemia, or erythrocyte glucose-6-phosphate dehydrogenase (G6PD) deficiency. You can experience iron overload if you have one of these conditions and use large amounts of vitamin C.

## **Vitamin E**

- Consult your doctor before taking vitamin E if you take warfarin (Coumadin).
- Consult your doctor before taking high doses of vitamin E if you have a vitamin K deficiency or a history of liver failure.
- Consult your doctor before taking vitamin E if you have a history of any bleeding disorder such as peptic ulcers, hemorrhagic stroke, or hemophilia.
- Discontinue using vitamin E 1 month before any surgical procedure.

For more information see the Safety Appendix

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