

Controversial Practices and Unproven Methods in Allergy

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KEY CONCEPTS

- There have been an increasing number of patients who are using complementary therapies for chronic conditions.
- Unproven methods are increasingly being used for the diagnosis and treatment of allergic diseases.
- Unproven methods are procedures or therapies that are not supported by scientific evidence and have no basis in the pathophysiology of allergic disease.
- Inappropriate methods are procedures and therapies that are legitimate but are used inappropriately.
- It is important for the practicing allergist to become familiar with both accepted and unproven practices.

Introduction

The process of diagnosing and treating allergic disease is complex and at times elusive. It requires a thorough history and physical examination and, in certain situations, complementary laboratory tests. Most of the tests which are performed today have undergone rigorous scientific evaluation for proof of effectiveness and safety. They must also have established physiological significance when used to diagnose a particular disease. Nevertheless, there are a growing number of unconventional, unproven, and inappropriate procedures used by some in order to diagnose allergic disease. Some of these “tests” are legitimate but are misused in their application to the diagnosis of allergy. Other “tests” have no basis in the pathophysiology of allergic disease. It is important for those practicing allergy and immunology to become familiar with all diagnostic procedures. Some may be unsuitable for allergy diagnosis for several reasons. For example, a procedure may be based on an unproven theory. Others are legitimate tests used inappropriately. Some procedures do not have the ability to diagnose any disease. It thus becomes apparent that standardization and a controlled evaluation of procedures before their use are imperative for proper patient care. The following information should be useful because there have been an increasing number of patients who are using complementary therapies for chronic

conditions. One study found that complementary therapies were usually used alongside conventional treatment [1]. Patients felt empowered to take control over their condition rather than feel dependent on medication [1]. These patients may present at the beginning of their search with a multitude of questions regarding a proposed specific diagnostic procedure or they may present having been involved in a questionable, perhaps expensive procedure, resulting in a questionable diagnoses.

Definitions

Standard practice is that which is performed by the majority of physicians in the community. It encompasses those procedures and treatments which have been scientifically proven to be effective and safe. Before describing and critiquing the following procedures and therapies it is important to first attempt to categorize each one. Thus first certain approaches can be considered to be “unproven,” and are also at times referred to as “complementary” or “alternative.” These types of tests or treatments are those that are not based on any clear rationale based on acceptable allergy pathophysiology, and their effectiveness is not supported by scientific evidence. Although they may appear well-constructed they do not seem capable of either diagnosing or treating an allergic disease. Some of these procedures have been loosely adapted from proven methods that are currently available for the diagnosis and treatment of allergic disease. Often one of the reasons why these tests have not been examined scientifically is that their methodology

is vague and is often difficult to reproduce. Other procedures are categorized as being “inappropriate.” This means that the test itself is a validated test used to diagnose certain conditions; however, in these cases the procedure is being inappropriately applied.

“Controversial” tests

Skin endpoint titration

During the 1940s, Rinkel developed the method of endpoint skin testing [2]. He found that this method was a useful guide in determining a patient’s sensitivity and the information found could be used in determining a safe and effective dose for immunotherapy. Variations of this method have been used for both the diagnosis and treatment of inhalant and food allergies.

Method

The procedure involves intradermal testing with 5-fold serial dilutions of extract. A 7-mm whealing response is considered reactive. The endpoint is defined as the weakest dilution that produces a positive skin reaction and initiates a progressive increase in the diameter of the wheals with each stronger dilution tested [3]. The optimal starting dose is usually 0.01–0.02 ml of extract. The optimal therapeutic dose, defined as a dose at which symptoms are controlled on immunotherapy, is reached after the endpoint dilution is given weekly in increasing increments. Rinkel anticipated a relief of patient symptoms at a dose of 0.5 ml of the endpoint dilution.

Conclusion

There have been several trials over the years that have looked at the efficacy of the Rinkel method. Van Metre *et al.* published several studies which supported the Rinkel method as valid in quantifying skin sensitivity to ragweed pollen and found the method comparable with *in vitro* leukocyte histamine release and radioallergosorbent assay testing (RAST) [4]. While variations of this method of skin testing are being practiced today without any risks, using the results to determine optimal dosing of immunotherapy is questionable. In the opinion of many, most of the time this “dose” is an underestimation resulting in ineffective treatment.

Unproven tests

Applied kinesiology

Kinesiology refers to the science of motion techniques. It is a belief by some that certain diseases, including allergic reactions, may cause a weakening of skeletal musculature. Some believe that by using applied kinesiology one may diagnose allergic disease. This is commonly applied to the diagnosis of food allergy.

Method

Allergens to be tested are placed in stoppered glass bottles. In some cases a glass vial containing a specific allergen is placed on or near the body of the patient, or in other cases, the patient is asked to hold the vial. During allergen “exposure,” muscle strength is tested. A positive test is said to be indicated by observed weakening in muscle strength. There are variations to the standard test which include “surrogate” testing in which a relative of the patient undergoes testing for the patient.

Conclusion

In 1988, Garrow [5] published a study of blinded and open challenges of allergen using applied kinesiology and looking at the reproducibility and efficacy of the test. The study reported no significant difference between frequencies of positive reactions to placebo versus allergen. Therefore, at this time, there appears to be no proof of the efficacy or reproducibility of the method of kinesiology in diagnosing food allergy.

Provocative testing and neutralization

Elicitation of a limited reaction by delivering allergen via the transdermal, subcutaneous, intradermal, or bronchial route are a part of an allergy practice. These procedures provide a wealth of information in the diagnosis of several allergic diseases. Such tests include: prick and intradermal skin test, intranasal, subconjunctival, oral tests and methacholine challenge. These approaches differ from provocative testing and neutralization in that they have undergone repeated scientific validation in studies with both patients and normal controls.

The provocative–neutralization method was introduced by Lee in 1961 for the diagnosis of food allergy [6]. The provocation is performed by intradermal, subcutaneous, or sublingual routes. It is currently used to diagnose and treat allergic disease and sensitivities to a wide variety of substances. The items tested are not necessarily those suspected by the history. They can include such chemicals as: formaldehyde, phenol, ethanol, and hormones such as progesterone [7].

Method

The patient is given an intradermal/subcutaneous dose of allergen extract using 5-fold serial dilutions (Rinkel method). The patient is observed for 10 minutes and any symptoms are recorded. If the patient remains symptom free then increasing doses of extract are given until symptoms do occur. Once these symptoms occur, the patient is immediately given injections of weaker dilutions of the same extract until symptoms are resolved. This amount of extract is considered the “neutralizing dose” and is then used for future treatment [8].

The technique appears vague and imprecise. There is no generally established validated protocol for performing the provocative testing and neutralization. In addition, there is no consensus on establishing what a positive test is. Symptoms may be quite extensive and non-specific and may include: headache, nasal symptoms, chest symptoms, ear reactions, gastrointestinal reactions, skin eruptions or itching, or general reactions such as fatigue, chills, muscle pain, or drowsiness [9]. There has been no general agreement on the role of wheal diameter in reporting a positive test. Some interpret an increase in wheal size as a further indication of a positive test.

Sublingual provocation testing and neutralization has been advocated by some in the diagnosis and treatment of food allergy. It was first described by Hansel in 1953 [10] as a diagnostic and therapeutic technique. The method consists of placing allergenic extract underneath the tongue and waiting 10 minutes for the appearance of symptoms. If symptoms occur then the patient is given a more dilute solution of the same extract. The neutralizing dose is used as treatment prior to or after eating meals containing the offending food if the food cannot be avoided.

Given the fact that a single item needs to be tested one at a time and requires waiting 10 minutes between each dilution, it comes as no surprise that a single complete provocative-neutralization might take an entire day. Testing multiple items may take many days. Therefore, this test is time consuming and can be costly.

Conclusion

There have been approximately 15 studies published looking primarily at the efficacy of provocative testing and neutralization. Eight of these studies were double-blinded. Only one study contained a control group. The majority of the studies were not able to demonstrate any benefit from neutralizing solution compared with placebo. Crawford *et al.* [11] performed a double-blinded study in 61 subjects with a history of reactions to five common foods. The authors were unable to demonstrate reproducibility of results from sublingual food testing. Kallin and Collier [12] in a double-blind study compared neutralizing effects of sublingual or subcutaneous food extracts versus saline placebo. The authors found that in 70% of patients, treatment with saline placebo was "relieving." Draper [13] in a study of 121 patients with inhalant allergy, found that only 38% of positive provocation tests correlated with a positive food challenge test. One of the most well-structured double-blind studies was that by Jewett *et al.* [14]. This study of 18 patients with symptoms previously provoked by intracutaneous testing were tested with food extracts or placebo. The rate of positive responses was similar between placebo and food extracts.

In conclusion, overall these studies fail to confirm the efficacy of provocative testing and neutralization in the diagnosis and treatment of allergic disease.

Neutralization therapy

Neutralization of allergic symptoms is an extension of provocation-neutralization testing described earlier. This type of treatment, also called "relieving therapy," consists of self-administered doses of allergen extract at a concentration which "neutralizes" symptoms provoked during the prior provocation testing [7]. This treatment may be used by some to relieve present symptoms and to prevent anticipated symptoms and for continuous maintenance doses twice weekly. These doses can be given either by injection or sublingual. The patient can change and discontinue or restart treatment as they deem necessary.

Theory

A number of theories have been brought forth to try and explain neutralization of symptoms. A common belief among some practitioners is that this type of therapy induces immunological tolerance. Controlled, double-blind, multicenter studies have reported that sublingual, provocative food testing did not discriminate between placebo controls and food extracts used in neutralization therapy [9]. In addition, there appear to be no long- or short-term studies looking at the efficacy of this therapy.

Conclusion

As a result, since there is no known mechanism for neutralization of symptoms and no clear scientific evidence demonstrating its effectiveness, this form of therapy is not generally recommended in the treatment of allergic conditions such as food allergy.

Cytotoxic leukocyte testing

Also known as "Bryan's" test, this form of allergy testing was adapted by Bryan in the 1960s. Initially designed to help aid physicians in diagnosing allergy, the theory behind the test is that the addition of specific allergen *in vitro* to whole blood or to serum leukocyte suspension will reduce the white blood cell count or result in the death of leukocytes. It has been claimed by some to be useful for the diagnosis of both food and inhalant allergy [15]. The newer ALCAT test currently available functions in a similar way in that it measures volumetric shifts in white blood cells upon incubation with antigens. The blood cells are passed after an incubation period through a narrow channel and are measured by an electronic instrument. The sizes are displayed as either cell diameters or as cell volumes. The company claims that their test will identify exactly which foods or chemicals are responsible for triggering a variety of symptoms including: joint pain, headaches, asthma, obesity, ADD/hyperreactivity, chronic fatigue among others.

Method

The technique involves collecting the buffy coat from a drop of patient's blood and placing it on a microscope slide

coated with dried extract of food or other allergen/substance and then observed microscopically for alteration in the appearance of white blood cells [16]. Once a fair number of white cells have been located, they are rated for degree of destruction. A single sample of blood can be tested to a panel of foods and other substances.

Conclusion

There is no theoretical basis for the cytotoxic test, since there is no evidence for a general cytotoxic mechanism in allergic disease. The test itself is not standardized and has never been shown in controlled trials to be effective in the diagnosis of food or inhalant allergy. Franklin and Lowell [17] reported that there was no significant difference in white blood cell counts in blood exposed to ragweed extract versus saline in ragweed-sensitive individuals. Lieberman *et al.* [18] could not demonstrate clinical correlation with test results in study patients and found inconsistent results when patients were tested more than once. Benson and Arkins [19] found the test was associated with a high degree of false positives. In regards to ALCAT, one abstract, from the company homepage, assessed the degree of correlation between ALCAT and the results of oral double-blinded food challenges found an almost 84% correlation between the two tests. However, this small study had some significant limitations and no recent larger studies are available [20].

Electrodiagnosis (Vega testing)

Electrodiagnosis is also known as electroacupuncture according to Voll (EAV), electrodermal screening (EDS), bioelectric functions diagnosis (BFD), or bioenergy regulatory technique (BER) [21]. Some practitioners believe that the presence of specific allergy can lead to a change in the electrical potential of the skin. These changes are then said to be detected by Vega machines or bioresonance devices.

Method

In this procedure a sample of food extract is placed in a container in contact with an aluminum plate. This is then placed between the skin of the patient and a galvanometer. Electrical activity of the skin is measured at certain "allergy points." For example, there are certain points on the lower extremities which are said to correspond to food allergy and points on the upper extremities which are said to correspond to inhalant allergies [15]. These results are entered into a computer which prints a list of allergies for the patient. Children are assessed by testing the parent first, and repeated with the parent holding the child's hand.

Conclusion

This type of procedure appeals to those patients who are reluctant to undergo any involved and potentially uncomfortable diagnostic procedures such as skin testing. Also, the use of computers, galvanometers, and "print outs" appear "state

of the art" to some patients. Semizzi *et al.* [22] assessed the accuracy of electrodermal testing in 72 allergic patients compared with healthy controls. They found no significant difference in skin electrical response between the two groups.

Radionics

Method

Radionics is based on the concept that all life forms are submerged in the electromagnetic energy field of the earth. And that a disease will be reflected by changes or "imbalances: in an individual's electromagnetic field said to lie outside the normal electromagnetic spectrum. Practitioners claim to treat disease by restoring normal energy balance. Sometimes the operator is with the patient, and sometimes the operator "connects" with the patient at a distance using an object such as a lock of hair, blood sample, or photograph.

Conclusion

This technique has not been subject to formal study, and there is no published evidence that it is effective for the assessment or treatment of any disorder [23].

Iridology

Method

This is based on the concept that each part of the body is represented by a corresponding part of the iris. A person's state of health is determined by the color, texture, and location of pigment flecks in the eye. Imbalances are treated with dietary supplements or herbal medicines.

Conclusion

Studies have shown that iridologists are unable to distinguish patients with disease from those who are healthy [23,24].

Body chemical analysis

Some practitioners claim that detection of any amount of inorganic or organic chemical in body fluid may indicate a toxic exposure and may explain the presence of disease. They postulate that certain substances may be toxic to the immune system leading to a state of sensitivity to the environment [2]. Some of these substances include: vitamins, drugs, chlorinated hydrocarbons, volatile organic chemicals, pesticides, and metals.

Method

Specific tests include gas chromatographic mass spectrophotometry analysis of body fluids and tissue, quantitation of chemicals in serum and other body fluids and breath analysis [3].

Conclusion

These procedures are highly sensitive and are able to identify chemicals in virtually every individual, even those who

do not report symptoms. This is why a strong clinical correlation is important in conjunction with this type of testing. In certain situations and in certain individuals, it may be appropriate to evaluate for chemical poisoning in order to properly diagnose a disorder. It is important to note that many of the laboratories performing these tests are deficient with respect to quality assurance so, for example, contamination of samples remains a major source of error [3].

Inappropriate tests

IgG antibodies

Immunoglobulin E (IgE) antibody in response to allergens causes the release of mast cell mediators which are important in the immediate-type symptoms of anaphylaxis or atopic disease. Sensitivities to certain allergens can be diagnosed by detecting IgE in the serum by RAST. Many laboratories can test in a similar fashion for the presence of immunoglobulin G (IgG) to certain foods. There are those practitioners who measure circulating IgG antibody reactive with food antigens in diagnosing food allergy. The patient then may receive therapy in the form of elimination and rotation diets. It is this construct, that while IgG may not be important in the immediate-type reactions to certain foods, it may be important in delayed-type reactions such as depression, apathy, fatigue, myalgias, and gastrointestinal complaints [25]. Diagnosis of delayed-type reactions is challenging and while conventional IgE RAST alone cannot diagnose these types of reactions there are no published double-blind, placebo-controlled studies that demonstrate that such symptoms are related to particular foods as identified using such tests.

IgG antibodies are not known to have a role in the pathogenesis of atopic disease and food allergy. Certain levels of IgG to food antigens as well as other environmental antigens may be found normally and their presence, as of yet, has not been shown to be associated with atopic disease. Therefore, measurement of antigen-specific IgG has not been recommended as a form of diagnosing food allergy in the clinical setting.

Lymphocyte subset counts

Quantitative counting of leukocytes bearing one or more surface markers known as cluster of differentiation (CD) markers is helpful in the diagnosis of some forms of lymphocyte cellular immunodeficiencies. For example, measuring CD4 lymphocytes is part of the standard procedure for diagnosis and management in human immunodeficiency virus [2]. Lymphocyte subset counts may be labile and non-specific. Levels may not be elevated in traditional allergic diseases but may be elevated in those with viral illnesses, for example. Use of these tests to diagnose forms of allergy or other presumed immunological disorders is generally considered inappropriate and can lead to inappropriate treatment of a patient.

Pulse test

Coca in 1953 reported that tachycardia occurring 5–90 minutes after exposure to a food or inhaled material is a reliable indicator of food allergy [26].

Method

The test dose can be given by any route including injection. A change of 10bpm is thought to be diagnostic by some, but the procedure has never been standardized. This test has no relationship to the diagnosis of allergic disease.

Unproven therapy

Neutralization therapy

This topic is discussed earlier in the section entitled “Provocation–Neutralization.”

Rotation diets

Theory

This particular type of diet recommends that a certain food not be eaten more than once every four to five days [3]. Part of the rationale is that if the patient is allergic to most or all foods, by eating them frequently, he or she runs the risk of becoming increasingly sensitized to that food and possibly other foods.

Conclusion

If a patient does have clinical sensitivity to a particular food then he or she will develop symptoms after contact with that food irrespective of rotation schedule. However, if a patient demonstrates “subclinical sensitivity” to a certain food, that is, no symptoms but evidence of specific IgE by testing, then each exposure to that food will increase sensitivity and likelihood of a future reaction. There is thus no scientific data supporting the efficacy of this type of diet.

Buteyko breathing technique

Theory

This technique is promoted as a drug-free asthma therapy. It is based on the concept that carbon dioxide is a natural bronchodilator. Slowing the rate of breathing by this logic would then raise carbon dioxide levels, resulting in symptomatic improvement. One recently visited website made a “12-month unconditional guarantee” that by following these exercises you could “outgrow your asthma.”

Conclusion

Controlled studies have demonstrated symptomatic improvement and reduction in medication use in some patients, but no changes in carbon dioxide levels or measurements of lung function [27]. There is no evidence that there is any impact on the inflammatory components of asthma.

Advanced allergy elimination

Theory

This treatment is based on the concept that “allergen” is perceived by the brain as a threat to the body’s well being. Exposure to allergen disrupts the flow of nervous energies from the brain to the body via “meridians,” resulting in symptoms [23]. Acupressure is applied to both sides of the spinal column while the patient is in direct contact to purported allergen.

Conclusion

This approach lacks scientific rationale or published evidence of efficacy.

Orthomolecular therapy

Theory

This refers to the use of supplements and/or vitamins administered in large quantities either parenterally or orally to treat numerous medical and psychiatric conditions [3]. Practitioners of this therapy will commonly measure levels of vitamins in the serum or urine to determine the amount needed for correction. This type of therapy has been used in a wide variety of diseases. For example, antioxidant supplements such as vitamin E, C and glutathione have been used to treat allergic disease based on the theory that allergic inflammation generates free radicals which can cause oxidative damage to tissues [28].

Conclusion

There have been no controlled studies looking at this type of therapy and is not a recommended treatment of any disease at this time. Large doses of certain vitamins can accumulate in the body and lead to toxic effects.

Mercury amalgam removal

Theory

Silver–mercury amalgam has been used in dental fillings for over 100 years. There have been many claims from physicians and dentists that certain patients may develop sensitivity to this material. Subsequently, it has been blamed for the development of a wide array of symptoms [3]. These claims have led to the removal of these types of fillings.

Conclusion

There is no sound clinical evidence for the claims that mercury amalgam is responsible for the development of a multiplicity of somatic complaints.

Urine autoinjections

In 1930 Oriel and Barber reportedly found protein-like substances in the urine of allergic individuals during acute exacerbations of allergic disease [29]. Urine obtained from sensitive individuals applied intradermally to those individuals with the same sensitivities resulted in a positive

skin test. This was not the case for the same urine applied intradermally in a non-atopic individual [25]. These practitioners felt that these “urine proteins” can be isolated by chemical extraction and given to the patient as a form of therapy in a series of intradermal/subcutaneous injections.

In 1947, the procedure was reintroduced by Plesch [30]. He describes a system of collecting fresh urine from a patient and after sterilization, injecting set amounts intramuscularly. Various reactions would occur within hours of injection and include: fever, diarrhea, hypotension, shortness of breath, and vomiting. He found that by performing these injections in patients with various syndromes such as jaundice, allergic disease, gastrointestinal symptoms, and dermatological symptoms there was a decrease in symptoms. There are however, no controlled studies to support neither the efficacy nor the safety of the procedure. In fact, in rabbits, urine autoinjection may lead to the formation of autoantibodies to glomerular basement membrane (GBM) and result in nephritis. Although this has not been demonstrated directly in humans, it is possible that receiving these urine autoinjections could induce immune complex disease. It has been established that in humans, anti-GBM antibodies can lead to the development of Goodpasture’s syndrome. Therefore, at this time, the American Academy of Allergy and Immunology has taken the position that this procedure is unproven, without scientific basis, and potentially dangerous [15].

Inappropriate therapy

Clinical ecology

Clinical ecology is based generally on two concepts. One is that a large number of chemicals and foods can be responsible for illness in the absence of abnormal laboratory tests and physical findings; and the other is that the immune system is functionally depressed as a result of exposure to certain chemicals in the environment [31]. This is not to be confused with toxic illnesses which produce a number of symptoms and abnormal laboratory tests in response to a particular toxin. Those who practice clinical ecology believe that patients with chemical hypersensitivity syndrome, also known as environmental hypersensitivity disorder, or 20th century disease, or induced immune dysregulation syndrome have symptoms which are a result of low-level, long-term exposure to environmental chemicals. The doses which cause these syndromes are far below those established in the general population to cause harmful effects [32]. The agents are sometimes referred to as “incitants” or “offenders,” and they include foods, food additives, and synthetic and natural chemicals such as: pesticides, detergents, perfumes, vehicle exhaust, and natural gas. Symptoms are often generalized, frequently affecting more than one organ system including the cardiac, gastrointestinal, respiratory, genitourinary, and neurological systems.

Theory

Clinical ecologists [33] have theorized that environmental illness is a result of the development of sensitivity to novel synthetic chemicals. Others believe that these chemicals act as haptens inducing IgG formation and immune complex formation [34]. Environmental illness has also been thought to be the result of a non-specific autoimmune process. What still needs to be established is a possible mechanism for this disease process; however, there are several concepts that clinical ecologists use to account for patient symptoms. "Total body load" and "Chemical overload" draw an analogy between the immune system and a container. The immune system is said to have a limited capacity for handling antigens. Once a patient develops symptoms in response to an environmental antigen this then indicates that the immune system has been exceeded. "Masking" is a concept in which a patient, who is sensitive to a certain food, may eliminate symptoms by eating the food on a regular basis. "Spreading phenomenon" refers to sensitivity to one antigen leading to the development of sensitivity to multiple other antigens [3].

Diagnosis

A detailed history within provocation-neutralization testing remains the mainstay of diagnosing environmental illness by clinical ecologists. Occasionally blood tests looking at immunoglobulin, complement, or specific chemical levels are used to aid in diagnosis.

Treatment

Consists mainly of avoidance measures, elimination diets, neutralization therapy, and in some cases as in *Candida* hypersensitivity syndrome, drug therapy.

Anti-Candida drugs for *Candida* hypersensitivity syndrome

Theory

Candida albicans is yeast which maintains a role as part of the body's normal flora. There are those who believe that it is this particular organism that is the cause of a condition termed "yeast hypersensitivity syndrome" or "*Candida* hypersensitivity syndrome." Proponents of this hypothesis believe that the syndrome is caused by an overgrowth of *Candida albicans* in the gastrointestinal tract leading to local inflammation as well as a more generalized toxic response. This response is thought to be secondary to a hypersensitivity reaction to a toxin which the organism secretes. As a result, symptoms range from recurrent or persistent candidal infections to chronic gastrointestinal symptoms such as bloating, diarrhea, constipation, and heartburn. Central nervous system symptoms have also been reported including depression, chronic fatigue, and memory problem [3].

Methods

There is no established method of diagnosing this syndrome. Diagnosis is most commonly made by history alone

and not with specific laboratory measures. There have been reports of practitioners performing allergy testing in order to document sensitivity to *candida*.

Treatment

Patients are first warned to avoid broad-spectrum antibiotics and systemic steroids since these medications may potentiate *candida*. They are given minute doses of oral nystatin until symptoms have resolved. If symptoms persist, treatment can be changed to another anti-candidal drug such as ketoconazole or amphotericin B. In addition to anti-candidal drugs, patients are also started on yeast-free, sugar-free diets. It is thought by some that by eating simple sugars there is an increase in growth of *candida* in the gut [35]. *Candida* allergy shots are also included in the treatment regimen of some patients.

Conclusion

Books and lay press articles have been published; support groups have been formed, all in the hopes of establishing a connection between yeast and disease. However, a scientific basis for this syndrome has never been established. The reports that do circulate are largely anecdotal. In 1990, Dismukes *et al.* [36] published the first randomized, double-blind, crossover study looking specifically at the effect of treatment with oral and vaginal nystatin compared with placebo in 42 pre-menopausal women presumed to have *Candida* hypersensitivity syndrome. Results from their work showed that while nystatin therapy did reduce vaginal symptoms, the efficacy of treatment for systemic symptoms including depression and chronic fatigue was not established. There was no significant reduction in systemic symptoms compared with placebo. Therefore, the study could not establish a therapeutic benefit of nystatin therapy in a patient with *Candida* hypersensitivity syndrome.

Elimination diets

Theory

The elimination of multiple foods has been recommended by some practitioners when multiple food allergies have been discovered on skin testing. This type of diet is also recommended by others who believe that through elimination diets one may "boost" the immune system [3].

Methods

Once the patient is diagnosed with sensitivity to multiple foods, either by unconventional testing or perhaps history, they are placed on highly restrictive diets in order to prevent further symptoms. Most of the time patients are given supplements of vitamin, minerals, or amino acids [21].

Conclusion

There is no evidence that by eliminating multiple foods one may improve the functioning of the immune system.

In fact, placing patients on such restrictive diets may lead to harmful effects of malnutrition.

Multiple chemical sensitivity syndrome

Theory

Multiple chemical sensitivity (MCS) syndrome or idiopathic environmental intolerances (IEI), as suggested by the WHO/IPCS workshop in 1996, has been used to describe a constellation of symptoms which overlap with those of environmental illness but overall remains a distinct entity. This disorder is characterized by a wide variety of symptoms including somatic, cognitive, and affective symptoms, caused by low-level exposure to environmental chemicals [37]. Symptoms commonly involve almost every major organ system and are thought to result from sensitivity to certain chemicals. Chronic fatigue, depression, headache, and dizziness are commonly reported symptoms. Little is known about the pathophysiology of this condition, but its proponents claim that through certain mechanisms such as disruption of immunological/allergy processes, alterations in nervous system function, changes in biochemical pathways, or changes in neurobehavioral function chemicals cause tissue damage [38]. This may be accomplished through processes such as free radical generation, immune complex formation, or hapten formation.

Methods

Patients with this condition often manifest certain psychological features such as anxiety, depression, somatization, conversion, and phobia [3]. This makes it especially challenging in establishing a diagnosis of MCS. The diagnosis of MCS is, however, made if symptoms cannot be explained by abnormal tests but are associated with a documented environmental exposure. The lack of objective findings of disease such as: physical exam and laboratory tests cast doubt on the validity of MCS as a clinical disease.

Critique

The concept of multiple chemical sensitivities in the absence of any objective data remains its advocates' greatest challenge. At the present time, there is no scientific evidence that MCS should be regarded as a true clinical entity, but rather it appears to be based on an association of a wide range of symptoms to a particular or varied number of varied environmental chemicals.

Clinical ecology is inadequately supported in the literature. Both diagnostics and treatments have not been proven to be of any consistent efficacy or benefit. Part of the difficulty in evaluating clinical ecology and environmental disorders is that it is virtually impossible to establish a cause and effect relationship. There is such a varied number of possible "triggers" of symptoms.

Conclusion

Many of the subspecialty groups including the American Academy of Allergy Asthma and Immunology and the American College of Physicians have issued position papers looking at several of the above-mentioned procedures and therapies. It was the goal of this chapter to provide definitions of controversial, unproven, and inappropriate procedures and treatments and provide examples of each so that it might provide insight into remote practices of allergy. There appears no reproducible scientific basis for any of the treatments, conditions, or procedures discussed. By examining each theory and method, we can become more aware of the importance of scientific evidence and standardization of procedures in our daily practice. The history, physical exam, selective skin tests, and appropriate laboratory tests remain the standard of care in first evaluating the allergy patient. However, as we have seen this may not always be the case. Patients may be asked to undergo rigorous, expensive, invalidated and even painful testing. They may be given diagnoses and treatments, which may lead to both physical and mental deterioration. We have also seen that many "validated" tests can be misused to diagnose allergic disease. Many supporters of these procedures have misinformed the public by implying that they have been clinically proven. Therefore, it becomes the responsibility of physicians to educate patients regarding such practices of allergy. It also becomes our responsibility to design proper clinical trials to definitively establish the merit or failure of these tests.

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PART 4

Adverse Reactions to Food Additives