

Unproved diagnostic and therapeutic approaches to food allergy and intolerance

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Purpose of review

Alternative and complementary medicine approaches to allergic disorders are commonly used by patients. Not all have been subjected to experimental analysis to support or refute their validity in the armamentarium of a practitioner. This review covers some of the most common unproved alternative or complementary approaches to diagnosis and therapy that we see in use by patients. These include the use of specific IgG to foods accompanied by rotary diets, provocation–neutralization testing and therapy, applied kinesiology followed by acupressure or acupuncture, and changes in cell size upon in-vitro exposure of leukocytes to food extract (using automated assays going under various trade names) followed by elimination diets or rotary diets.

Recent findings

There continues to be a dearth of well performed studies investigating these approaches in the literature, but many testimonials have been posted on websites of practitioners using these methods attesting to their effectiveness. Several recent studies have refuted the use of applied kinesiology and provocation–neutralization in diagnosis. The placebo effect must not be overlooked as a potentially important factor in some approaches.

Summary

There have been no studies supporting the use of these techniques, and several have refuted their utility. A beneficial placebo effect may be responsible for the perceived clinical effectiveness in many cases of food intolerance.

Keywords

food allergy, kinesiology, provocation–neutralization, alternative, complementary, acupuncture, rotary diet

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Abbreviation

NAET Nambudripad's allergy elimination technique

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Introduction

The term 'food allergy' is all-encompassing to the public, describing a multitude of ailments and reactions believed to be associated with food ingestion. Physicians, however, use the term to describe a condition or reaction resulting from an immune response to a food that results in an adverse reaction. The European Academy of Allergy and Clinical Immunology published a position paper in 1999 that reviewed the disorders attributed to food allergy or intolerance in detail and the reader is referred to this summary [1]. We will review the current literature (or most recent literature) from 1999 to 2002 on several of the most common diagnostic and therapeutic techniques used in complementary and alternative medicine for food allergy/intolerance. The techniques will be separated into diagnostic modalities and therapeutic modalities, because there is often overlap in therapies that are paired with the different diagnostic techniques (e.g. the rotary diversified diet). However, provocation and neutralization will be discussed together as they are generally not separated.

Methods

PubMed, Complementary and Alternative Medicine (CAM) on PubMed, MEDLINE journal articles, the websites of the American Academy of Environmental Medicine, the *Journal of Naturopathic Medicine* (volume 1), and the *Journal of Alternative and Complementary Medicine* (August 2000–December 2002) were screened for experimental papers on the diagnostic and therapeutic techniques included herein. The National Institutes of Health Computer Retrieval of Information on Scientific Projects (CRISP) database was searched to look for National Institutes of Health-funded studies dealing with alternative or complementary approaches to food allergy, but none was located.

Diagnostic modalities

The evaluation of adverse reactions to foods starts with a detailed history and physical examination of the patient. Recent reviews have outlined suggested strategies to follow in the further work-up of a patient, on the basis of whether the practitioner suspects an intolerance or an immune-mediated disorder [2]. However, practitioners of alternative and complementary medicine and some allopathic practitioners do avail themselves of techniques for diagnosis that are unproved for application to food-related disorders or to the work-up of vague symptoms that many believe are food related (such as 'brain fog' or

fatigue). Other techniques are entirely without scientific rationale (in the traditional allopathic model of health and disease, that is). Measurements of food-specific serum IgG or its subtypes, sublingual or intradermal 'provocation' with food extracts, and applied kinesiology are commonly used, in our experience. Other tests sometimes used include in-vitro assays of changes in cell morphology or size upon exposure to food antigens (using a Coulter counter or similar automated equipment), the 'pulse test', and electrodermal testing.

Measurement of food-specific IgG, IgG4 or food immune complexes

Food-specific IgG panels are advertised as IgG radio-allergosorbent tests and vary in offering total IgG towards a food, or IgG4, with or without food immune complex assays. There are several large commercial laboratories in the United States that offer this testing domestically and to customers abroad. This testing is considered unproved for use in food intolerance or allergy. Its proponents state that such antibodies can identify food intolerances that cause or contribute to chronic fatigue, headache, 'sinus', hyperactivity, irritable bowel syndrome, arthritis, difficulty concentrating, and almost any somatic or mental symptom. It is normal to produce specific IgG, IgG4 and IgA (most of which is intraluminal) to commonly eaten foods without manifesting symptoms of food allergy [3,4]. In a recent study of children with peanut or cow's milk allergy and normal, age-matched controls [4], the specific IgG antibody values in milk-allergic patients were no different from those of the controls. In the controls, the presence of food-specific IgG was correlated with the regular ingestion of that food; thus, if the food was avoided, levels could be expected to be lower. The same can be said for food immune complexes in relation to regular ingestion. For instance, in another recent report [5•], 12 out of 37 human breast milk samples contained ovomucoid in an immune complex with IgA. No studies have combined IgG levels with verified double-blind, placebo-controlled food challenges to investigate the possible links with objective or subjective symptoms. An intriguing preliminary study [6] reported elevated IgG and IgA levels to cow's milk in children with recurrent abdominal pain, but actual OD ranges were not reported, no food challenges were performed in this group, and no measurement of specific IgE was made to see if the elevated IgG and IgA levels were concurrent with IgE. At present, there is thus no evidence to support the diagnostic efficacy of food-specific IgG in any particular disorder. One disease reported to be related to extremely high levels of IgG to food antigens, visualized in a precipitin assay, is food-induced pulmonary hemosiderosis. This has been reported rarely in children with cow's milk hypersensitivity and in case reports with egg and pork [7,8]. No recent publications in Pubmed or MED-

LINE in the past decade have contained references to more contemporary measurements of IgG by enzyme-linked immunosorbent assay in these rare cases.

Provocation-neutralization

Provocation-neutralization testing to foods involves either sublingual or (more commonly) intradermal 'provocation' by a test antigen, followed by an observation period of 10 min after each injection, at which time the wheal response is measured and any subjective symptoms are reported. Symptoms such as drowsiness, dry mouth, an inability to concentrate or headache are considered a positive challenge, meaning that the individual is 'allergic' to the food. The patient is then given a different dose of the antigen as either a sublingual drop or another injection until the 'reaction' is 'neutralized'. This 'neutralization' dose would then be taken in a desensitization series or to neutralize a reaction [9–11]. Adverse outcomes of such testing are rare. However, there was a report of angioedema after the application of sublingual drops when a patient had an IgE-mediated food hypersensitivity [12]. Practitioners normally avoid this by not testing patients who have a history suggestive of an IgE-mediated reaction. We recently described a patient with systemic mastocytosis, including extensive skin involvement, who underwent provocation-neutralization and had a severe, life-threatening reaction as a result of massive mediator release after intradermal injections [13]. Practitioners of provocation-neutralization may not be internal medicine or pediatric medicine trained, and may not be aware of uncommon or rare medical conditions responsible for a patient's symptom complex, instead attributing symptoms to 'allergy' [13].

Two blinded, controlled studies were published in 1990 [14] and 1999 [15], showing that the testing relied on a placebo response. Both studies were double-blinded and placebo-controlled, but practitioners of the technique criticized the earlier study on methodological grounds. Fortunately, the Nova Scotia Environmental Health Centre sought to reinvestigate the issue; the results confirmed the first study, and the group concluded that provocation of symptoms by intradermal testing should not be used to make diagnostic (or therapeutic) decisions [15]. It should now be considered a disproved technique, rather than unproved.

Applied kinesiology

Applied kinesiology, or muscle response testing, is frequently used to diagnose food or environmental sensitivities. Practitioners state that they can detect both IgE and non-IgE-mediated allergy or intolerance based on positive or negative energy balances that manifest as muscle weakness. During this procedure the patient holds a vial with a specific food item in one hand while

the practitioner most commonly tests the muscle strength of the opposite arm by applying light pressure to the forearm. (If performed when the patient is supine, the arm is usually held erect approximately perpendicular to the body, and the practitioner applies pressure just proximal to the wrist.) If the practitioner can overcome the strength of the patient's arm, the individual is deemed to be 'allergic' to the specific contents in the vial. A review article written by Klinkowski and Leboeuf [16] over a decade ago evaluated 20 studies on applied kinesiology. According to the authors, none of the studies fulfilled basic research criteria; therefore, no valid conclusions could be drawn. A study in Germany published in 2001 [17**] concluded that there was no inter-tester reliability and no correlation with specific IgE, IgG or lactose breath hydrogen testing. Another recent study [18] attempted to prove that applied kinesiology is not subjective. Investigators devised equipment that could evaluate force and displacement. Mathematical procedures were used to analyse the data. Their conclusion was that applied kinesiology can 'reliably and objectively' discriminate the facilitation or inhibition of a muscle. The study failed to mention an important variable: the individual being tested and their role in the procedure [18]. A final study to be summarized here, also from Germany in 2001 [19**], looked at individuals with a clinical history of insect venom allergy and positive allergy tests including skin tests (prick and intradermal) and specific IgE antibodies by ImmunoCAP (Pharmacia, Uppsala, Sweden). The study, which was blinded, using venom and placebo vials for muscle testing, concluded that kinesiology as a diagnostic tool is no better than random guessing. The weight of the evidence to date suggests that this diagnostic modality is not validated when subjected to scrutiny.

Cytotoxicity and current equivalents: in-vitro cell assays

In the 1970s and 1980s, cytotoxic food testing was popular, also called 'Bryan's test' after the primary author [20]. The test hinged on the theory that the morphology of peripheral blood mononuclear cells was affected by contact with foods to which a patient is 'allergic', reflecting activation of the cells. A dried film of food extract on a slide was the substrate to which a fresh drop of whole blood was added. Any morphological change was considered positive. This test was shown to be non-reproducible [21]. However, the core concept behind this test – that of leukocytes reacting to food antigen exposure in a way that predicts allergies or intolerances – drives several current assays available to patients. The tests use modern Coulter system machines in a modified way. For example, in one assay, a citrated blood sample is obtained and diluted 1:5, and is then applied to cuvettes containing freeze-dried food extracts and incubated for 90 min; up to 50–100 food antigens are

checked on one patient [22]. The blood is run on a Coulter system counter to assess cell volume compared with a sample of the patient's blood that has not been exposed to food antigen. Leukocytes or platelets can be assessed and changes in any can be considered significant. There are no recently published, peer-reviewed studies to review on this assay; its use is not supported by the available literature [23].

Pulse test

The 'pulse test' is often incorporated into provocation–neutralization sessions as an additional objective measure of a response, but it is sometimes used alone. A change in the pulse of 16 beats per minute from baseline is considered to be positive for an intolerance or allergy after a sublingual drop, intradermal injection, or open challenge. There are no blinded clinical trials to support or refute the use of this test, which could be partly a result of the observation time of up to 2–3 h that may be required to watch for a 'delayed reaction', depending on how the test is utilized [24].

Electrodermal testing

Electrodermal testing involves placing the patient in a circuit with a machine that uses a galvanometer to measure skin conductance. The patient holds the negative electrode in one hand and the positive electrode is applied to certain acupuncture points. A sealed glass vial of the food extract is put in contact with an aluminum plate within the circuit. If there is a drop in conductance, 'allergy' is diagnosed on the basis of the perturbation in the electromagnetic field. Two double-blind, placebo-controlled studies of this technique were recently published, in 2001 [25**] and 2002 [26**]. Both used environmental allergens, such as dust mite, cat or pollens as antigens rather than foods, but the results have wide-ranging implications. In the first, a popular electrodermal measurement device called the Vegatest (Vega Medizinische Geräte, Schiltach, Germany) was used to compare the diagnostic capability of electrodermal testing to skin-prick tests using house dust mite and cat allergens. Over 1500 individual tests were performed in total on 15 atopic and 15 non-atopic volunteers. The testing was not able to distinguish the two groups [25**]. Similarly, the DBE204 (Tekav Srl, Rovigo, Italy) electrodermal device was also unable to distinguish between allergens and negative controls, and thus no differences between atopic and control patients were observed. The poor reproducibility of the method was noted in particular [26**].

Therapeutic modalities

The treatment options presented to patients diagnosed with food allergy or intolerance via alternative and complementary techniques vary from simple avoidance to elaborate diets or acupuncture. 'Neutralization'

therapy in the context of 'provocation' was already discussed above.

Rotary diversified diets

Rotary diets, or the 4-day rotation diet, are unproved diet therapies most commonly recommended for individuals with positive specific IgG or food immune complex assays, but also in several other situations. In our experience, it is common for patients to receive, as part of the fee that is paid to the remote laboratory, a personalized rotary diversified diet plan to follow. The diet was first used in 1934, with the idea that it would help a patient avoid cumulative food reactions [27]. This therapy has been used to treat individuals with chronic fatigue syndrome [28], environmental hypersensitivity disorder [29], food allergy, and food intolerance, sometimes in combination with other lifestyle modalities, homeopathy or neutralization therapy [30]. It is felt that rotation is necessary to prevent the continued sensitization to specific foods [28,30], preserve the tolerance acquired by prolonged elimination of the food [28], and as a prophylactic measure in allergic individuals [27]. Foods are organized into biological groups (citrus, fungi, mulberry, etc.). The diet allows one to eat all members of a food group on a specified day. Each day allows for several different groups, and a specific quantity is not restricted [29]. The cycle rotates every 4–7 days. Foods to which the individual is sensitive are eliminated. A literature search did not reveal any clinical trials evaluating the effectiveness of rotary diets. However, a study published in 1998 assessed adherence to rotary diets [30]. The results revealed that the diets were very difficult to follow, and individuals frequently consumed foods that were not allowed on a particular day. Adherence to this technique appears to be difficult. In addition, nutrition is of concern given that one can only consume from specified groups. This method does not seem practical and it is completely without objective evidence to support its use.

Nambudripad's allergy elimination techniques

Nambudripad's allergy elimination techniques (NAET) are reported to be a revolutionary treatment for allergy and allergy-related conditions. This adaptation of acupuncture was developed by Devi S. Nambudripad. She stated that the treatment was discovered when she integrated techniques from her various fields of study and combined them with her personal experience with food allergies [31••]. NAET practitioners are reported to diagnose and treat allergies in a non-invasive, drug-free, natural manner. Success in treating pollen-induced allergic rhinitis, sinus problems, non-IgE-mediated food intolerances or sensitivities, as well as the techniques' effectiveness in treating IgE-mediated food allergy (including peanut and shellfish) is also stated in her text

[31••]. Dr Nambudripad feels that these conditions are caused by energy blockages and imbalances.

The diagnostic method used by NAET is muscle response testing, or kinesiology, as discussed above. After the diagnostic testing is completed, the patient is treated with acupuncture or acupressure on specific points to drain the energy blockages out of the body while the patient holds the allergen [31••]. After treatment, the patient is asked to remain in the office for several minutes. They are then retested by applied kinesiology with the substance to which they were 'allergic'. If upon retesting they are strong, the patient is then advised to avoid the allergen for the next day. After the avoidance period, the patient may then be re-exposed to the allergen. A review of the literature revealed no study looking specifically at NAET as a therapeutic option for food allergy, thus it is unproved at this time. Nor has traditional acupuncture, disassociated from the diagnostic portion of NAET, been evaluated as a therapy for food allergy in a controlled trial.

With NAET, there is the potential for an anaphylactic reaction if a patient with severe food allergies seeks such a therapy and tests themselves by oral challenge away from a physician's office after completing the NAET sessions successfully. This particular technique highlights the very real importance of asking patients about their use of complementary and alternative therapies, and engaging in a partnership with them.

Other reviews covered homeopathy, medicinal herbs and supplements that are used in general 'allergy' conditions. The latter also need to be reviewed with the patient to ensure no drug-supplement interactions [32,33]. Worth mentioning is preliminary research in a murine model of food allergy that is bound to generate much public interest as the investigators pursue future human applications. In this model, a decoction of 11 herbs used in traditional Chinese medicine for allergy and gastrointestinal conditions was able to abrogate anaphylactic reactions to peanut in the peanut-sensitized mice [34••].

Conclusion

Many subjective symptoms are associated with the ingestion of food. This is not surprising, considering that much of our daily life revolves around the procurement, preparation and ingestion of foodstuffs. Adverse reactions may be immune mediated, a true food 'allergy', or non-immune mediated, a 'food intolerance', which is far more common. In many cases, we can acknowledge to our patients that we truly do not know all the possible effects of various phytochemicals, lectins, lipids, proteins and fibers on humans, and that the possibility of various unexplained adverse reactions to specific foods is real. We can then offer blinded

challenges to the suspected food(s). Such an acknowledgement may keep patients from spending money on unproved diagnostics or treatments because 'my regular allergist didn't believe me'. Some patients may have beliefs about foods and intolerances that cause lifestyle hindrances, but hold these beliefs so dear that they are not interested in the further evaluation of their adverse reactions. However, if a patient is pursuing significant or just plainly difficult dietary restrictions, and especially if a patient is the recipient of restrictions at the hands of someone else (e.g. children), then blinded food challenges should be pursued to determine whether there is a link of a specific symptom, or most commonly, to prove a lack of association.

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