

## NUTRITIONAL THERAPY FOR GASTRIC PERMEABILITY

### *Interrupting the Perpetual Cycle of Food Allergies and Inflammation*

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## Background

### **The allergy epidemic**

Allergy is a response by the immune system which results in inflammation. Food allergies are a growing medical conundrum associated with a range of symptoms from eczema, diarrhea, and fatigue to debilitating conditions like arthritis, autism and anaphylaxis. (1,2) To date, doctors have primarily recommended strict food avoidance and epinephrine for immediate IgE allergic responses such as peanut or shellfish allergies. Skin tests or RASTs are used to identify IgE allergy levels, and oral immunotherapy is now being approved for use under hospital supervision. Yet this treatment does not address the underlying cause or prevent allergies. Another type of allergy is also complicating the picture - the delayed IgG type-3 allergy also referred to as *non-IgE mediated response* or delayed hypersensitivity. New studies on IgG allergy are linking this type allergy to atherosclerosis and obesity. (190) This elusory condition does not yet have established blood testing standards. Patients are burdened with food elimination and challenge tests and food avoidance is the only proven therapy. Such diets can severely impact quality of life on many levels, comparable to diabetes, arthritis, asthma and IBS. (4)

### **Roots tangled in gastric permeability and gut inflammation**

We know very little about how or why allergies develop or evolve. The most promising research illuminates the origin of food allergy and related auto-immune conditions as a "leaky gut" featuring *intestinal permeability* where undigested food particles and toxins pass through the gut lining in open *tight junctions* and force the liver to form antigens and immune complexes that can settle into tissues throughout the body. Food allergy is just one of many conditions that manifest from gastric permeability (6, 7); this condition is being linked to a wide range of chronic disorders including asthma, celiac disease, Crohn's disease, depression, diabetes, liver disease, and pancreatitis. (5, 18, 28, 68) Inflammation in chronic heart failure, traumatic brain injury, and cerebral stroke are also affiliated with reduced permeability. (177) In rats, increased gastric and small intestinal permeability appeared before the development of both insulinitis and clinical diabetes. Diabetes is being linked to celiac disease and gut inflammation, (17) and celiac is linked to joint inflammation and specific types of arthritis. (159) Anaphylaxis from severe IgE allergy can also have roots in the intestine where a concentration of mast cells reside, hold IgE antibodies, and store/release histamine which causes the varied intense symptoms. Mast cells generate a number of substances that increase permeability, including histamine and serotonin. (8) Studying this network of challenges in the immune system through intestinal function is a powerful new approach in health and nutrition research.

## A proposal

As a complement to the limited treatments for food allergy, I'm proposing a four-pronged nutritional therapy to help reduce and reverse the damaging effects of gastric permeability: **A) reduce intestinal permeability, B) reduce excessive histamine and IgE response, C) reduce inflammation in the body, and D) balance and build awareness.** An increasing number of studies are identifying factors that increase or decrease permeability as it has become a major factor in autoimmune disease. IgE and histamine reduction may improve symptoms because there is an increased risk of adverse histamine reactions with increased gut permeability. (185) Reducing inflammation systemically dramatically supports the immune system, and intestinal inflammation can increase allergy sensitization by increasing gut permeability. (185) Changes in nutrition and lifestyle, with awareness and integrative medicine, can help balance the body and correct nutritional deficiencies common with food allergy and malabsorption.

## Therapy A: Reducing permeability

### Tests

The current standard for evaluating permeability is the Lactulose and Mannitol Test which analyzes the ability of mannitol and lactulose sugar molecules to permeate the intestinal lining.

### Drugs & alcohol

- **Medications, including aspirin and NSAIDs (31) can significantly increase permeability.**

Drugs are often designed to penetrate the intestinal lining for enhanced delivery by increasing permeability, potentially leading to GI side effects. Glutamine reduces the effect of permeability from NSAIDs when taken close in time. (63) Probiotics reduce intestinal permeability (41) and counteract increasing effects of NSAIDs possibly by a) stimulation of the expression of gastric mucins, b) decreases in bacterial overgrowth by competitive exclusion and blocking binding, c) stimulation of local immune responses, d) release of antioxidant substances. (48) Cases of drug abuse and addiction should be treated professionally.

- **Gastric permeability is a serious complication in cancer treatment.**

Permeability is associated with mucositis in chemotherapy patients (178), irradiation in animals (180), and toxicity in cancer patients (179). Alanyl-glutamine (stable dipeptide of glutamine) appears to help prevent the permeability resulting from chemotherapy. (37)

- **Alcohol increases permeability and promotes growth of gram-negative bacteria.**

Research suggests that alcohol-induced permeability increases with the overproduction of nitric oxide (181), naturally produced during exercise. Alcohol consumption should be avoided to reduce permeability, and addiction should be treated with outside help. Alcohol-induced intestinal permeability and liver damage may be reduced by diets supplemented with oat or zinc. (41, 47, 22) Alcohol seems to play a role in creating the zinc deficiency, possible from oxidative stress. (36) L-glutamine prevents the permeability caused by acetaldehyde. (57) Glutamine food sources include beef, chicken, fish, beans, and dairy products. (71) Probiotic *L. rhamnosus* also reduced permeability and inflammation in alcoholic rats. (23) Research found that epidermal growth factor prevents permeability caused by alcohol. (56) Salivary epidermal growth factor plays a role in gastric health and is regulated by dietary inorganic iodine. Epithelial growth factors are also found in deglycerated licorice, glandular extracts and stevia and have potential for treating IBD. (58, 63)

## *Bacteria & fungus*

- **Inflammation from bacteria or other interactions can affect the tight junctions in the intestine's epithelium. (26) Pathogenic bacteria such as *H. pylori* are linked to infection and allergic reactions. (25) *Helicobacter* species seem to be "barrier breakers" in the intestines of susceptible individuals.**

*H. pylori* tests are available when the bacteria is suspected as a source of stomach irritation. Wasabi shows bactericidal activities against *H. pylori*. (27) Plant extracts that have proven successful against *H. pylori* are turmeric (most efficient), cumin, ginger, chili, borage, black caraway, oregano and licorice. Extracts of turmeric, borage and parsley also prevented *H. pylori* from adhering to the stomach. (29) Berries have also proved to be antimicrobial. (59) Galactans in black currant seeds may stop *H. pylori* from adhering to the gastric mucosa in humans. (60) Interestingly, arabinogalactan proteins also inhibited *H. pylori*. (61) Arabinogalactans (AG) are in plant fibers and are starting to appear in commercial teas and bars as prebiotics. Probiotics also prevent pathogens from adhering to the epithelium and reduce permeability. (30) More research is needed to determine the dosage and effectiveness of foods, herbs and spices on pathogenic and non-pathogenic bacteria.

Careful washing, thorough cooking and quick consumption of perishable foods can prevent ingestion of bacteria. Broad-spectrum antibacterial foods can be easily integrated into the diet for additional protection, noting that foods may act differently on unique bacteria. The strongest antimicrobial properties were found in thyme, oregano (marjoram and oregano), mint, cinnamon, salvia and clove. (54) Salicylic acid has proved to inhibit replication of bacteria (50) and is found in blueberries, blackberries, apricots, and raisins. Cashew fruit, available in the U.S. as cashew fruit juice, contains antimicrobial compounds. (86) Some essential oils have also been found to inhibit harmful intestinal bacteria without harming beneficial ones, including caraway, lavender, ajowan, and bitter orange. (51) In another study, essential oils of thyme, peppermint, caraway seed, pennyroyal, and fennel proved antibacterial. (52) Essential oils can also work together more powerfully, as in the case of clove and rosemary essential oils against bacteria and fungus. (53) Adequate vitamins and minerals may also prevent invasion; in one study on rats fed a Western diet with inulins and fructooligosaccharides, the intestines were vulnerable to salmonella yet protected with dietary calcium. (55) Professional guidance is important for determining proper dosages and applications for different pathogens.

- **Yeast such as *Candida albicans* can increase permeability; (184) as it changes from a yeast to fungus, it forms rhizoids which break intestinal walls.**

A diet to reduce *Candida* may help reduce permeability, avoiding yeast-containing foods, mold-supporting foods, and concentrated sugars. A diet high in fiber with low-starch vegetables and high protein foods including nuts and seeds may prevent *Candida* overgrowth. Supplements that are known to counter candidiasis include digestive enzymes, probiotics, grapefruit seed extract, essential fatty acids, and vitamins and minerals in cases of deficiency.

## *Environment & Lifestyle*

- **Stress increases permeability and inflammation locally or systemically (10), affiliating with chronic conditions such as liver disease and Crohn's disease. Even exertional stress through intense exercise can cause permeability and lead to heat stroke or anaphylaxis, possibly in combination with consumption of allergens. (11)**

Changes to work, lifestyle, and nutrition are important in reducing stress. Regular exercise and meditation help reduce stress. Professional help can assist in managing stress and anxiety.

- **High-intensity exercise may combine with food allergens to cause anaphylaxis in some cases, possibly through permeability. (7) Crustaceans and wheat flour are the most common allergens in exercise-induced anaphylaxis. (24)**

Reducing or avoiding intense exercise is important after eating suspect allergens, especially where there is history of exercise-induced anaphylaxis. Studies in mice showed that high intestinal heat can also increase permeability. (110)

## Nutrition

- **Recent studies show that IgE can trigger reactions in the intestine that compromise the epithelial barrier. (112, 113)**

Reducing the immune burden on the intestinal barrier may promote healing and enhance permeability. Allergen avoidance is recommended for IgE (immediate) allergy, though immunotherapy may help in some cases.

- **Zinc depletion increases permeability and cell disintegration with exposure to a common mycotoxin. Zinc supplementation restored homeostasis in one study. (32, 40)**

If a deficiency is diagnosed, zinc may benefit through supplementation or adding foods high in zinc such as oysters and crab. Beef and cooked cabbage are also good food sources for zinc. (43)

- **Calcium plays a role in permeability.**

Calcium has been associated with increased permeability in animals, though the mechanism is complex. (182)

- **Certain foods appear to increase permeability.**

Supporting evidence for treating permeability through nutrition is growing rapidly. A wide range of compounds and their related foods are being identified and analyzed. Legumes contain high levels of saponins which, in binding to the lining, cause increased intestinal permeability. Rats fed on diets containing kidney bean showed increased intestinal permeability. (21) Even potatoes can disrupt the gut lining and increase leakage. The glycoalkaloids in potatoes seem responsible for this degradation and aggravation of IBD. (15) Tomatoes also increase gut permeability, more potent than potato in vitro. (17) Excessive dietary fat increases permeability in animals. (175)

Sweet peppers, mushrooms, glucose, saponins, L-tryptophan, linoleic acid, chitosan, medium chain fatty acids and surfactants can increase permeability, (12,13,19) and are detailed as follows: Saponins can promote leaky gut and are found in alfalfa, agave, fenugreek, ginseng, red onions, paprika, and soybeans. Quillaja found in foaming root beer has extremely high concentrations of saponins. Quinoa is a concentrated source of saponin, though commercial quinoa has removed the saponin. Hot peppers, cayenne, and paprika contain both saponins and capsaicin which can increase gut permeability. (14) Tryptophan is highest in egg whites, spirulina, cod, soybeans, and parmesan cheese. Linoleic acid is highest in safflower oil, grape seed oil, and poppy seed oil. Chitosan is high in the shells of crustaceans and fungi. Medium chain fatty acids are found in coconut oil and palm kernel oil. Surfactants include mono and di-glycerides common to in bakery products, frozen desserts, toppings, and peanut butter. Surfactants include the popular lecithin used in baked goods, chocolate, instant foods, candy, and cooking spray. Margarine, dressings, and shortenings contain emulsifiers which are surfactants.

Cooking by grilling, broiling, or frying in moderate to high temperatures increases the production of toxic AGEs (advanced glycation end products). AGEs induce inflammation and are associated with increased allergenicity and increased intestinal permeability. (195) Roasted peanuts, for example, have much higher allergenicity than raw peanuts. (195)

Reducing the consumption of these foods under medical guidance may be helpful in cases of permeability. Where food addiction is an obstacle, professional help should be employed. Recent findings have built a stronger case for food addiction and the need for more research and support, as the restriction-binge cycle may be an obstacle. (42)

- **Certain foods may decrease permeability.**

Adding foods and probiotics to reduce permeability may benefit conditions under medical guidance, though food interactions, amounts, and relative effectiveness have not yet been determined. Probiotics help reduce intestinal permeability and also play a role in reducing inflammation. (169) Their effect may be related to impact on IgE, as probiotics prevented IgE-related eczema in infants. (193) Recent studies show that high IgA in early life is linked to reduced IgE-related allergies later, and probiotics also helped promote production of IgA. (160) Probiotics are always best taken on an empty stomach. The gut flora and strain of probiotics affect the immune system in different ways, and further research is needed for selective treatment.

Foods that reduce permeability include eicosapentaenoic acid, gamma-linoleic acid, casein, lactoglobulin from cow's milk, nutmeg, and piperine (black pepper). (12,15) Eicosapentaenoic acid (EPA) can be found in oily fish or microalgae, and gamma-linoleic acid ( $\gamma$ -linoleic acid or GLA) can be found in borage oil, evening primrose oil, blackcurrant seed oil, hemp seed oil, and spirulina. Insoluble fiber such as cellulose has also been found to decrease gut permeability in some studies.

Some amino acids show support; L-cysteine reduced intestinal permeability and inflammatory responses in animals. (49) Cysteine is found in high-protein foods like eggs, poultry, pork, yogurt, red pepper, garlic, onions, broccoli, Brussels sprouts, and oats. (71) Arginine reduced permeability in animals (176) and is high in peanuts, various tree nuts, tuna, salmon, and chicken. A balanced set of aminos are in quinoa, buckwheat, and amaranth.

Certain flavonoids, known for antioxidant activity, may benefit; the green tea polyphenol epigallocatechin gallate (EGCG) prevents epithelial permeability. (123) In one study, green banana and pectin improved permeability and diarrhea in children. (20) Quercetin, found in onions, tea, apples and red wine, enhances the intestinal barrier. (35) Crude rhubarb appears to reduce permeability in septic patients. (183)

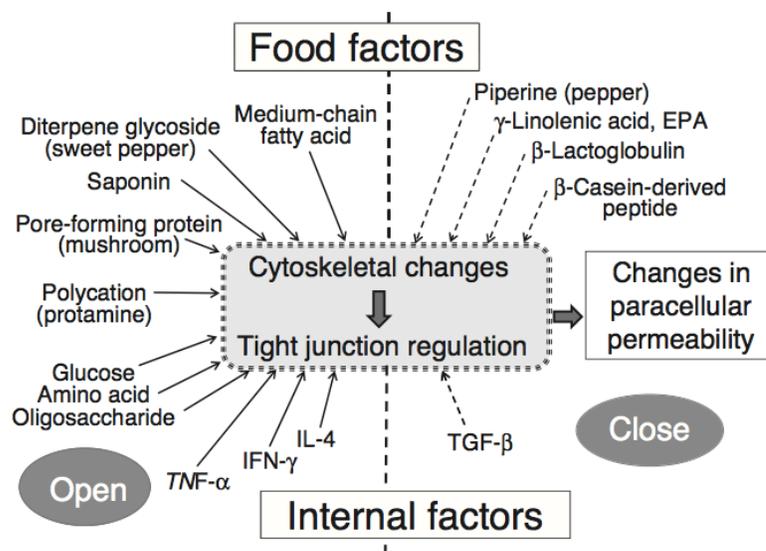


Figure 1. Examples of Foods and Factors That Affect Permeability (12)

## Therapy B: Reducing histamine & IgE allergy symptoms

### Tests

Allergen-specific IgE antibody tests or RAST tests measure antibodies against specific allergens in the blood. Skin allergy tests are generally preferred by doctors to replace or confirm blood tests, though the skin tests can be uncomfortable for sensitive individuals.

### Nutrition

- **Histamine intolerance can be mistaken for food allergies and can result from allergies and gastrointestinal diseases. Certain foods increase histamine in the body.**

If histamine intolerance is diagnosed, a histamine-restricted diet will be necessary, eliminating products for a trial period like aged cheese, fermented soy, fermented vegetables, brewer's yeast, shellfish, many fin fish and canned fish, shellfish, chicken, dry pork sausage, beef sausage, uncooked egg whites, strawberries, tomatoes, eggplant, spinach, chocolate, pineapple, vinegar and alcohol. Processing and storing food can increase histamine content. Impaired histamine metabolism is associated with food allergies (186) and diet may help control symptoms.

- **Immunotherapy can reduce symptoms of IgE allergy, but long term effects of the IgG increase are not defined.**

Oral immunotherapy or desensitization, as recommended by a doctor, may relieve symptoms of IgE allergy. However, IgG levels increase as a result of immunotherapy, blocking the allergic response, and this defensive glycoprotein can turn proinflammatory in autoimmune disease. We do not yet understand the long-term effects of IgG or immunotherapy. (105)

- **Artificial ingredients and highly processed foods increase IgE and burden the intestine and liver.**

A new study reveals that IgE antibodies against processed food antigens are increased 3-8 times their raw food counterparts. (109) Consume raw foods and whole foods without preservatives, additives, artificial flavors, or excessive processing. Avoid contamination by washing produce before eating.

- **Some foods and compounds break down histamine or inhibit allergic reaction.**

Fermented foods and lactic acid bacteria have been researched for their anti-allergy effects – useful in cases where histamine intolerance is not an issue.

Vitamin B6, copper and C stimulate the activity of DAO in the body which breaks down histamine. (43, 106) If DAO is inhibited, histamine can collect in the body and results in symptoms of histamine intolerance - a type of intolerance. DAO is produced in high concentrations during pregnancy which may explain why food allergies often go into remission during pregnancy. In one study, 2 g vitamin C reduced histamine levels 38 percent after 6 weeks. (87) Diets low in vitamin A and C are also affiliated with higher asthma symptoms. (84)

It has recently been discovered that phenolics such as caffeic, chlorogenic and ferulic acids interact with peanut allergens and reduce their IgE binding. (60) Phenolics create blue, blue-red, and violet pigments in plants and function as antioxidants and anti-inflammatory and anticoagulants in the body. Apple, cabbage, garlic, grapefruit, onion, orange, radish, raspberry, spinach, tarragon, thyme, chamomile, and yarrow are high in both caffeic and

ferulic acid. (43) Deseret Biologicals show apple and olives as both containing caffeic and chlorogenic acid. New research also reveals that polyphenol-enriched apple extract reduces IgE allergy response in mice. (156) Phycocyanin, the blue pigment found in spirulina, reduces histamine release in animals in vivo. (33) The luteolin flavonoid also helped inhibit allergic reactions. (97). Luteolin has shown anti-inflammatory activity in other studies as well. (81) Luteolin is found in green peppers, celery, onion leaves, and chamomile tea. (89, 94) Luteolin is a major flavonoid in rooibos tea. Nettle, high in phenolics, also reduces histamine activity related to allergic rhinitis. (191) More research is needed to establish specific phenolic levels and antiallergy potential of common foods.

Copper amine oxidase (histaminase) metabolizes histamine. Copper-containing amine oxidases can be found in bacteria, yeasts, mushrooms, various plants, and animals, and pea seedlings are currently being studied for extracting copper amine oxidase. (108)

A new commercial supplement "Histame" boosts DAO in the body to purportedly reduce histamine.

- **IgE allergies may associate with obesity.**

IgE levels for food allergens were higher among obese and overweight children in a recent study. (168)

### *Genetics, Birth & Infancy*

- **Genetic susceptibility is demonstrated in cases of allergy-related conditions like celiac and inflammatory bowel disease, but needs further study considering possible triggers. (38)**
- **Various factors protect or increase likelihood of allergy development from womb to childhood.**

Prenatally, Caesarian section and high maternal age increase likelihood of childhood food allergy. (39) Avoidance of smoking and alcohol during pregnancy and lactation also reduce risk of allergy in early childhood. (44)

During infancy, a recent study suggested that avoiding dust mite and food allergens in infancy help reduce allergic disease in the first 8 years of life. (45) Research has contradicted popular belief that breastfeeding protected children from atopic disorders; results showed breastfeeding inhibits asthma (in early childhood) but *not* food allergy and atopic dermatitis. (46) A recent study corroborated that breastfeeding does not protect against food allergy. In fact, this study challenged the existing recommendations of delaying solid foods for infants. Late introduction of eggs (>10.5 mo), oats (>5.5 mo), and wheat (>6 mo) were significantly related to food allergies, as well as sensitization to egg allergies. Potatoes (>4 mo) and fish (>8.2 mo) were the most important foods related to sensitization to any inhalant allergen. Eggs were significantly associated with cow's milk allergy, and wheat was the most important food in developing wheat allergy. In summary, eggs, oats, and wheat were strongly related to food sensitization, whereas potatoes and fish were strongly related to inhalant sensitization. (88)

### *Environmental toxins, pollen & cross-reactivity*

- **Environmental toxins can burden the immune system, increase inflammation, and aggravate allergy symptoms.**

Avoid exposure to environmental toxins that tax the immune system like formaldehyde, industrial and traffic smog, wood preservatives, microbial toxins, additive-rich food, nicotine, alcohol, pesticides, solvents, amalgam-heavy metals. (9) Test for airborne allergies and reduce exposure to pollen, mold, and other toxins by monitoring air quality and pollen indices before outdoor exercise. Home dampness, mold, and tobacco smoke are associated with increased allergy symptoms. (161, 162) Wash linens in hot soapy water to reduce the common dust mite allergen. The use of bleach results in less IgE allergy symptoms, but higher frequency of use may lead to more respiratory symptoms. (155)

- **Cross-reactivity between foods, substances or pollens can increase allergic reactions.**

The environmental factors become even more harmful when the body cannot differentiate between allergens and other similar environmental proteins. This cross-reactivity can occur with biologically related plant families, as in legumes or tree nuts, or between unrelated proteins such as birch pollen and apple fruit, latex and banana, and peanut and tomato. (117) Awareness of cross-reactivity and testing for both airborne and food allergens are important when symptoms are present.

## Therapy C: Reducing inflammation

### Tests

Testing for hs-CRP (high-sensitivity C-reactive protein) levels reflect general inflammation and is being associated with an increasing number of conditions including cardiovascular disease, arthritis, diabetes and some cancers. Testing for additional inflammatory markers like plasminogen activator inhibitor-1, interleukin-6 and serum amyloid A is becoming even more useful in evaluating disease and risk. (145) IgG antibodies do not cause histamine release but can induce potentially harmful inflammation under certain circumstances. (135) The ELISA (Enzyme Immunoassays) test is offered by different labs for determining IgG levels for over a hundreds of foods and spices, but its accuracy is debated in the medical community. It would be useful to test for inflammatory markers and IgG levels before and after therapy.

### Environment & Lifestyle

- **Mood and attitude play a major role in inflammation.**

Anxiety is correlated with high CRP levels. (132) In another study, depression is linked to inflammation, though the correlation is stronger among hostile individuals and greater in women than men. (133) Data from the Multi-Ethnic Study of Atherosclerosis showed a very high association between pessimism and inflammation. (134) Various techniques – including biofeedback – may be employed to reduce anxiety and stress to help affect inflammation.

- **The airborne toxins in our environment contribute to inflammation in the body.**

New research is revealing how the lungs link air pollution to inflammation and autoimmune diseases. (114) Pollution clearly affects hs-CRP levels and other cardiovascular markers of oxidative stress and inflammation. (115)

- **Sleep may have some benefit on inflammation in women.**

A recent study found CRP levels higher among women - not men - who slept 5 hours or less. (139)

- **Exercise appears to reduce inflammation in some cases, with weight loss as a major co-factor.**

Total cholesterol and inflammation marker plasminogen activator inhibitor-1 are much lower in athletes than sedentary individuals. (147) Similarly, fibromyalgia patients show a decrease in inflammatory markers after aquatic exercise. (148) Multiple studies confirm that exercise alone may not decrease CRP levels, and weight loss is considered a major co-factor in reducing inflammation.

- **Medical Qigong may improve inflammation as studied in cancer patients.**

CRP levels improved in a study of cancer patients who used medical Qigong twice a week. (140)

## Nutrition

- **Identifying IgG allergies and controlling consumption may help reduce inflammation.**

The 4-day food rotation diet is a popular approach to reducing the IgG (delayed) allergy load and promote intestinal healing. A food elimination diet, under medical supervision, will help reveal problem foods and avoid them. It may take up to five days of strict avoidance to reveal the changes in symptoms associated with a food or chemical. For celiac patients, the exclusion of wheat, rye, and barley is the only effective treatment, and the safety of oats for celiac still remains unclear.

- **Certain foods and compounds can increase inflammation.**

Different macronutrients are being linked to inflammation which is linking obesity and diabetes. (118, 119) Meals high in saturated fat raise biomarkers of inflammation that lead to cardiovascular disease. Partially hydrogenated vegetable oils were associated with higher CRP levels. (137) It is notable that combining high fat with antioxidant-rich vegetables seems to be protective, (120) and combining orange juice with high-fat, high-carb meals prevented inflammatory stress. (142) Refined grains raised inflammatory factors in a recent study. (146)

CRP levels increase with glucose levels, even without diabetes, in communities studied. (143) High-glycemic load diets also increase CRP levels. (144)

High-heat-treated diet is also linked to risk of cardiovascular disease and lower insulin sensitivity, omega-3s, and vitamins C and E. (196) Acrylamide, a compound in starchy foods like potato chips and bread, is associated with an increase in hs-CRP levels and risk for atherosclerosis. (141) Acrylamide levels rise with frying, baking, or roasting above 120°. (89) Slow boiling of foods or roasting at reasonable temperatures may help reduce acrylamides and prevent inflammation and diabetes.

Carrageenan, a very common additive used to thicken and stabilize food and body care products, can disrupt the intestinal lining, and research suggests it promotes inflammation. (193) Carrageenan is common in alternative milks, ice cream, diet soda, beer, toothpaste, shampoo, and pharmaceuticals.

- **Certain foods and compounds can decrease inflammation.**

The complex pathways of inflammation can be interrupted and inhibited at many different levels by *dietary polyphenols* to benefit a range of conditions. Oats contain polyphenols that may protect against heart disease, colon cancer, and skin irritation. (121) Many polyphenols show COX and LOX inhibition, an anti-inflammatory combination that drugs cannot yet replicate. A number of compounds such as quercetin, caffeic acid (in coffee beans), phenethyl ester (in honeybees), resveratrol (in red grape skins), indole-3-carbinol (in Brassica vegetables) inhibit NF- $\kappa$ B, a genetic-inducing factor in inflammation. (122) Recent studies reveal that the degree of roasting coffee correlates with the reduction in inflammation and oxidative stress. (127) Olive oil, rich in polyphenols, was also found to affect genes affiliated with atherosclerosis. (34) Berries, also high in polyphenols, were found to reduce the signs of liver damage and markers of inflammation. (125) Green tea is high in polyphenols and is linked to a range of anti-inflammatory activity. (165) New research suggests that rhubarb, high in polyphenols, may protect the gut barrier and reduce inflammation. (13) Cooking often changes the levels of polyphenols in foods, so further research is necessary for therapeutic use. Generally, high intakes of carotenoids, vitamin C, and fruits and vegetables are associated with lower hs-CRP levels. (136)

The Mediterranean-style diet (whole grains, vegetables, fruits, nuts, and olive oil) continues to show positive results in improving inflammation and other major health factors in metabolic syndrome. (120)

Dairy also improves inflammation associated with obesity. (153) This activity may be due to bovine glycomacropeptide, a component of cow's milk, which limits intestinal inflammation in animals through lymphocyte activity. (126)

Cocoa shows anti-inflammatory activity in trigeminal ganglion neurons, a factor in migraines and TMJ. (130)

Curcumin (tumeric), ginger, black pepper, cinnamon, have proven anti-inflammatory activity. (163, 164, 166 ,167)

Proteolytic enzymes such as bromelain can best help reduce inflammation (170) when taken without food.

Reducing trans- and saturated fatty acids intake and increasing the consumption of omega-3 fatty acids help reduce inflammation, though specific mechanisms and cases are still unclear. Omega-3 fatty acids derived from fish, but not from flaxseed oil, suppresses inflammation in recent studies. (3) Omega-3 fatty acids also show oral antibacterial activity. (5) Eicosapentaenoic acid (EPA) is an omega-3 fatty acid found in fish oil as well as spirulina and microalgae. Interestingly, a high fat diet appears to prevent cardiac benefits from fish oil. (4)

One study shows that a six-fold increased alpha-linolenic (ALA) intake lowers CRP levels, (124) though this may be due to EPA. Alpha-linolenic acid is found in flaxseed, canola oil, kale, broccoli, Brussels sprouts and various nuts. Nuts also contain magnesium, fiber, L-arginine, antioxidants and MUFAs (monounsaturated fatty acids), purported to offer protection for inflammation and insulin resistance. Walnuts have been studied most, but it is likely that other nuts share similar properties. (154)

Multiple studies link increased magnesium intake with lowered hs-CRP levels. (138, 157) Magnesium is found in pumpkin seeds, spinach, chard, seaweed, soybeans, salmon, halibut, cocoa, sunflower seeds, and sesame seed.

High intake of vitamin B6 showed protection against high CRP levels in a recent study. (189) Foods containing high levels of B6 include red and green peppers, casaba melon, cod fish, spinach, and garlic. Vitamin K is also associated with reduced inflammation. (151) Spinach, Brussels sprouts, Swiss chard, green beans, asparagus, broccoli, and kale are high in vitamin K. (43) Vitamins and minerals are usually best taken with meals for greater absorption with the exception of B12, iron and folic acid. Despite vitamin D popularity, results have been inconclusive regarding its association with CRP levels. (150)

L-arginine shows benefits for cardiovascular risk, including lowering blood pressure. (197) Glutamine also reduces the inflammatory response in studies. (195) Amino acids are emerging as key players in reducing inflammation.

### **General trends and limitations in research**

Though the mechanisms are unclear, higher inflammation levels (CRP) are associated with obesity. (131) Many factors such as weight loss, fat consumption, and lifestyle contribute to the complexity of the inflammation equation. For example, one study linked a high-fat diet to inflammation of the airway and lung and not systemic inflammation. (128) Dietary intervention can reduce inflammatory activity, as revealed in a study of changes in adipose tissue. Supplements containing resveratrol, green tea extract, a-tocopherol, vitamin C, omega-3 polyunsaturated fatty acids, and tomato extract were used in this *nutrigenomics approach*, a promising therapy for controlling or reducing inflammation. (152)

Other research has not been able to identify how the consumption of fish and fiber reduce inflammation. Trends between genders and ethnicities are not established, and individual responses further complicate research. In the case of Crohn's disease, self-reported data from hundreds of patients showed no consistency in foods that benefitted the condition. (129) Overlapping studies conducted on various cancers may provide new clues, as cancer risk is being linked to inflammation.

## Therapy D: Balancing & building awareness

### Tests

- **Vitamin and mineral testing can be helpful with limitations.**

While nutritional deficiencies may not cause food allergies, gut permeability, or inflammation, they are associated with these conditions. (158) Tests for vitamin and mineral deficiencies may be useful in identifying and tracking comorbid conditions as well as treatment effectiveness. It must be noted, however, that blood testing has inherent limitations including broad, controversial ranges for normal and abnormal levels, unreliable methods, susceptibility to recent food intake, and general inconsistency between labs. The healthy values are derived from populations of 'healthy' people which may not reflect optimal levels for age, ethnicity, gender, or individual. Most importantly, high or low circulating blood levels of vitamins and minerals may reflect a metabolic problem that may not be resolved through supplementation. Vitamins and minerals have not been proven as an independent therapy for most conditions, but deficiencies are linked to disease by association and supplementation is generally supportive and safe within limits.

- **Additional tests can evaluate metabolism, glandular function and intestinal pathogens.**

When gut permeability, food allergy, or inflammation is a problem, intestinal pathogens, metabolic dysfunctions and glandular imbalances may also be present. Testing the function of the thyroid, liver, kidneys, and adrenal glands can determine the scope of disease. Invasive bacteria, parasites, and heavy metals are also affiliated with allergy and permeability and testing can help define treatment. Some tests can also evaluate efficiency of energy metabolism and oxidative stress, though in most cases the links between test results and conditions are undefined. It is important to get professional help in choosing reliable tests, deciphering the results, and developing a individualized wellness plan.

### Adjusting diet & lifestyle

- **The right health partner and team of practitioners can help achieve best results.**

*Team-based care* through integrative medicine promises greater success in treating complex allergy and immune-regulated conditions. Addressing mind, body, and spiritual needs can potentially enhance the healing process and long-term results. (171) An integrative approach, including nutritional support, can manage the range of symptoms and imbalances with tests, diagnoses, treatment, and follow-up.

- **Food diaries or journals can help track allergies, consumption, and symptoms.**

Personal health tracking journals, including food diaries, can help monitor health conditions, trace symptoms to foods or other triggers, and support weight loss. (173)

- **Individualized use of foods and supplements may help achieve nutritional balance.**

Over-supplementing with vitamins and minerals for conditions rooted in gastric permeability or malabsorption has potential to harm. (64) Carrier proteins in the intestine can be damaged in a leaky gut and cannot transport the necessary vitamins and minerals. Professional nutritional therapy must be individualized to address all possible factors contributing to the condition including motivation, intolerances, environment, and lifestyle.

For example, in the case where permeability may be primarily affected by stress levels, dietary recommendations may begin with reduced caffeine, salt, spices, and sugar while increasing consumption of fish, asparagus, garlic, spinach, and avocado. Foods and supplements with magnesium, B vitamins, and calcium may also benefit the nerves. In this manner of individualized therapy, nutrition for gastric permeability can complement food avoidance or immunotherapy and potentially prevent future allergy development and disease.

- **Nutritional education is essential to understanding and improving allergies and diet.**

Food sensitivities and allergies can drastically affect diet and lifestyle, and proper education can help reduce the impact. (174) Understanding food labels, balancing diet, and choosing food alternatives can be difficult or impossible without professional help.

- **An intensive intervention program has more potential for long-term success.**

Food allergies and associated issues of gut permeability require dietary changes, and studies are showing that such changes are not effective in the long-term unless intervention is highly intensive. (172) The popular Mayo Clinic has just launched a more integrative, intensive diet that involves a rapid weight-loss and habit-changing phase with the help of a journal. Patient-driven techniques like this may intensify the program in the short-term, but further studies are needed to determine long-term motivating factors.

## Summary

Protecting the gut from permeability and the subsequent perpetual cascade of inflammation responses is a promising new step in treating a wide range of conditions from hives to diabetes. Medication, including over-the-counter drugs, and alcohol may play a significant, unrecognized role in making the intestine vulnerable to pathogens through permeability. Foods such as potatoes, legumes, and saponin-rich substances like mono and di-glycerides can also increase permeability. Probiotics, certain amino acids, omega-3 fatty acid, some flavonoids, and other foods may help reduce permeability. Reducing histamine, through certain vitamin and minerals and foods like apple and olives, can support the immune system. Identifying and avoiding IgE allergies may also prevent inflammation during the healing process. Reducing inflammation is essential to healing and may be supported by avoiding inflammatory foods including fried starchy foods, sugary foods, and refined grains. Anti-inflammatory foods may support healing through various compounds in foods like green tea, dark roasted coffee, nuts, red grapes, olive oil, and fruits and vegetables rich in carotenoids and vitamin C.

Most importantly, an integrative approach that incorporates these dietary changes can target multiple aspects of health and address the complex nature of autoimmune events that can perpetuate chronic symptoms. Nutritional therapy has the potential to offer safe, economical support to complement or replace medication without the side effects that complicate healing.

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