Selected Abstracts

Immunology & Food Allergy

Alpha Education
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Selected Abstracts & Citations: Immunology & Food Allergy

This collection of abstracts from the medical literature and citations to the literature is considered to be a supplemental text to the books Food Allergy and Immunology Notes by Stephen Gislason MD.

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Recommended Reading

1. Food Allergy is an introduction to the nature and management of food-related immune mediated disease. The relevance and application of diet revision using the Alpha Nutrition Program is explained. For the advanced reader, download Immunology Notes.
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Food Allergy Abstracts

Preface

The subject of food allergy is fascinating from many points of view. In my opinion, it is one of the more important topics in the study of practical medicine and one of the most ignored. The ignorance of delayed patterns of food allergy among physicians is embarrassing. Official denial is understandable; since powerful vested interests are threatened by the possibility that food allergy is a cause of common of endemic diseases. Denial is the best defense if you are marketing foods that cause disease, but are generally considered to be "safe foods."

This collection of abstracts and references is part of an introduction to the study of food allergy recommended to all who are interested in the food causes of disease. The theory and practice are discussed in two other books Managing Food Allergy and Immunology Notes; the abstracts are supplementary to these texts. This volume also lists references papers published before 1985 that established delayed patterns of food allergy as mechanisms of immune mediated disease that may underlie the most common and unsolved disease processes.

The alert reader of the abstracts will notice considerable differences in the opinions stated, especially about the prevalence and mechanisms of food allergy. A brief introduction to this complicated subject will allow the reader to develop a perspective on the play of variables in the often confused medical mind.

There are rich leads for further research, good insights for clinicians, and a good resource for patients and their families who usually have solve food-related diseases on their own.

Stephen Gislonson MD, 2014
A Very Brief Introduction

The concept of immune responses to food antigens is useful in understanding many diseases. Many of the major unsolved diseases of our civilization are either degenerative and/or inflammatory and many are recognized to be inflammatory, immune-mediated, hypersensitivity diseases. The term "hypersensitivity" refers to immune-mediated processes that lead to disease. As we consider the possible role of food antigens in causing or contributing to immune-mediated diseases, we look for opportunities to help patients with simple and safe therapeutic strategies such as diet revision.

The basic phenomena that concern us are:

- Food antigens activate immune networks
- Activated immune networks produce symptoms
- Long-term activation of immune networks causes chronic disease, often featuring inflammation in target organs.
- The food supply is the most abundant and continuous source of antigenic material.

Rheumatic diseases, autoimmune diseases, multiple sclerosis, insulin-dependent diabetes, thyroiditis, psoriasis are examples of hypersensitivity diseases that involve humoral and cell-mediated immunity. The common specific problems that are related to allergy include asthma, rhinitis, atopic dermatitis, urticaria, anaphylaxis, angioedema, allergic gastroenteropathy, and allergic arthritis. Many patients will express several of these hypersensitivity phenomena over a lifetime and demonstrate an underlying tendency to be hypersensitive. An important concern is the possibility that the chemical soup created by our civilization drives increasing numbers of individuals into hypersensitivity illness.

The advocates of a broad definition of food allergy run the risk of being evangelical. The conviction that food allergy is a ubiquitous cause of disease comes from knowing the benefits of careful diet revision in medical practice. Many books in the popular literature proclaim the benefits of diet revision and a ground swell of interest and concern has engaged an ever-enlarging group of patients.

Often, the patient who benefits from proper diet revision is distanced from a medical profession who is either not interested or denies the problem of food allergy. Some of the issues that arise are semantic and
political, but other issues involve the very complex biology of food-body interactions that are not well understood. Other issues involve the changes in the food supply that have accelerated in the past few decades. When you do not know about food allergy, you are surrounded by mysterious diseases. When you know about food allergy, several common illness patterns begin to make more sense. Linda Gamlin writing about food allergy in the New Scientist stated that:

"Evidence is growing that many debilitating and chronic symptoms of ill health come from an intolerance for certain foods… The medical establishment remains largely hostile to the notion, leaving the field open to the medical fringe… the main problem is the plethora of symptoms and the variations from one patient to another. Doctors working with food intolerance report more than 40 possible symptoms and conditions...the severity also varies. Some patients are said to have nothing more than the occasional migraine or bout of fatigue, while at the other end of the scale the sufferer is unable to work or lead any sort of normal life."

In response to allergy lobby groups in the USA, the US Congress passed a bill that requires notice on the labels of foodstuffs that contain eight of the most common food allergens. The Food Allergen Labeling and Consumer Protection Act, will require plain English labeling by the year 2006 of products containing wheat, milk, soy, peanuts, tree nuts, fish, shellfish, or eggs. These account for an estimated 90% of all food allergies. The bill also requires the Food and Drug Administration to develop a definition of the term "gluten-free" to help those with celiac disease and who require a gluten free diet for other reasons. 


Multiple Mechanisms

Since there are multiple effects following ingestion of food, no explanation of adverse reactions to foods based on one mechanism alone will ever account for the multiplicity of effects reported and observed. The range of disorders that can be considered food-related and amenable to diet revision therapy is surprisingly broad. It is helpful to consider three categories of disorders:

1. commonly recognized syndromes
2. specific diseases
3. nonspecific illness

Specific diseases that have well-defined pathological definitions are diagnosed by objective criteria. However, common syndromes are just collections of symptoms with descriptive names such as irritable bowel syndrome, migraine, panic disorder, and depression. Chronic fatigue and fibromyalgia are not diseases in the nosological sense with discrete and objective pathology. They need a process interpretation. Treatment should be directed at removing the cause of these maladaptive dysfunctions.

The following concepts suggest a whole-system's way of thinking about body process, patients' symptoms and disease causation:

The human body is viewed as sensitive and reactive to its environment. It is appropriate for a patient to report sensitivity and reactivity to food, beverages, water, air and other features of the environment.

Emotional, intellectual, and physical sensitivity-reactivity are different expressions of the same biological properties.

Body surface protection involves cellular response systems. Immune sensors act in concert with nervous systems sensors to respond to threats at the body-environment interfaces.

All body surfaces continuously monitor the ambient environment. Surveillance provides protection against non-self antigens. An interactive, often synergistic effect of molecular stressors in air, food, water, and drugs should be predicted and accounted for.

The digestive tract surface begins with the lips and extends to the anus. This is an outside surface, strictly speaking. Most foods contain molecules which can act as antigens, and excite immune responses. The response to food is complex and variable, never consistent.

The digestive tract does not always process food well, and may permit the routine absorption of antigenic large molecules. Digestive tract function is easily disturbed by inappropriate food selection, infection, toxins, malnutrition, and drugs.

The pattern of multi-system disorder in patients with food allergy is understood as a consequence of somewhat chaotic antigen entry and distribution. The most important variables are food choices eating behaviors, dose and frequency of food ingestion, the interaction of food input on digestive procedures, adequacy of gastrointestinal tract surface defenses, and gastrointestinal tract permeability.

Digestive tract responses to perceived threats include expulsion mechanisms - vomiting, diarrhea, crampy abdominal pain; inflammatory defense - swelling, bloating, pain and
tenderness; and deterrent experiences - nausea, heartburn, vague discomforts, fullness, loss of appetite.

The digestive tract immune network tends to tolerance of molecular stressors or antigens that appear regularly. The eruption of symptoms of food allergy may represent the sudden loss of tolerance, rather than new or different sensitivities.

**Allergy Polemics**

There is confusion about the nature and mechanism of allergic reactions. The confusion begins with the struggle over the meaning of the term "allergy" among allergists and continues into the community where many improvised and nonsense tests and treatments for "food allergy and sensitivity" have become popular. The term "Food Intolerance" has been applied to metabolic derangements that occur when enzyme deficiencies such as lactase deficiency lead to intolerance of otherwise normal nutrients. Many physicians are more comfortable with the term "food intolerance" and are prepared to diagnose, for example, lactose intolerance when patients complain of gas, bloating and diarrhea. Other physicians prefer the term "food sensitivity" when a patient insists that eating certain foods bother them. A common distinction in the allergy literature between food allergy and intolerance since 1984 has not helped to resolve the uncertainty about what mechanisms are operating in which patients. The growing tendency to limit the description "allergy" to those reactions that are IgE-mast cell mediated and to refer to symptom production otherwise as "food intolerance."

Hill reported four clinical syndromes in children with milk allergy proven by cow's milk challenge in a hospital.

1. Anaphylactic - urticaria, angioedema, acute stridor, wheeze, and syncope.
2. Episodic vomiting and/or diarrhea
3. Severe Colic
4. Chronic ill-health with multisystem disease, associated with failure to thrive and/or chronic diarrhea, and/or eczema, and/or bronchitic, wheezing symptoms.

These children also fell into three groups according to the nature and timing of symptoms following challenge with cow's milk.

**Immediate onset**, within one hour: skin eruptions, vomiting, coughing, wheezing, stridor; high incidence of IgE antibodies to milk.

**Intermediate onset**, gastrointestinal symptoms developing within 24 hours with irritability, colic, vomiting, diarrhea. Low incidence of IgE antibodies. IgA deficiency was common.

**Delayed onset**: skin, respiratory, gastrointestinal tract and systemic symptoms, e.g. diarrhea 24 hours after milk challenge in an infant failing to thrive, serum IgG anti-milk antibodies and elevated total IgM.

**Type 1 Food Antigens**

The type 1 model of allergic disease encourages us to search for specific food allergens and to trace the occurrence of similar allergic substances in related foods. An allergic reaction to peanuts, for example, suggests that the peanut protein sensitizer may appear
in related legumes like peas or soybeans. This “cross-reactivity” has been noted for several food groups. Patients may react to both inhaled and ingested food antigens.

Interesting connections between cross-reacting foods and airborne reactions also occur with Type 1 allergy. For example, a 50 year old man experienced an anaphylactic reaction to sunflower honey. Investigation showed that he reacted to pollens of compositae family plants - daisy, dandelion, and sunflower. The same man also reacted to raw celery; celery sensitive people often cross react to birch pollens. Honey contains pollen the bees have collected and can be allergenic. Schwartz et al reported on three patients with carrot and celery reactions. One developed nasal and ocular itching handling raw carrots and ingestion would cause throat swelling, hoarseness, and dyspnea. Another patient had swollen lips, itchy throat, and nasal blockage 30 minutes after eating iceberg lettuce. The authors suggest a correlation between fruit and vegetable reactivity and birch pollen reactivity. Patients sensitive to raw fruits and vegetables may tolerate the same food if it is well cooked.

The study of food antigens or allergens has focused on the special antigens that produce immediate allergic reactions. A profile of antigenic proteins suggests that glycoproteins of a certain size and weight are common allergens. These proteins can be isolated from foods and are used to skin test sensitive individuals. Specific protein antigens have been characterized from a variety of foods, particularly cow’s milk, eggs, soybeans, peanuts, fish, crustaceans, wheat, oats, corn, rice, citrus, and some other foods. Gelatin is a collection of animal proteins made from skin and bones that can trigger typical type allergy. Reactions to gelatin-containing foods do occur. Reactions to gummy bears, jellos, licorice, marshmallows, fruit yogurt, instant whipped cream, and puddings are examples.

Laboratory studies of the interaction of proteins and antibodies present in the blood of sensitive individuals have confirmed the immediate hypersensitivity model of allergy as a reaction between specific food proteins and specific IgE antibodies.

The IgE model of allergy is satisfying to researchers, because of its simplicity and the ease of testing for sensitization; but, it selects only a special population of people with Type 1, IgE-mediated allergy. While this is an important reaction pattern, some physicians have claimed it is the only valid form of allergic reactions to food. Their opinion is not acceptable.
Delayed Food Allergy Patterns

Non-IgE mechanisms are responsible for other forms of food allergy that are prevalent and produce symptom complexes both systemically and in target organs such as the gastrointestinal tract. The central idea is that food proteins or peptides derived from these proteins enter the body and act as antigens. The immune responses to foreign proteins are delayed, complex and variable. Flu-like symptoms are typical manifestations of the delayed patterns of food allergy. Patients often complain of fatigue, irritability, aching, and cognitive dysfunction.

The concept of delayed patterns immune reactions to food proteins provides both a theoretic and practical basis for interpreting symptoms of patients with both specific diseases and non-specific syndromes. The presence of food allergy is concealed in a variety of diagnoses such as migraine headaches, asthma, eczema, irritable bowel syndrome, depression, panic disorder, and arthritis. Patients with these problems tend to have two or more manifestations concurrently in a matrix of non-specific symptoms. Our grand theory of hypersensitivity disease attempts to explain these illness complexes as expressions of reactive immune networks, responding to food and airborne antigens.

Delayed reactions begin in the gastrointestinal tract mucosa and spread inward to any body tissue if food antigens enter the circulation and interact with the circulating immune system. Incoming antigens tend to form immune complexes, and can injure target organs by triggering inflammatory responses in a variety of ways. Knicker stated: "Delayed adverse reactions to foods are exceedingly varied, and may involve virtually any organ system. Some reactions are classically allergic (the same list described for immediate reactions alone), and at times may reflect delayed IgE-mediated mechanisms. Others involve a single organ system, or multiple organ systems with puzzling combinations of symptoms."

The gastrointestinal tract (GIT) is central to understanding all food allergy mechanisms. In addition to digestion of food and absorption of nutrients, the gastrointestinal tract acts as a secretory organ, and an immune sensing device responsible for immunization against incoming antigens and tolerance to frequently appearing antigens. The gastrointestinal tract mucosa secretes a variety of peptide mediators in response to food stimulation, and may release prostaglandins, leukotrienes and cytokines that cause systemic symptoms such as flushing, fever, sweating, fatigue, and cognitive dysfunction. The gastrointestinal tract may "leak" and allow the passage of antigenic molecules into the lymphatics or blood. Systemic disease is downstream from a reactive, leaky gastrointestinal tract.

The permeability of the GIT determines how much antigenic material gets inside. Increased permeability to food and microbial antigens sets the stage for systemic problems. The spectrum of systemic disease from increased permeability to food and microbial antigens can be seen in patients with Crohn's and Celiac disease; both are prototypes of food allergic disease. The surface epithelium is a sophisticated nutrient processor-transporter, influenced by immune cells which lie below and between epithelial cells. These ideas are useful in developing a biological understanding of patients who get irritable, reactive bowels from ingesting food to which they have become sensitive.

Understanding associated changes in gastrointestinal tract permeability will help to explain why food-sensitive patients with bowel symptoms are likely to have systemic manifestations of food allergy including CNS effects.
The gastrointestinal tract mucosa secretes a variety of peptide mediators in response to food stimulation. The release of prostaglandins, leukotrienes and cytokines cause systemic symptoms such as flushing, fever, sweating, fatigue, and cognitive dysfunction. The gastrointestinal tract may "leak" and allow the passage of antigenic molecules into the lymphatics or blood. Systemic disease is downstream from a reactive, leaky gastrointestinal tract. Coombs, McLaughlin, Brennerman, Gerrard, Knicker, Hill, Brostoff, Egger, Walker and numerous others have made conspicuous efforts to elucidate the delayed forms of food allergy. These patterns of illness involve the most profound immune mechanisms since food antigens enter the circulation, interact with the circulating immune system, form immune complexes, and can injury target organs by triggering inflammatory responses in a variety of ways.

**Diet Revision as Therapy**

Careful application of diet revision therapy will reveal the fundamental significance of the food supply in the production of many common diseases. Diet revision should fit into the medical model as a first-stage combined diagnostic and treatment procedure. In a rational world, diet revision would be used to identify and treat patients who have food-related disease. The non-responders would proceed through further diagnostic and treatment procedures. Knicker stated that: "To diagnose adverse reactions to foodstuffs the clinician chiefly need to be satisfied that the ingestion of a food predictably and repeatedly causes disease. It is not necessary to know the precise triggering mechanism or which mediators of inflammation are activated. Such information is difficult to obtain, often requiring considerable laboratory investigation beyond the scope of clinical practice."

The Alpha Nutrition Program is offered as a diet revision algorithm, a versatile method of diet revision. This program was developed as practical medical management of food-related illnesses. The original design of the program was based on the management of food allergies. Food allergy often co-exists with digestive and absorption disturbances, as well as metabolic and biochemical problems. The bias of the program toward solving the problem of delayed pattern food allergy is an important advantage over other systems of diet revision. The "elimination diet" has been the allergist's main tool of diagnosis and treatment. Single foods or selected food groups were omitted from the patient's diet. Often elimination lists were based on the results of allergy skin or other tests. The IgE model of allergy postulated that single foods were responsible for symptom production and that their avoidance would leave the patient asymptomatic. Dietitians are usually equipped with avoidance lists that show a variety of products that contain the food or food group to be avoided.

The assumption is that the patients existing diet is perfectly adequate and eliminated offending foods will leave the patient intact with good nutrition. If skin tests were positive to several foods the patient would receive several elimination lists and would often feel frustrated and confused about what to eat.

Many food-related illnesses cannot be resolved by elimination strategies, nor can good nutrition be assured. More comprehensive diet revision completely re-designs the patient's food supply. The first step is to ask the patient to eat only a few foods; to return to a basic set of well-tolerated foods until symptoms remit and then reintroduce foods much in the way of infant-feeding practice.
First foods are based on the concept of a hypoallergenic diet. The “hypoallergenic or oligoantigenic” diet is a selection of foods that are thought to be well tolerated by the majority of patients. Many “few-foods” lists have appeared in the literature. They vary with local taste and custom. The consensus has always been that the high risk foods - milk, wheat, rye, barley, eggs, soya, corn, citrus, nuts, chocolate, coffee and processed foods with additives and preservatives are avoided.

Egger and his colleagues, for example, chose lamb, chicken, potatoes, rice, banana, and apple as the first foods in their oligoantigenic diet. Supplements of vitamins and minerals are included to improve the nutritional value of the diet. Following a successful remission of symptoms foods were reintroduced one at a time to assess their reactivity.

Darlington and Ramsey suggested that diet therapy should begin with elimination of all foods that might be causing symptoms, followed by single food re-introductions to discover which foods reproduce symptoms. They listed corn, wheat, cow's milk, pork, oranges, oats, rye, eggs, beef, coffee, malt, cheese, grapefruit, lemon, tomato, peanuts, and Soya as the foods most likely to cause arthritis.

Gerrard stated: "Foods seem to play a part in severe chronic disorders which have no recognized aetiology. To establish the role of foods in precipitating these disorders we need hospital units where patients can be fasted and then tested individual with foods, with biochemical and immunological studies if required. Investigations such as these are inexpensive and, when foods are implicated, the treatment, food avoidance, is cheap. When food avoidance prevents headaches, the irritable bowel syndrome, arthralgias, and depression, it is more effective and less costly than traditional treatment, and the observation also throws light on the aetiology of the disorder."

Hamburger, reviewed some of confusing and controversial aspects of food allergy. He stated: "The diagnosis and management of food allergy today cannot be practiced with the "facts" alone. To help our patients I used everything available- diet, support, trial and error, placebo, lab and skin tests, reassurance and medications. The 'art of medicine' was never more challenged than in the care of the possibly food-allergic, food intolerant patient."
General Abstracts

New insights into innate immune mechanisms underlying allergenicity.

Novel Immunotherapy Approaches to Food Allergy


Abstract  Despite reaching high percentages of desensitization using allergen-specific immunotherapy (SIT) in patients with food allergy, recent studies suggest only a low number of patients to reach persistent clinical tolerance. This review describes current developments in strategies to improve safety and long-term efficacy of SIT.

Recent findings  Modified allergens or tolerogenic peptides, ultimately optimized for human leukocyte antigen background of the patient, are explored for tolerance induction, whereas anti-IgE antibody (Omalizumab) may be used to facilitate SIT safety. Adjunct therapies to enhance efficacy may make use of Th1 polarizing agents, for example, CpG-oligodeoxynucleotides combined with modified allergen packaged in nanoparticles. Preclinical studies showed insulin-like growth factor-2, intravenous immunoglobulin, Tregitopes or allergen encased oligomannose-coated liposomes capable of inducing regulatory T-cells, recognized for their importance in clinical tolerance induction. Dietary intervention strategies utilizing herbal formula 2, VSL#3, nondigestible short-chain galacto-oligosaccharides and long-chain fructo-oligosaccharides (scGOS/lcFOS) plus *Bifidobacterium breve* M-16V or n-3 long-chain polyunsaturated fatty acids may facilitate safety and/or a favourable milieu for tolerance induction.

Summary  Combining SIT using (adapted) allergens or tolerogenic peptides with adjunct therapy may be essential to improve safety and/or efficacy. Beyond using targeted approaches, specific dietary components may be explored to reduce side-effects and support clinical tolerance induction by SIT.

Echocardiographic Alterations in a Child With Cow's Milk Allergy

A Case Report

Giuseppe Di Cara, Maria G Berioli, Anna Biscarini, Claudia Soldani, Piera Abate, Eleonora Ugolini, Giusiana Allocca, Maddalena Milioni

J Med Case Reports. 2012;6(299)

Abstract

Introduction: Cow's milk allergy is the most frequent food allergy in Europe and western countries and shows a wide spectrum of clinical features, including atopic dermatitis and gastrointestinal disease. To the best of our knowledge, this report is the first to describe Kawasaki disease-like clinical features and echocardiographic alterations which resolved after a cow's milk-free diet.
Case presentation: We report a case of a 9-month-old Caucasian girl with atopic dermatitis who developed clinical features commonly present in Kawasaki disease (erythematous skin rash, non-exudative conjunctivitis, fissured lips and neck lymph nodes), together with mild echocardiographic alterations (perivascular brightness, pericardial effusion) in the absence of fever. These features resolved within 2 weeks after the beginning of a cow's milk-free diet.

Conclusion: Kawasaki disease has recently been considered a possible risk factor for subsequent allergic disease secondary to immune dysfunction. This case report suggests that the immune-related alterations which are commonly present in allergic patients could be similar to the antigen-related immune response in Kawasaki disease and thus could lead to similar clinical features.

Mucosal Immunology (2010) 3, 104–110; doi:10.1038/mi.2009.138; published online 23 December 2009

M Wills-Karp, A Nath, K Page and C L Karp

Allergic diseases, which have reached epidemic proportions, are caused by inappropriate immune responses to a relatively small number of environmental proteins. The molecular basis for the propensity of specific proteins to promote maladaptive, allergic responses has been difficult to define. Recent data suggest that the ability of such proteins to promote allergic responses in susceptible hosts is a function of their ability to interact with diverse pathways of innate immune recognition and activation at mucosal surfaces. This review highlights recent insights into innate immune activation by allergens—through proteolytic activity, engagement of pattern recognition receptors, molecular mimicry of TLR signaling complex molecules, lipid-binding activity, and oxidant potential—and the role of such activation in inducing allergic disease. A greater understanding of the fundamental origins of allergenicity should help define new preventive and therapeutic targets in allergic disease.

IL25 elicits a multipotent progenitor cell population that promotes TH2 cytokine responses.


CD4+ T helper 2 (TH2) cells secrete interleukin (IL)4, IL5 and IL13, and are required for immunity to gastrointestinal helminth infections1. However, TH2 cells also promote chronic inflammation associated with asthma and allergic disorders2. The non-haematopoietic-cell-derived cytokines thymic stromal lymphopoietin, IL33 and IL25 (also known as IL17E) have been implicated in inducing TH2 cell-dependent inflammation at mucosal sites3, 4, 5, 6, but how these cytokines influence innate immune responses remains poorly defined. Here we show that IL25, a member of the IL17 cytokine family, promotes the accumulation of a lineage-negative (Lin-) multipotent progenitor (MPP) cell population in the gut-associated lymphoid tissue that promotes TH2 cytokine responses. The IL25-elicited cell population, termed MPPtype2 cells, was defined by the expression of Sca-1 (also known as Ly6a) and intermediate expression of c-Kit (c-Kitint), and exhibited multipotent capacity, giving rise to cells of monocyte/macrophage and granulocyte lineages both in vitro and in vivo. Progeny of MPPtype2 cells were competent antigen presenting cells, and adoptive transfer of MPPtype2 cells could promote TH2 cytokine responses and confer protective immunity to helminth infection in normally susceptible Il25−/− mice. The ability of IL25 to induce the emergence of an MPPtype2 cell population identifies a link between the IL17 cytokine family and
extramedullary haematopoiesis, and suggests a previously unrecognized innate immune pathway that promotes TH2 cytokine responses at mucosal sites.

**Food allergy: separating the science from the mythology.**


Numerous genes are involved in innate and adaptive immunity and these have been modified over millions of years. During this evolution, the mucosal immune system has developed two anti-inflammatory strategies: immune exclusion by the use of secretory antibodies to control epithelial colonization of microorganisms and to inhibit the penetration of potentially harmful agents; and immunosuppression to counteract local and peripheral hypersensitivity against innocuous antigens, such as food proteins. The latter strategy is called oral tolerance when induced via the gut. Homeostatic mechanisms also dampen immune responses to commensal bacteria. The mucosal epithelial barrier and immunoregulatory network are poorly developed in newborns. The perinatal period is, therefore, critical with regard to the induction of food allergy. The development of immune homeostasis depends on windows of opportunity during which innate and adaptive immunity are coordinated by antigen-presenting cells. The function of these cells is not only orchestrated by microbial products but also by dietary constituents, including vitamin A and lipids, such as polyunsaturated omega-3 fatty acids. These factors may in various ways exert beneficial effects on the immunophenotype of the infant. The same is true for breast milk, which provides immune-inducing factors and secretory immunoglobulin A, which reinforces the gut epithelial barrier. It is not easy to dissect the immunoregulatory network and identify variables that lead to food allergy. This Review discusses efforts to this end and outlines the scientific basis for future food allergy prevention.
Gastrointestinal eosinophils in health, disease and functional disorders

Nature Reviews Gastroenterology and Hepatology 7, 146-156 (March 2010) | doi:10.1038/nrgastro.2010.5

Nicholas Powell, Marjorie M. Walker & Nicholas J. Talley  About the authors

Eosinophils are potent innate immune cells that home to the gastrointestinal tract where they participate in host immunity to luminal pathogens, and help to maintain intestinal epithelial homeostasis. However, these cells are now recognized to have key functions in the pathogenesis of numerous other disorders of the gastrointestinal tract, including primary eosinophilic gastrointestinal disease, common functional conditions, such as dyspepsia, and also in gastrointestinal disorders in patients with allergic disease. We are just beginning to understand the potential pathological role of eosinophils in gastrointestinal disease, and it is increasingly likely that gastroenterologists and histopathologists will need to account for the presence of gastrointestinal eosinophils and relate their presence to gastrointestinal symptoms. This Review discusses the role of gastrointestinal eosinophils in health and disease, including their associations with functional and allergic disorders.

Determination of T-cell fate by dendritic cells.

Sandra S Diebold.  Immunology and Cell Biology (2008) 86, 389–397; doi:10.1038/icb.2008.26; published online 1 April 2008

Dendritic cells (DC) are professional antigen-presenting cells with a unique T-cell stimulatory aptitude that play a crucial role in the instruction of adaptive immune responses upon infection. By controlling the initiation of a diverse set of effector functions, which are suitable for the elimination of a wide range of pathogens, DCs form the pivotal link between the innate and the adaptive immune system. The innate pattern recognition pathways that trigger DC activation are central for skewing of the adaptive immune responses that are subsequently induced. Thus innate activation not only precedes adaptive immune activation, it also controls it and tailors the effector functions to the requirements of the infection. The adaptive immune response has to match the nature of the infection, but this does not only concern the type of pathogen, it is also affected by the localization of the infection. Tissue homeostasis has to be ensured and thus tissue-derived environmental factors influence the functional activity of activated DCs and thereby contribute to shaping of the immune response. Adaptive immune responses are vital for the elimination of pathogens, have the potential to attack tumor cells and play a detrimental role during transplant rejection and in a variety of autoimmune diseases. Better understanding of the mechanisms that control the induction of different T-cell effector functions will enable the development of strategies to manipulate the immune system in the context of vaccination, tumor immunotherapy, transplantation and autoimmunity.
Determinants of systemic manifestations of food allergy

J Allergy Clin Immunol 2000 Nov;106(5 Suppl):S251-7
Sicherer SH . Elliot and Roslyn Jaffe Food Allergy Institute, Division of Allergy and Immunology, Department of Pediatrics, Mount Sinai School of Medicine, New York, NY, USA.

The myriad of systemic manifestations induced by food hypersensitivity responses is testament to the ability of localized exposure to foods in the gastrointestinal tract to result in symptoms in distal target organs. Cow's milk protein, for example, may induce hives (urticaria), atopic dermatitis, isolated gastrointestinal symptoms, or severe generalized anaphylaxis in different individuals or in the same person at different times. These diverse manifestations are the result of complex interactions among the causal food protein, gut, immune system, and target organs. The dynamic state of these interactions is demonstrated by the development of food tolerance in most subjects and by the ability to experience the development of new allergies in some subjects. This review explores the variety of clinical manifestations of food hypersensitivity disorders in the context of the question: What determines the local or systemic expression of food allergy in a given individual at a particular time? Evidence is provided for both systemic and local immune activation. The role of food-protein chemistry, absorption and processing of ingested allergen, immune responses (type, degree, and specificity), and target organ hyperreactivity are considered as determinants in the expression of food allergic disorders.

Presentations of food allergy

Ann Allergy Asthma Immunol 2001 Apr;86(4):414-20
Bahna SL  Division of Allergy and Immunology, University of South Florida/All Children's Hospital, Saint Petersburg 33701, USA. bahnas@allkids.org.

OBJECTIVE: This presentation is designed to critically review information on presentations of food hypersensitivity reactions that may be considered unusual regarding the source or nature of allergen, route of exposure, or clinical manifestation. DATA SOURCES: Information has been gathered primarily through a thorough search of the English literature relevant to human subjects. Some clinical cases were also included from the author's own clinical experience. STUDY SELECTION: Information summarized here was critically selected on the basis of proven or acceptable scientific validity. RESULTS: The findings indicate that food allergy presentation can be unusual in three main aspects. First, the offending allergen may not be the obvious food that was ingested or be a food protein incorporated in a nonfood product. Second, systemic reactions can be provoked by very minute quantities of food allergens that may even get access through noningestant routes, eg, inhalation, odor, skin contact, or mucous membrane contact. Third, the clinical manifestations are not limited to the few gastrointestinal, cutaneous, and respiratory symptoms with which we are generally familiar. CONCLUSIONS: The extent of food allergy presentation is more than has been generally realized. Our awareness of such unusual presentations adds new knowledge and should
prompt our interest in carefully evaluating patients with obscure allergic reactions for possible food allergy.

**What makes a food protein an allergen?**

*Curr Allergy Asthma Rep 2004 Jan;4(1):43-6  (ISSN: 1529-7322)*

Bannon GA

Food allergens are almost always proteins, but not all food proteins are allergens. This one statement sums up the purpose of this article, defining the difference between an innocuous food protein and a food allergen. The simplest answer is that a food allergen has the ability to first elicit an IgE response, and then, on subsequent exposures, to elicit a clinical response to the same or similar protein. However, this simplistic answer avoids the more complex issues of defining the biochemical characteristics that allow a food protein to survive the extremes of food processing, escape the digestive enzymes of the human gastrointestinal tract, and interact with the immune system. More than 700 allergen sequences have been identified from food and nonfood sources. However, despite increasing knowledge of the structure and amino acid sequences of the identified allergens, only a few biochemical characteristics can be associated with food allergens. Food allergen characteristics, including abundance of the protein in the food; multiple, linear IgE binding epitopes; resistance of the protein to digestion and processing; and allergen structure are discussed, and the possible reasons they predispose some food proteins to become allergens are suggested.

**Adverse reactions to foods.**

*Med Clin North Am. 2006; 90(1):97-127 (ISSN: 0025-7125)*

Nowak-Wegrzy A; Sampson HA

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Food allergy encompasses a variety of immune-mediated adverse reactions to foods. IgE-mediated, cell-mediated, and mixed-mechanism food allergy disorders are recognized. Over the past 2 decades, the prevalence of food allergy doubled and its phenotypic expression increased in Westernized societies. Major food allergens have been identified for many common foods. Laboratory diagnosis of food allergy relies heavily on the detection of food-specific IgE antibodies, but novel approaches include tests for T-cell-mediated disorders and tests for prediction of tolerance. OFC remains the diagnostic standard for food allergy. Management of food allergy focuses on avoidance of the offending foods, nutritional support, and prompt recognition and treatment of acute food allergic reactions. Anti-IgE monoclonal antibody is the first potential therapy for food allergy that is under-going testing in clinical trials.
Severe food anaphylaxis:

107 cases registered in 2002 by the Allergy Vigilance Network.

*Allerg Immunol (Paris)* 2004 Feb;36(2):46-51  (ISSN: 0397-9148)

Moneret-Vautrin DA; Kanny G; Morisset M; Rance F; Fardeau MF; Beaudouin E

**BACKGROUND:** The prevalence of food allergies increases, relating to diet modifications. The consumption of new foods--exotic foods or foods originally used for animal feed, new proteins, neo allergens due to the use of new technologies and soon, Genetically Modified Foods--are in the spotlight. **OBJECTIVE:** It is essential to develop a system of food allergy vigilance encompassing the full range of foods being consumed. Understanding this imperative leads logically to the suggestion of developing an allergy vigilance network taking advantage of the ongoing experience of allergists "on the ground". **METHODS:** The French Allergy Vigilance Network is subscribed to by 302 allergologists (267 of whom are French). The aims of the Network are to record cases of severe anaphylaxis, to establish an epidemiological data bank from prospective multicenter studies, and to monitor the allergic risk from novel foods. **RESULTS:** In 2002, 107 cases of severe anaphylaxis were recorded: anaphylactic shock--59.8% (one fatal), systemic reaction--18.7%, laryngeal angio-edema--15.9%, acute severe asthma--5.6% (one fatal). The main allergens identified were peanuts, nuts, shellfish, lupine flour and wheat flour. Action has been taken as a result: information by industry on inadequate labeling, withdrawal of wrongly labeled batches, and university hospital centers have been encouraged to establish the allergenic safety of their catering services. **CONCLUSION:** Setting up such a network in other countries would lead to a significant advance in knowledge of the peculiarities of allergies.

Food allergy, the hidden culprit.


Food is frequently the trigger of commonly encountered primary care allergic problems. This paper includes a review of the prevalence, immunology and pathophysiology, manifestations, and factors that influence the development of food allergy. The focus is on the delayed or cyclic reaction. History and associated physical findings are identified. Diagnosis and recommendations for management of the disease process, including lifestyle impact, are discussed.

Use of a chemically defined hypoallergenic diet (Vivonex) in the patients with suspected food allergy

Author Dockhorn RJ; Smith TC  Source *Ann Allergy*, 1981 Oct, 47:4, 264-6

The use of a hypoallergenic diet was evaluated in patients suspected of food allergy/intolerance. Symptom scores for one week of regular diet were compared with symptom scores while taking Vivonex. Results indicate that patients had fewer symptoms while on Vivonex than during the preceding week of normal diet.


Review of the atopic diseases suggests a redefinition of the term "atopy" is indicated to reflect new information that has become available during the 60 years since the term was introduced. Atopy may be viewed as a manifestation of a still undefined defect. It is characterized by certain clinical findings and frequently by derangement of the immune and autonomic nervous systems. The atopic diseases are a group of seemingly unrelated conditions—eczema, asthma, rhinitis, hypertrophic sinusitis, and perhaps vernal conjunctivitis and migraine—which cluster in individuals and families. In the respiratory tract and eye, eosinophils in the tissues and secretions are characteristic and are not dependent on the presence of immediate hypersensitivity. Symptoms suggestive of basophil and mast cell mediator release are common to all the atopic diseases, and there is some evidence that nonimmunologic mediator release is enhanced in atopic patients. In the most clearly defined atopic diseases, eczema and asthma, approximately 80% of patients have an increased IgE response to normal environmental allergens. Accompanying and perhaps underlying these enhanced IgE responses are deficiencies of T cell numbers and function particularly in the suppressor T lymphocytes. Evidence exists that decreased beta-2-adrenergic and increased cholinergic and alpha-adrenergic responsiveness accompany and perhaps underlies the atopic diseases irrespective of the presence or absence of allergy.

Multiple food allergies.

Author Speer F Source Ann Allergy, 1975 Feb, 34:2, 71-6

This paper is devoted to a study of multiple food allergy, here defined as sensitivity to three or more foods. The purpose of the study is to report findings obtained from a study of 250 private patients and to show what type of persons develop this condition, how it affects them, and what their common allergens are. It was found that multiple food allergy occurs in both sexes and at all ages but is more common in boys than in girls and more common in women then in men. The clinical manifestations were much like those caused by the more familiar inhalant allergy but with a much more widespread constitutional disturbance. The great majority of patients (86%) also reacted to such air-borne allergens as molds, pollens, house dust, and animal epithelials. This indicates that food allergy and inhalant allergy are fundamentally the same phenomenon. The common food allergens were such everyday foods as milk, chocolate, corn, egg, tomato, peanut, and citrus fruits.

Specific adaptation.

Author Randolph TG Ann Allergy, 1978 May, 40:5, 333-45

In this paper the key to the diagnosis, treatment and prophylaxis of chronic illnesses based on individual susceptibility to foods, drugs, food-drug combinations and environmental chemicals is discussed thoroughly.
Immunology of delayed food allergy.

Author Breneman JC
Address Western Michigan University, Galesburg, USA.
Source Otolaryngol Head Neck Surg, 113: 6, 1995 Dec, 702-4

Abstract Studies here and abroad are stockpiling evidence that immunoglobulin E explains only a small part of food allergy. Involvement of the entire immune system is evident if the more prevalent delayed-type food allergy is to be explained. To adequately diagnose food hypersensitivity a testing technique must be used that identifies delayed food allergy, such as the patch test here described, along with a test that diagnoses immediate immunoglobulin E-mediated food allergy.

Chemically defined diet in the diagnosis of food sensitivities

Author Hughes EC
Source Ann Allergy, 1978 Jun, 40:6, 393-8

A chemically defined diet of low allergenicity was used to provide complete nutritional support for a week in a referred group of 27 patients. Food-sensitive patients remitted 70% of their allergy symptoms, supporting a diagnosis of dominant food etiology. For those the diet was continued while selected foods were orally challenged. Safe diets were thus established in about three weeks of largely patient-executed effort. Patients without remission were given concentrated attention toward establishing other etiologies. Remission was thus achieved in 85% of the cases.

Prevalence and severity of food allergy--need for control.

Author Hourihane JO
Address Department of Immunobiology, Institute of Child Health and Great Ormond Street Hospital, London, UK.
Source Allergy, 1998, 53:46 Suppl, 84-8

Abstract Food allergy is an increasingly recognized manifestation of atopy. Patient and public awareness of food allergy is also increasing. Justifiable demands are being made for better medical guidance of the practice of food labelling for industry and catering businesses. Such advice must bear in mind the relative frequency and severity of allergies to certain foods. Some commonly allergenic foods (milk, egg, soya, wheat) are staple components of the diets of populations, used widely in prepared foods. The frequency of the allergies to these foods and their widespread uses means they and their derivatives must be declared on food labels. Less commonly used foods such as fish, shellfish, peanut, and tree nuts demand declaration due to the severity of reactions induced in the admittedly more rare, but increasingly common, sufferers of these allergies. Reactions to more unusual foods are increasingly being identified, and the "minimum" list is likely to be extended in the future.

Joint complaints and food allergic disorders.

Author Denman AM; Mitchell B; Ansell BM
Source Ann Allergy, 1983 Aug, 51:2 Pt 2, 260-3
An important problem in investigating food allergic diseases is to adduce evidence that specific diseases of unknown cause may be attributable to food allergy. Polyarthritis is a good example of the difficulties involved in such studies because it is a very heterogeneous disorder and generalizations about aetiology are unlikely to prove correct. We have observed transient synovitis in both children and adults which is caused by food allergy. On the other hand we have not been able to show that food allergy demonstrably contributes to juvenile chronic arthritis or to rheumatoid arthritis in adults. The arthritis associated with inflammatory bowel disease undoubtedly responds to elemental diets and the mechanism of this remission warrants further investigation.

**Ear Nose and Throat**

**Mechanisms in adverse reactions to food. The mouth and pharynx.**

Author Pastorello EA; Incorvaia C; Ortolani C
Address Istituto di Medicina Interna Malattie Infettive e Immunopatologia Universita degli Studi di Milano, Italy.

Source Allergy, 50: 20 Suppl, 1995, 40-5

Symptoms appear immediately at the site of contact with the food when a susceptible allergic patients eats the offending food. Allergy to fresh fruits and vegetables, associated with all kinds of pollinosis, is the more frequent cause of Oral Allergy Syndrome.

**Allergy in Ménière's disease, fluctuating hearing loss**

Author Endicott JN; Stucker FJ
Source Laryngoscope, 1977 Oct, 87:10 Pt 1, 1650-7

Several clinical reports suggest allergy as a causative or associated factor in the etiology of Ménière's Disease or endolymphatic hydrops. The A.A.O.O. subcommittee reported in 1972 its criteria for a therapeutic improvement in Ménière's Disease. This important report allows for clinical studies to proceed in a scientific manner using the subcommittee's criteria to evaluate the results. In an ongoing study utilizing a double-blind crossover technique, fourteen Ménière's patients have been evaluated for allergies utilizing the Rinkle and Lee techniques for inhalent and food allergies. Several cases directly relate symptoms to specific food ingestion and were given challenge food tests.

**The role of allergy in fluctuating hearing loss.**

Author Powers WH
Source Otolaryngol Clin North Am, 1975 Jun, 8:2, 493-500

A method for the selection of patients with fluctuating hearing loss and Meniere's disease for allergic evaluation is presented. An approach to the diagnosis and treatment of these
problems is reviewed. Seventy-two patients with Meniere's disease who met the criteria of the American Academy Subcommittee on Equilibrium and Its Measurements were evaluated. Thirty-two per cent of the 62 patients receiving allergy therapy or allergy and metabolic therapy responded to treatment. Half required a combination of metabolic and allergy management, whereas the other half responded to allergy therapy alone.
Common manifestations of cow's milk allergy in children.


Abstract  Cow's milk allergy was diagnosed in 79 patients, all of whom had signs and symptoms of allergies other than milk intolerance. In addition to difficulties with infant feeding and diarrhoea, clinical features included constipation, vomiting, intestinal colic, growth retardation, and psychological disturbance, as well as eczema and asthma. All were reversible after milk withdrawal, which suggests that the allergic basis of such symptoms may have been underestimated. In most cases, one or both parents were atopic and the child had been bottle-fed from birth. There were no breast-fed children of non-atopic parents in this series.

Role of food allergy in serous otitis media

Author Nsouli TM; Nsouli SM; Linde RE; O'Mara F; Scanlon RT; Bellanti JA
Address Department of Pediatrics, Georgetown University School of Medicine, Washington, DC. Source Ann Allergy, 73: 3, 1994 Sep, 215-9

BACKGROUND. The relationship between IgE-mediated hypersensitivity and recurrent serous otitis media has not been completely established. OBJECTIVE. The purpose of the present study was to examine the prevalence of food allergy in patients with recurrent serous otitis media. METHODS. A total of 104 unselected patients (age range 1.5 to 9 years, mean 4.6 years) with recurrent serous otitis media were evaluated for food allergy by means of skin prick testing, specific IgE tests, and food challenge. Patients who were allergic to food(s) underwent an exclusion diet of the specific offending food(s) for a period of 16 weeks. A non-double blinded food challenge was performed with the suspected offending food(s). Their middle ear effusion was monitored and assessed by tympanometry (Welch Allyn Model 23600) during the pre-elimination, elimination and challenge diet phases. RESULTS. There was a significant statistical association, by chi-square analysis, between food allergy and recurrent serous otitis media in 81/104 patients (78%). The elimination diet led to a significant amelioration of serous otitis media in 70/81 (86%) patients as assessed by clinical evaluation and tympanometry. The challenge diet with the suspected offending food(s) provoked a recurrence of serous otitis media in 66/70 patients (94%). CONCLUSIONS. The possibility of food allergy should be considered in all pediatric patients with recurrent serous otitis media and a diligent search for the putative food allergen made for proper diagnostic and therapeutic intervention.
Prevalence of allergy in Meniere's disease.

Author Derebery MJ; Berliner KI
Address House Ear Clinic and House Ear Institute.
Source Otolaryngol Head Neck Surg, 2000 Jul, 123:1 Pt 1, 69-75

OBJECTIVES: The goal of this study was to determine the prevalence of allergy in a population of patients with Meniere's disease. METHODS: A survey was mailed to all patients with Meniere's disease seen at our institution from 1994 to July 1998 (n = 1490). As a control group, 172 patients with otologic problems other than Meniere's disease completed the same survey. RESULTS: Of 734 respondents with Meniere's disease, 59.2% reported possible airborne allergy, 40.3% had or suspected food allergies, and 37% had had confirmatory skin or in vitro tests for allergy. These prevalence rates were significantly higher than those found in the control group, of which 42.7% reported having or suspecting airborne allergies and 25% had or suspected food allergies (differences all significant at P< or =0.005). CONCLUSION: The prevalence of allergy appears to be much higher in patients with Meniere's disease than in the general population or the population of patients visiting an otologic clinic for other symptoms.

Allergic management of Meniere's disease

Author Derebery MJ
Address House Ear Clinic and House Ear Institute, Los Angeles, CA 90057, USA.

The effect of allergy immunotherapy and elimination of suspected food allergens was evaluated in patients with Meniere's disease. A total of 137 patients with Meniere's disease for whom allergy treatment had been recommended were identified and were mailed and returned a symptoms questionnaire. One hundred thirteen had received allergy treatment; 24 did not have treatment and served as a control group. Information regarding history, signs and symptoms, allergy test results, and audiologic data were obtained by chart review. The 113 patients treated with desensitization and diet showed a significant improvement from pretreatment to posttreatment in both allergy and Meniere's symptoms. Ratings of frequency, severity, and interference with everyday activities of their Meniere's symptoms also appeared better after allergy treatment than ratings from the control group of untreated patients. Vertigo control results, by use of the American Academy of Otolaryngology-Head and Neck Surgery classification, categorized 47.9% as class A or B. Hearing was stable or improved in 61.4%. Patients with Meniere's disease can show improvement in their symptoms of tinnitus and vertigo when receiving specific allergy therapy. The inner ear may be the target, directly or indirectly, of an allergic reaction.
Prevention and management of food allergy.

Author Businco L; Bruno G; Giampietro PG
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The phenotypic expression and natural history of food allergy vary widely according to the patient's age, disease presentation and type of offending food. Prevention of food allergy might be achieved by altering the dietary factors responsible for the sensitization and phenotypic expression of the disease. Owing to the peculiarity of the atopic status, a minute amount of allergens can trigger both sensitization and symptoms in atopic individuals. The oral dose of beta-lactoglobulin causing sensitization can be estimated to be between 1 ng and several milligrams. In food allergy, sensitization and treatment are allergen specific; therefore, for primary prevention (avoiding sensitization) and secondary prevention of food allergy (avoiding symptoms in an already sensitized subject), a product without immunogenic and allergenic epitopes should be given in each case. Babies of atopic parents are particularly prone to develop food allergy and for this reason they are called high-risk babies. Cow's milk is the most commonly offending food in both gastrointestinal and cutaneous manifestations. Cow's milk proteins are potent allergens and around 2.5% of infants experience cow's milk allergy in the first years of life. The major risk factors for cow's milk allergy are positive family history of atopy and early exposure to cow's milk proteins. Hydrolysate formulae have been developed for the purpose of reducing the allergenicity of cow's milk proteins. More recently, partially and extensively hydrolysed formulae have also been used for feeding babies with a high risk of atopy for the prevention of cow's milk allergy. However, according to the results of a recent randomized controlled study, only an extensively hydrolysated formula, and not a partially hydrolysated formula, significantly decreased the prevalence of cow's milk allergy.

Late onset reactions to food challenge, low serum interleukin-10 in patients with atopic dermatitis and food allergy.

Author S?as Y; Kekki OM; Isolauri E Address Department of Paediatrics, University of Turku, Turku; Department of Dermatology, University of Tampere Medical School, Tampere, Finland.
Source Clin Exp Allergy, 2000 Aug, 30:8, 1121-8

BACKGROUND: Aberrant cytokine production in vitro has been associated with atopic disease. No study has as yet been made of the circulating cytokine profiles in atopic patients with food allergy in response to oral allergen challenge. OBJECTIVE: To assess the effect of oral allergen challenge on the serum cytokine concentrations in patients with atopic dermatitis and food allergy. METHODS: Serum concentrations of interleukin (IL)-10, transforming growth factor beta 1, IL-1ra, IL-6, IL-5, IL-4 and interferon (IFN)-gamma were measured before and after double-blind, placebo-controlled food challenges (DBPCFC) (n = 73). Before DBPCFC, combined skin prick and patch testing was performed for cow milk, egg, soybean and cereals, and production of IFNgamma, IL-4, IL-10 and tumour necrosis factor alpha (TNFalpha) was determined in supernatants of cultures of peripheral blood mononuclear cells (PBMCs) stimulated by cow milk. RESULTS: The oral food challenge triggered immediate onset exanthematous reactions in 22 cases and late onset eczematous reactions in 29. The late-reacting cases had more
positive skin patch test and negative skin prick test reactivities with allergenic food, and they had lower serum IL10 concentrations than immediate-reacting cases. In challenge-positive cases, IL-10 concentrations increased from 2.9 (0.1-5.04) pg/mL to 3.9 (1.2-8.3) pg/mL in response to DBPCFC, $P = 0.05$, median (interquartile ranges), but not in those tolerant to cow milk. PBMCs of patients with cow milk allergy but not of those tolerant to cow milk generated TNFalpha in response to cow milk in vitro. CONCLUSION: These results indicate that oral allergen challenge in atopic patients with food allergy triggers systemic release of IL-10. Patients with late onset reactions were found to have lower serum IL-10 concentrations than their immediate-reacting counterparts. Considering that IL-10 is an inhibitory cytokine of delayed-type hypersensitivity, low IL-10 in late-reacting patients may explain the high frequency of their positive skin patch tests combined with negative skin prick tests.

Infants & Children

Alterations in the gut microbiotas of children with food sensitization in early life

Chien-Chang Chen et al. Pediatric Allergy and Immunology published online: 21 JAN 2016

We hypothesized that food sensitization (FS) in children could be linked to specific gut microbiota. The aim of our study is to quantify and evaluate differences in gut microbiota composition between children with FS and healthy controls. A case–control study of 23 children with FS and 22 healthy children was performed. Individual microbial diversity and composition were analyzed via parallel barcoded 454 pyrosequencing targeting the 16S rRNA gene hypervariable V3–V5 regions. The children with FS exhibited lower diversity of both the total microbiota ($p = 0.01$) and the bacterial phylum Bacteroidetes ($p = 0.02$). In these children, the number of Bacteroidetes bacteria was significantly decreased and that of Firmicutes were significantly increased compared with the healthy children. At the genus level, we observed significant increases in the numbers of Sphingomonas, Sutterella, Bifidobacterium, Collinsella, Clostridium sensu stricto, Clostridium IV, Enterococcus, Lactobacillus, Roseburia, Faecalibacterium, Ruminococcus, Subdoligranulum, and Akkermansia in the FS group. We also found significant decreases in the numbers of Bacteroides, Parabacteroides, Prevotella, Alistipes, Streptococcus, and Veillonella in this group. Furthermore, linear discriminant analysis (LDA) coupled with effect size measurements revealed the most differentially abundant taxa (increased abundances of Clostridium IV and Subdoligranulum and decreased abundances of Bacteroides and Veillonella), which could be used to identify FS.

Conclusions
Our results showed that FS is associated with compositional changes in the gut microbiota. These findings could be useful for developing strategies to control the development of FS or atopy by modifying the gut microbiota.
Dietary Intervention in Infancy and Later Signs of Beta-Cell Autoimmunity


Early exposure to complex dietary proteins may increase the risk of beta-cell autoimmunity and type 1 diabetes in children with genetic susceptibility. We tested the hypothesis that supplementing breast milk with highly hydrolyzed milk formula would decrease the cumulative incidence of diabetes-associated autoantibodies in such children. In this double-blind, randomized trial, we assigned 230 infants with HLA-conferred susceptibility to type 1 diabetes and at least one family member with type 1 diabetes to receive either a casein hydrolysate formula or a conventional, cow’s-milk-based formula (control) whenever breast milk was not available during the first 6 to 8 months of life. Autoantibodies to insulin, glutamic acid decarboxylase (GAD), the insulinoma-associated 2 molecule (IA-2), and zinc transporter 8 were analyzed with the use of radiobinding assays, and islet-cell antibodies were analyzed with the use of immunofluorescence, during a median observation period of 10 years (mean, 7.5). The children were monitored for incident type 1 diabetes until they were 10 years of age.

Results: The unadjusted hazard ratio for positivity for one or more autoantibodies in the casein hydrolysate group, as compared with the control group, was 0.54 (95% confidence interval [CI], 0.29 to 0.95), and the hazard ratio adjusted for an observed difference in the duration of exposure to the study formula was 0.51 (95% CI, 0.28 to 0.91). The unadjusted hazard ratio for positivity for two or more autoantibodies was 0.52 (95% CI, 0.21 to 1.17), and the adjusted hazard ratio was 0.47 (95% CI, 0.19 to 1.07). The rate of reported adverse events was similar in the two groups.

Conclusions

Dietary intervention during infancy appears to have a long-lasting effect on markers of beta-cell autoimmunity — markers that may reflect an autoimmune process leading to type 1 diabetes. (Funded by the European Commission and others; ClinicalTrials.gov number, NCT00570102.)
Clinical spectrum of food allergy in children.

Author Hill DJ; Hosking CS; Heine RG

The prevalence of atopic diseases is increasing worldwide for reasons that are not clear. Food allergies are the earliest manifestations of atopy. This review defines the foods most commonly involved in allergic reactions and identifies an emerging group of syndromes in which food allergy is involved. A study of the frequency of food allergies in Australia and South-East Asia has recently shown that egg, cow's milk and peanut are the most common food allergens in Australia, but there were divergent results from different regions of South-East Asia. It is not clear whether the differences in reactivity to foods are due to genetic or cultural factors, but the findings raise the possibility that genetic susceptibility to food allergy may operate at the T-cell level modulated by the major histocompatibility complex. The Melbourne Milk Allergy Study defined a wide range of clinical symptoms and syndromes that could be reproduced by dietary challenge. A subsequent analysis of the infants with hypersensitivity to cow's milk and other multiple food proteins identified a new syndrome, multiple food protein intolerance of infancy. Food challenges demonstrated reactions developing slowly days after commencement of low-allergen soy formula or extensively hydrolysed formula. Follow-up at the age of 3 years showed that most children with this disorder tolerated most foods apart from cow's milk, egg and peanut. Atopic dermatitis affects about 18% of infants in the first 2 years of life. In a community-based study we have shown a very strong association (RR 3.5) between atopic dermatitis and infants with immunoglobulin E allergy to cow's milk, egg or peanut. Family studies on these infants have shown a link between atopic dermatitis and the genomic region 5q31 adjacent to the interleukin-4 gene cluster. Infantile colic (distress) affects 15-40% of infants in the first 4 months of life. Many theories of causation have been proposed, but a study from our centre showed that dietary modification, particularly that of breastfeeding mothers whose infants present with colic before the age of 6 weeks, alleviated symptoms. Colic associated with vomiting has been attributed to gastro-oesophageal reflux (GOR). This has been considered primarily a motility disorder, but a secondary form resulting from food protein intolerance has been described recently. We have also recently identified a group of infants with distressed behaviour attributed to GOR who have failed to respond to H2-receptor antagonists, prokinetic agents and multiple formula changes. Symptoms resolved on commencement of an elemental amino acid-based formula. In two-thirds of the patients, symptoms relapsed when challenged with low-allergen soy formula or extensively hydrolysed formula. We propose that a period of food protein intolerance is a part of the normal development of the immune system as it encounters common dietary proteins in infancy and early childhood. Future targets for research are development of appropriate dietary and management strategies for these entities and identification of genetic markers for these disorders.
Food allergy: two common types as seen in breast and formula fed babies.

Author Gerrard JW; Shenassa M
Source Ann Allergy, 1983 Jun, 50:6, 375-9

Cow’s milk allergy can develop in both breast and formula fed babies. The allergy developing in breast fed babies is triggered by trace amounts of antigen, tends to cause severe reactions and may persist for several years. The allergy developing in formula fed babies is triggered by large amounts of antigen, is not associated with either positive prick tests or with anaphylactic reactions and often subsides spontaneously.

Children with allergic rhinitis and/or bronchial asthma treated with elimination diet

Author Ogle KA; Bullock JD Source Ann Allergy, 1980 May, 44:5, 273

Three hundred and twenty-two children under one year of age with respiratory allergy and negative inhalant skin tests were placed on a six-week hypoallergenic diet consisting of Meat Base Formula, beef, carrots, broccoli and apricots. Two hundred and ninety-two or 91% showed significant improvement of respiratory symptom scores during the trial. On subsequent oral food challenge symptoms were reproduced in only 51% of the children. Milk greater than egg greater than chocolate greater than soy greater than legumes greater than cereals were most commonly involved. Skin tests with food allergens rarely correlated with challenge results. One hundred and seventeen or 40% later developed inhalant respiratory allergy. Only 6% of the children studied five years or longer showed any evidence of food sensitivity. The data suggest (1) infants with respiratory allergy will respond to hypoallergenic diet, (2) symptoms may or may not reappear on food challenge, (3) food allergy tends to be "outgrown" and (4) many "grow into" inhalant respiratory allergy.

Prevention of atopic diseases in high risk babies

Author Bruno G; Milita O; Ferrara M; Nisini R; Cantani A; Businco L Address Department of Pediatrics, University of Roma La Sapienza, Italy. Source Allergy Proc, 14: 3, 1993 May-Jun, 181-6; discussion 186-7

Several studies have demonstrated that dietary and environmental manipulations in the first months of life have a protective effect on the development of allergic diseases in babies "at risk" of atopy. We have prospectively followed up 174 "high risk" infants who underwent dietary and environmental manipulations, such as exclusive breast-feeding for the first 6 months of life, supplemented if necessary with soy-protein formula (Isomil, Abbott), delayed weaning beyond the 6th month of life, and rigorous environmental manipulations for the elimination of house-dust mite and passive smoking. The low prevalence of atopic disease (10%) and the trivial course of the allergic manifestations in this "at risk" population confirm the effectiveness of this preventive program. Moreover, this study demonstrates that the incidence of atopic dermatitis peaks at 6 months, and decreases until it disappears. Food allergy appears only at 6 months and may disappear later. The incidence of asthma peaks at 6 and 36 months and decreases at low levels in the intervals. Allergic rhinitis develops not sooner than 36 months.
**Multiple food allergy: a possible diagnosis in breastfed infants.**

Author de Boissieu D; Matarazzo P; Rocchiccioli F; Dupont C Address Unit de Gastroentérologie Pédiatrique, Hôpital Saint Vincent de Paul, Paris, France.
Source Acta Paediatr, 1997 Oct, 86:10, 1042-6

Six infants suspected of food allergy during breastfeeding were evaluated using prick tests, total IgE, RASTs and intestinal permeability measurements during fast and provocation with mother's milk. An elimination diet was undertaken in mothers, removing first cow's milk protein (CMP), then, when inefficient, all foods suspected on the clinical history or a positive prick test in the child, followed by oral challenges in mother's diet with the corresponding food. The sole CMP-free diet in mothers always proved insufficient. In four, an additional diet excluding two to three other foods cleared the symptoms. Oral provocations in mother's diet with those foods were positive in all. In two, mothers turned down a diet excluding more than four foods, symptoms cleared while feeding the child with an extensively hydrolysed formula, whereas challenges with mother's milk induced immediate reactions. Intestinal permeability was altered during provocation tests with mother's milk sampled before maternal diet. Food allergy during breastfeeding may be due to multiple foods and the inefficacy of the sole CMP elimination in mothers does not rule out food sensitization.

**Occurrence of the major food allergen, ovomucoid, in human breast milk as an immune complex**

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Research Institute for Food Science, Kyoto University, Uji, Japan.

The major food allergen, ovomucoid (molecular weight of 28 kDa) could be detected in 12 of 37 human breast milk samples by using three types of enzyme-linked immunosorbent assay. By gel-filtration, ovomucoid in breast milk was only eluted in the fractions corresponding to a molecular weight of about 450 kDa, suggesting its occurrence as an immune complex with IgA. In fact, almost the same elution profile as that for ovomucoid was obtained for its immune complex with IgA by gel-filtration.
Food Protein-Induced Enterocolitis Syndrome (FPIES) is a symptom complex of severe vomiting and diarrhea caused by non-IgE-mediated allergy to cow's milk and/or soy in infants. Symptoms typically begin in the first month of life in association with failure to thrive and may progress to acidemia and methemoglobinemia. Symptoms resolve after the causal protein (usually sensitivity to both cow's milk and soy) is removed from the diet. Symptoms recur approximately 2 hours after reintroduction of the protein along with a coincident elevation of the peripheral blood polymorphonuclear leukocyte count. The sensitivity is usually outgrown by 3 years of age. The purpose of this review is to delineate the characteristic clinical features, diagnosis and management of FPIES. Furthermore, infantile FPIES will be discussed in relation to clinical syndromes that share features with it ("atypical FPIES") and other food-allergic disorders affecting the gastrointestinal tract.

Egg allergy predicts respiratory allergic disease

Sensitization to hen's egg early in life has been proposed as a predictor for respiratory allergic disease during childhood. However, symptomatic egg allergy in infancy has not been studied in this context. In 1989, a cohort of consecutive births was recruited. Data on family history of atopy and environmental factors were collected. At 4 years of age, 1,218 children were seen of whom 981 were skin-prick tested with a range of food and aero-allergens. Of the 1,218 children, 29 (2.4%) had suffered symptomatic egg allergy (20 during infancy). Egg allergy in infancy was associated with increased respiratory (asthma, rhinitis) allergic disease (odds ratio [OR] 5.0, 95% confidence intervals [CI] 1.1-22.3; p < 0.05) at 4 years of age, with a positive predictive value (PPV) of 55.0%. The addition of infantile eczema to egg allergy increased the PPV to 80% whereas the addition of family history of atopy had no effect. Egg allergy also increased aero-allergen sensitization (OR 6.1, CI 1.1-37.5; PPV 61.1%; p < 0.05). As a predictor for respiratory allergic disease and aeroallergen sensitization, it carried a high specificity but poor sensitivity. Hence, egg allergy in infancy, especially when coexisting with eczema, increases respiratory allergic symptoms and aero-allergen sensitization in early childhood.
**Hydrolysed cow's milk formula improves symptoms of gastroesophageal reflux**

and reduces the gastric emptying time in infants.

Allergol Immunopathol (Madr) 2002 Jan-Feb;30(1):36-41 (ISSN: 0301-0546)

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BACKGROUND: About 20 % of infants fed with breast-milk substitutes suffer from Gastro Esophageal Reflux (GER) and 1/3 of them also show Cow's Milk Allergy (CMA) symptoms. METHODS: We planned this study to assess by dynamic echography the usefulness of an Extensively Hydrolysed Cow's Milk Formula (eHF) in infants suffering from GER. Ten infants showing GER symptoms and 10 normal babies, all fed with breast-milk substitutes, were enrolled. Clinical symptom scores related to GER were assessed for one week. The Gastric Emptying Time (GET) was determined by means of dynamic echography after feeding with cow's milk-derived formulae and again after a week feeding with eHF in subjects previously showing GER symptoms. RESULTS: All infants with a clinical diagnosis for GER showed an abnormally high average GET in comparison to normal subjects (205 vs 124 min, p = 0.000). Switching to the eHF led to a significant clinical improvement (p = 0.0039) especially in babies skin-test and RAST positive to cow's milk, and to a significant decrease toward the normal value of the GET (167 min, p < 0.001). CONCLUSIONS: The eHF tested improves GER symptoms in infants suffering from this disease. Our experience confirms and supports the use of dynamic echography as a reliable, simple, and non-invasive diagnostic method for infants with an increased GET associated with clinical symptoms of GER.

**Gastrointestinal occult hemorrhage and gastroduodenitis in cow's milk protein intolerance.**


Coello-Ramirez P; Larrosa-Haro A

We are reporting on four infants with cow's milk protein intolerance who presented with hypochromic anemia and occult gastrointestinal hemorrhage. Esophagogastroduodenoscopy revealed erosive gastritis or gastroduodenitis in all cases. Management with a cow's milk-free diet led to a favorable clinical and hematological outcome; the endoscopic inflammatory image disappeared after the cow's milk-free diet trial. Challenge with cow's milk led to gastrointestinal symptoms and to impaired D-xylene absorption. The data presented suggest that some patients with cow's milk intolerance may have gastroduodenitis resulting in occult gastrointestinal hemorrhage and hypochromic anemia.
Gastroesophageal reflux disease, colic and constipation in infants with food allergy.


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This review assesses the role of food allergy in the pathophysiology of gastroesophageal reflux disease, colic and constipation in infancy. RECENT FINDINGS: Frequent regurgitation, persistent crying and constipation are common clinical problems in infancy. A subgroup of infants with these conditions may respond to hypoallergenic diets, but only few randomized clinical trials have been conducted. Skin prick testing and food-specific antibody levels are usually not elevated in these infants, whereas atopy patch testing may diagnostic. The mechanisms by which cow's milk and other food allergens induce gastrointestinal motility disorders are not understood. Apart from cell-mediated reactions, non-immunological effects of food constituents on gastrointestinal motility and gut microbiota may be involved in the pathogenesis. In the absence of reliable diagnostic tests, dietary elimination and re-challenge are usually required to confirm food allergy. A trial of amino acid-based formula or an oligoantigenic maternal elimination diet may be indicated in infants who have failed conventional medical treatment. SUMMARY: Food allergy may contribute to gastroesophageal reflux disease, colic or constipation in infancy. Infants with these conditions often respond to hypoallergenic formula or a maternal elimination diet. Further research is needed to define the mechanisms and clinical markers of gastrointestinal food allergy in infancy.

Autism Spectrum Disorders and Allergy

Harumi Jyonouchi.: Observation from a Pediatric Allergy/immunology Clinic

IgE-mediated allergic diseases (e.g., allergic rhinoconjunctivitis, atopic asthma and food allergy) are prevalent (up to 30%) in the general population and are increasing in developed countries. In infants and young children, non-IgE-mediated food allergy is also prevalent. In addition to easily recognized organ-specific symptoms, allergic diseases can cause neuropsychiatric symptoms, such as irritability and hyperactivity, in otherwise healthy individuals. This is also likely to occur in children with autism spectrum disorder (ASD). Moreover, the discomfort and pain associated with allergic diseases could aggravate behavioral symptoms in ASD children. Allergic conditions are easily treatable; however, ASD children may be underdiagnosed and/or undertreated for allergic and other common childhood diseases, in part due to their impaired communication skills. Practicing physicians should be aware of the potential impact of allergic diseases on behavioral symptoms and cognitive activity in ASD children. However, they also need to be aware that certain symptoms often attributed to 'allergy' by caregivers may not be immune mediated and should understand that behavioral symptoms can also be affected by many non-IgE-mediated causes.
Autism and Immune-Mediated Disease

Theoharides et al reported:” Autism spectrum disorders (ASDs) affect as many as 1 in 45 children and are characterized by deficits in sociability and communication, as well as stereotypic movements. Many children also show severe anxiety. The lack of distinct pathogenesis and reliable biomarkers hampers the development of effective treatments. Most children with ASD are often prescribed psychotropic medications, primarily risperidone and aripiprazole to reduce disruptive and aggressive behaviors, but these drugs have no effect on the core symptoms of ASD. In fact, recent studies have questioned the benefit of psychotropic agents and have highlighted frequent adverse effects such as weight gain, sedation, tremor, movement disorders and drooling. As a result, there is increased polypharmacy and risk of unwanted drug interactions.

Autoantibodies against brain epitopes in mothers of children with ASD and many such children strongly correlate with allergic symptoms and indicate an aberrant immune response, as well as disruption of the blood–brain barrier (BBB). Recent epidemiological studies have shown a strong statistical correlation between risk for ASD and either maternal or infantile atopic diseases, such as asthma, eczema, food allergies and food intolerance, all of which involve activation of mast cells (MCs). These unique tissue immune cells are located perivascularly in all tissues, including the thalamus and hypothalamus, which regulate emotions. MC-derived inflammatory and vasoactive mediators increase BBB permeability. Expression of the inflammatory molecules interleukin (IL-1β), IL-6, IL-17 and tumor necrosis factor (TNF) is increased in the brain, cerebrospinal fluid and serum of some patients with ASD, while NF-kB is activated in brain samples and stimulated peripheral blood immune cells of other patients of the brain could have great promise in the treatment of ASD. A number of perinatal allergic, genetic, environmental, immune and infectious factors may increase the risk of or contribute to the pathogenesis of ASD. These could act through activation of a unique tissue immune cell, the mast cell (MC). MCs derive from bone marrow progenitors and mature in tissues depending on microenvironmental conditions. In addition to histamine, stimulated MCs secrete other vasoactive and pro-inflammatory mediators such as the preformed kinins and proteases, as well as the de novo synthesized leukotrienes, prostaglandins, chemokines (CCXL8, CCL2), cytokines (interleukin (IL)-4, IL-6, IL-1, tumor necrosis factor (TNF)) and vascular endothelial growth factor (VEGF).

*MCs are not only considered critical for the development of allergic reactions, but also for immunity and inflammation. In fact, many studies have reported that allergic diseases in preschoolers are strongly associated with psychological and behavioral problems. We had proposed that MC-derived mediators could disrupt the blood–brain barrier (BBB) and cause ‘allergy of the brain or ‘focal encephalitis thus contributing to the pathogenesis of ASD. A number of recent reviews have now confirmed and expanded on these findings.

*Allergies and auto-immune diseases have been increasing significantly. Early reports indicated more frequent allergies in ASD children, with food allergies being the most prevalent complaint, often in the absence of elevated serum IgE or positive skin tests. A large epidemiological study of noninstitutionalized children 7-years-old showed that eczema was strongly associated with ASD and attention deficit hyperactivity disorder. Another study of atopic subjects and non-atopic subjects (n=6944) also showed a strong association between atopy and risk of both ASD and attention deficit hyperactivity disorder. A case control study of children and young patients with ASD (n=5565) and controls matched to birth year (1980–2003) and sex reported that
allergies, asthma and autoimmune disorders were diagnosed more frequently, with psoriasis occurring more than twice as often, in ASD patients than controls. An experimental study actually reported neurochemical changes and autistic-like behavior in a mouse model of food allergy. MCs can be activated by fungi, such as Aspergillus fumigatus which triggers IgE-independent MC degranulation and fungal zymosan induces leukotriene production from human MCs. Moreover, MCs can be stimulated by aluminum and mercury. Microglia, the innate brain immune cells, are important during healthy brain development because they may ‘prune’ neural circuits. However, abnormal microglia activation and proliferation could lead to focal inflammation and ‘choking’ of normal synaptic traffic as has been reported in brains of patients with ASD. A recent study of the transcriptomes from 104 human brain cortical tissue samples from patients with ASD identified gene clusters associated with increased microglia activation (M2) and decreased neuronal activity. As a result, microglia are now considered an important component of the pathogenesis of ASD.

“Human microglia express functional CRHR1159 and NTR3 (sortilin), activation of which leads to microglia proliferation.160 NTR3 has been implicated in neuronal viability and function and increased soluble sortilin has been associated with depression, corresponding to elevated levels of BDNF and VEGF. NT can be neurotoxic by facilitating N-Methyl-d-aspartate-induced excitation of cortical neurons. We recently reported that NT stimulates activation and proliferation of human microglia.164 We believe this is the first time that a neuropeptide elevated in ASD is shown to stimulate human microglia that are now believed to play a major role in the pathogenesis of ASD.39, 153, 154 NT can therefore stimulate both microglia and MCs. Severe cow’s milk induced colitis in an exclusively breast-fed neonate.

**Case report and clinical review of cow's milk allergy.**

Clin Pediatr (Phila) 1990 Feb;29(2):77-80 (ISSN: 0009-9228)

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Cow’s milk induced eosinophilic colitis presenting in the first week of life has been reported. The authors describe a 4-day-old female infant who presented with profuse rectal bleeding resulting in a hematocrit fall from 38% to 30% within 8 hr after hospital admission. Sigmoidoscopy revealed colonic mucosa that was red, edematous, and friable, with punctate hemorrhages. Rectal biopsy showed marked eosinophilic infiltration with multifocal hemorrhage. Further history indicated that while the infant had been exclusively breast-fed since birth, the nursing mother had been drinking 4-5 glasses of cow’s milk per day since delivery. Prick puncture skin testing of the infant was positive for cow’s milk protein. A serum radioallergosorbent test (RAST) for cow’s milk protein was positive. The infant’s serum IgE was 1.5 IU/ml. Rectal bleeding resolved when the patient was given a casein hydrolysate formula (Nutramigen, Mead Johnson Nutrition, Evansville, IN), and endoscopy one week later showed improvement, with only scattered areas of erythema, and no friability. We conclude that since the infant was exclusively breast-fed, the milk protein must have passed into the breast milk antigenically intact. Prenatal sensitization probably occurred. Cow’s milk induced allergic colitis should be considered in the differential diagnosis of colitis in breast-fed neonates.
**Allergic colitis presenting in the first day of life**


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Allergic colitis can occur within hours of birth and should be considered in the differential diagnosis of any newborn in whom hematochezia develops. This diagnosis should be considered after excluding infectious and anatomic disorders common to this age group. The diagnosis is supported by the healthy appearance of affected infants and specific proctosigmoidoscopic and histopathologic findings. Infants with allergic colitis usually respond to withdrawal of the offending antigen, by the use of hydrolyzed cow's milk protein formula or more elemental formulas, or if the infant has been breast fed, by the strict removal of the offending antigen from the breast-feeding mother's diet.

**Proctocolitis in breast fed infants: a contribution to differential diagnosis of haematochezia in early childhood.**

Postgrad Med J 2001 Apr;77(906):252-4  (ISSN: 0032-5473)

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Dietary protein induced proctocolitis in exclusively breast fed infants is rarely taken into consideration as a cause of rectal bleeding or blood streaked stool in the neonatal period and early infancy. Eleven babies are presented in whom it is believed that bleeding through the rectum was due to proctocolitis as a result of allergy triggered by cows' milk protein transferred to the infants via the breast milk. Colonoscopy was performed in five infants, revealing benign eosinophilic proctocolitis. Standard treatment was the exclusion of the allergen from the mother's diet. Resolution of visible rectal bleeding took place within 72 to 96 hours after elimination of the offending protein from the mother's diet.

**Food hypersensitivity in children.**

Author James JM; Burks AW Address Arkansas Children's Hospital, Little Rock.

Source Curr Opin Pediatr, 6: 6, 1994 Dec, 661-7

A variety of investigations of food hypersensitivity have been published over the past 18 months. These studies have focused on specific immunopathogenic, clinical, diagnostic, and prophylactic issues directly related to this allergic disorder. Whereas several of the reports have confirmed previous findings, significant pieces of new information have emerged. This review provides a practical summary of these scientific publications specifically related to food allergy.
Food allergy in children with hyperactivity, learning disabilities and/or minimal brain dysfunction.

Author Tryphonas H; Trites R  Source Ann Allergy, 1979 Jan, 42:1, 22-7

Ninety hyperactive children, 22 children with learning disability and eight emotional-inattentive children were tested for allergy to 43 food extracts using the in vitro radioallergosorbent test (RAST). Fifty-two percent of all children exhibited allergy to one or more of the foods tested. Within the hyperactive group a statistically significant association was found between the number of allergies and teachers' (Conners) scores of hyperactivity. This association was statistically significant only in those hyperactive children who also had learning disability and minimal brain dysfunction. A statistically weak association was also found between a small number of children clinically diagnosable as hyperactive and the number of allergies or total allergy scores. A causal relationship between food allergy and a small subgroup of children with a primary diagnosis of hyperactivity is suspected.

Food allergy: the major cause of infantile colitis.

Author Jenkins HR; Pincott JR; Soothill JF; Milla PJ; Harries JT  Source Arch Dis Child, 1984 Apr, 59:4, 326-9

Forty six children presented with colitis between 1977 and 1981, and all 8 of those below the age of 2 years had food allergic colitis which resolved completely after exclusion of certain foods. In most of the 8 the onset was soon after starting foods other than breast milk. The most common offending food was cows' milk protein, but soya (3 cases) and beef (1 case) were also implicated. A history of allergy in the child or family was common as were blood eosinophilia, high concentrations of serum IgE, and positive IgE antibodies. Colonoscopic appearances were distinctive and biopsies showed a noticeable increase in eosinophils and IgE-containing cells in the lamina propria. We suggest that food allergy is the major cause of colitis in infancy and that an exclusion diet is the treatment of choice.

Time course of allergy to extensively hydrolyzed cow's milk proteins in infants.

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We report on the follow-up of 22 infants allergic to cow's milk proteins who did not tolerate extensively hydrolyzed protein formulas. After successful use of an amino acid-based diet for a duration of 11.8 +/- 8.7 months, evolution differed according to the presence or absence of associated allergy to other foods. Cow's milk protein tolerance occurred earlier in the patients (n = 9) whose allergy was limited to cow's milk proteins and to extensively hydrolyzed protein formulas.
Food Allergy

The spectrum of cow's milk allergy in childhood. Clinical, gastroenterological and immunological studies.

Author Hill DJ; Davidson GP; Cameron DJ; Barnes GL
Seventeen of 52 children suspected of having cow's milk allergy had this diagnosis confirmed after milk challenge in hospital. A broad spectrum of reactions was observed including skin eruptions, respiratory symptoms and gastrointestinal disturbance. Not all patients with gastrointestinal symptoms showed small bowel mucosal damage. Only patients with skin reactions had positive skin tests. IgA deficiency and IgE elevation were common. Four patients had symptoms within 3 days of birth. Twelve children tolerated cow's milk by three years of age. Cow's milk allergy can cause a variety of symptoms. Challenge with milk for several days may be required before allergic manifestations can be demonstrated.

Food allergy: two common types as seen in breast and formula fed babies.

Author Gerrard JW; Shenassa M
Source Ann Allergy, 1983 Jun, 50:6, 375-9
Cow's milk allergy can develop in both breast and formula fed babies. The allergy developing in breast fed babies is triggered by trace amounts of antigen, tends to cause severe reactions and may persist for several years. The allergy developing in formula fed babies is triggered by large amounts of antigen, is not associated with either positive prick tests or with anaphylactic reactions and often subsides spontaneously.

Food intolerance and food allergy in children: a review of 68 cases.

Author Minford AM; MacDonald A; Littlewood JM
Source Arch Dis Child, 1982 Oct, 57:10, 742-7
The clinical and laboratory features of 68 children with food intolerance or food allergy are reviewed. Young children were affected the most with 79% first experiencing symptoms before age 1 year. Forty-eight (70%) children presented with gastrointestinal symptoms (vomiting, diarrhoea, colic, abdominal pain, failure to thrive), 16 (24%) children with skin manifestations (eczema, urticaria, angioneurotic oedema, other rashes), and 4 (6%) children with wheeze. Twenty-one children had failed to thrive before diagnosis. A single food (most commonly cows' milk) was concerned in 28 (41%) cases. Forty (59%) children had multiple food intolerance or allergy; eggs, cows' milk, and wheat were the most common. Diagnosis was based on observing the effect of food withdrawal and of subsequent rechallenge. In many children food withdrawal will mean the use of an elimination diet which requires careful supervision by a dietician. Laboratory investigations were often unhelpful in suggesting or confirming the diagnosis.
Controlled trial of oligoantigenic treatment in the hyperkinetic syndrome.

Author Egger J; Carter CM; Graham PJ; Gumley D; Soothill JF Source Lancet, 1985 Mar 9, 1:8428, 540-5

76 selected overactive children were treated with an oligoantigenic diet, 62 improved, and a normal range of behaviour was achieved in 21 of these. Other symptoms, such as headaches, abdominal pain, and fits, also often improved. 28 of the children who improved completed a double-blind, crossover, placebo-controlled trial in which foods thought to provoke symptoms were reintroduced. Symptoms returned or were exacerbated much more often when patients were on active material than on placebo. 48 foods were incriminated. Artificial colorants and preservatives were the commonest provoking substances, but no child was sensitive to these alone.

Oligoantigenic diet treatment of children with epilepsy and migraine

Author Egger J; Carter CM; Soothill JF; Wilson J Address Department of Neurology, Hospital for Sick Children, London. Source J Pediatr, 1989 Jan, 114:1, 51-8

We studied the role of oligoantigenic diets in 63 children with epilepsy; 45 children had epilepsy with migraine, hyperkinetic behavior, or both, and 18 had epilepsy alone. Of the 45 children who had epilepsy with recurrent headaches, abdominal symptoms, or hyperkinetic behavior, 25 ceased to have seizures and 11 had fewer seizures during diet therapy. Headaches, abdominal pains, and hyperkinetic behavior ceased in all those whose seizures ceased, and in some of those whose seizures did not cease. Foods provoking symptoms were identified by systematic reintroduction of foods, one by one; symptoms recurred with 42 foods, and seizures recurred with 31; most children reacted to several foods. Of 24 children with generalized epilepsy, 18 recovered or improved (including 4 of 7 with myoclonic seizures and all with petit mal), as did 18 of 21 children with partial epilepsy. In double-blind, placebo-controlled provocation studies, symptoms recurred in 15 of 16 children, including seizures in eight; none recurred when placebo was given. Eighteen other children, who had epilepsy alone, were similarly treated with an oligoantigenic diet; none improved.

Topographic mapping of brain electrical activity in children with food-induced attention deficit hyperkinetic disorder.

Author Uhlig T; Merkenschlager A; Brandmaier R; Egger J Address Institute for Child Health Research, Clinical Sciences Division, West Perth, Australia. Source Eur J Pediatr, 1997 Jul, 156:7, 557-61

In 15 children suffering from food induced attention deficit hyperkinetic syndrome, topographic EEG mapping of brain electrical activity was carried out following avoidance and ingestion of previously identified provoking foods. A crossover design was used and recordings were interpreted independently by two investigators, one of whom was blind to the order of testing. During consumption of provoking foods there was a significant increase in beta activity in the frontotemporal areas of the brain. This investigation is the first one to show an association between brain electrical activity and intake of provoking foods in children with food-induced attention deficit hyperactivity disorder. CONCLUSIONS: These data support the hypothesis that in a subgroup of children with
attention deficit hyperactivity disorder certain foods may not only influence clinical symptoms but may also alter brain electrical activity.

Diet treatment, enuresis, migraine, hyperkinetic behavior.


Twenty-one children with migraine and/or hyperkinetic behavior disorder which was successfully treated with an oligoantigenic (few-foods) diet also suffered from nocturnal and/or diurnal enuresis. On diet, the enuresis stopped in 12 of these children and improved in an additional four. Identification of provoking foods was by sequential reintroduction of the foods that were avoided on the oligoantigenic diet. In eight of the 12 children who recovered on the oligoantigenic diet and in the four who improved, reintroduction of one or more foods provoked a reproducible relapse of the enuresis. Nine children were subjected to a placebo-controlled, double-blind reintroduction of provoking foods. Six children relapsed during testing with incriminated foods; none reacted to placebo. Enuresis in food-induced migraine and/or behavior disorder seems to respond, in some patients, to avoidance of provoking foods.
**Bowel Disease**

The spectrum of gastrointestinal allergies to food.

Author: Walker-Smith JA; Ford RP; Phillips AD

Source: Ann Allergy, 1984 Dec, 53:6 Pt 2, 629-36

Gastrointestinal food allergies may be defined as clinical syndromes which are characterised by the onset of gastrointestinal symptoms following food ingestion where the underlying mechanism is an immunologically mediated reaction within the gastrointestinal tract. These gastrointestinal symptoms, principally vomiting and diarrhoea, sometimes abdominal colic, may be accompanied by other symptoms outside the alimentary tract. The clinical spectrum of these disorders ranges from acute anaphylaxis (rarely leading to death in infancy) to relatively minor symptoms which are difficult to distinguish from other disorders such as toddler's diarrhoea or psychological disorders. The same food, e.g. cow's milk, may produce a wide range of clinical manifestations. In the one individual, clinical features may change with age. The incidence of gastrointestinal food allergic disease is greatest in the first year of life and decreases with age. There are, broadly speaking, two categories of clinical syndromes which are related to speed of onset of symptoms: immediate and delayed. Those syndromes which manifest immediately after food ingestion are usually easy to diagnose and specific IgE tests and skin prick tests are frequently positive. Those which have a delayed onset of up to several days are difficult to diagnose, and currently available investigations may be unsatisfactory for routine use. In current clinical practice, gastrointestinal syndromes which can be manifestations of food allergy, may be grouped as follows: 1) immediate syndromes, including anaphylaxis and b) acute vomiting +/- diarrhoea in association with cutaneous and respiratory manifestations; and 2) delayed syndromes, including a) food-sensitive small intestinal enteropathies, b) food-sensitive colitis, c) multiple food allergy +/- enteropathy, and d) infantile colic

**Hypoallergenicity & efficacy of amino acid-based formula**

in children with cow's milk and multiple food hypersensitivities

J Pediatr 2001 May;138(5):688-93

Sicherer SH., Noone SA., Koerner CB., Christie L., Burks AW., Sampson HA
Division of Pediatric Allergy and Immunology, Department of Pediatrics, Mount Sinai School of Medicine, New York 10029-6574, USA.

AB - OBJECTIVE: To determine the hypoallergenicity and efficacy of a pediatric amino acid-based formula (AAF), EleCare, for children with cow's milk allergy (CMA) and multiple food allergies (MFA). STUDY DESIGN: Hypoallergenicity was determined by performing blinded oral food challenges in 31 consecutive children with documented CMA. Growth, tolerance, and biochemical response were evaluated during a nonrandomized feeding study with each child serving as his or her own control.

RESULTS: Thirty-one children (median age, 23.3 months; range, 6 months to 17.5 years) were recruited; 29 had MFA, 17 had acute reactions and cow's milk-specific IgE antibody,
and 14 had allergic eosinophilic gastroenteritis. At study entry, 23 were receiving another AAF; 13 had not tolerated extensively hydrolyzed formula. Eighteen subjects with allergic eosinophilic gastroenteritis and/or MFA were followed up while receiving AAF for a median of 21 months (range, 7 to 40 months), with biochemical analysis performed at 4 months. No statistically significant differences were observed in the change in weight or height National Center for Health Statistics z scores from entry; the percent of expected growth exceeded 90%. There was a small decline in percent eosinophils and increase in hemoglobin, hematocrit, and serum ferritin level (P < .05). Except for small increases in plasma leucine and valine levels (P < or = .006), the remaining biochemical markers were unchanged. CONCLUSIONS: The AAF was hypoallergenic and effective in maintaining normal growth for children with CMA and MFA.

**Food protein-induced enterocolitis syndrome**

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Enterocolitis induced in infants by cow's milk and/or soy protein has been recognized for decades. Symptoms typically begin in the first month of life in association with failure to thrive and may progress to acidemia and shock. Symptoms resolve after the causal protein is removed from the diet but recur with a characteristic symptom pattern on re-exposure. Approximately 2 hours after reintroduction of the protein, vomiting ensues, followed by an elevation of the peripheral blood polymorphonuclear leukocyte count, diarrhea, and possibly lethargy and hypotension. The disorder is generally not associated with detectable food-specific IgE antibody. There are increasing reports of additional causal foods, prolonged clinical courses, and onset outside of early infancy, leading to description of a food protein-induced enterocolitis syndrome. The disorder poses numerous diagnostic and therapeutic challenges. The purpose of this report is to delineate the characteristic clinical features and review the possible pathophysiologic basis to frame a rational strategy toward management.
Elemental diet as primary treatment of acute Crohn's disease


Acute exacerbations of Crohn's disease are usually treated with prednisolone or potentially more toxic immunosuppressive drugs or by surgery. In pilot studies replacing the normal diet by a protein free elemental diet also induced remission. A controlled trial was therefore conducted in which 21 patients acutely ill with exacerbations of Crohn's disease were randomised to receive either prednisolone 0.75 mg/kg/day or an elemental diet (Vivonex) for four weeks. Assessment at four and 12 weeks showed that the patients treated with the elemental diet had improved as much as and by some criteria more than the steroid treated group. Elemental diet is a safe and effective treatment for acute Crohn's disease.

Diet in the management of Crohn's disease.

Author Workman EM; Alun Jones V; Wilson AJ; Hunter JO Source Hum Nutr Appl Nutr, 38: 6, 1984 Dec, 469-73

Thirty-three patients with Crohn's Disease were studied to see if their symptoms were related to food intolerances. Initial treatment to produce remission of symptoms was total parenteral nutrition (20), elemental diet (2) or elimination diet (11). Twenty-nine patients reported specific food intolerances, and 21 of these remained in remission on diet alone, the mean length of remission being 15.2 months. The most important foods provoking symptoms were wheat and dairy products.

Nitrogen utilization of two elemental diets in Crohn's disease.

Author Vaisman N; Griffiths A; Pencharz PB Address Division of Clinical Nutrition, Hospital for Sick Children, Toronto, Ontario, Canada. Source J Pediatr Gastroenterol Nutr, 7: 1, 1988 Jan-Feb, 84-8

Energy, nitrogen absorption, and nitrogen utilization of two commercial elemental diets, Vivonex and Vital, were compared in 10 teenage boys and girls with Crohn's disease. The diets were given in random order as overnight feedings and were the sole source of nutrients for two consecutive periods of 3 weeks each. Urine and stools were collected for 48 h at the end of each 3-week period. Energy absorption was slightly better on Vivonex (p less than 0.05), although 95-100% of energy was absorbed with both formulas. Nitrogen absorption was not different for the two formulas, but nitrogen utilization was significantly better on Vital (28.6 +/- 12.9% versus 9.7 +/- 17.7%, p less than 0.01). This difference may be attributable to the different concentrations of sulfur-containing and aromatic amino acids in the two formulas.
Comparing prednisolone with an elemental diet plus antibiotics in Crohn's disease.

Author Saverymuttu S; Hodgson HJ; Chadwick VS Source Gut, 26: 10, 1985 Oct, 994-8

In a randomised clinical trial, patients with moderately active Crohn's disease received either prednisolone 0.5 mg/kg/day plus a normal diet, or an elemental diet plus oral framycetin, colistin and nystatin. Patients were assessed using the Crohn's disease activity index (CDAI), ESR, and faecal granulocyte excretion quantified by $^{111}$In-autologous leucocytes. Five patients were intolerant of the elemental diet plus antibiotics and were withdrawn from the trial within 72 hours. Sixteen patients completed 10 days treatment on each regime. Fifteen of 16 patients on elemental diet plus antibiotics and all 16 patients on prednisolone improved with marked, but statistically indistinguishable falls in CDAI, ESR, and faecal granulocyte excretion between the two groups. Thus a regime decreasing the intraluminal concentration of bacteria and complex food molecules, was associated with rapid improvement in activity of Crohn's disease. This suggests that these intraluminal factors play a role in maintaining inflammation and that their removal or alteration offers an approach to management.

Comparison of total parenteral nutrition and elemental diet in induction of remission of Crohn's disease

Author Jones VA Address Department of Community Medicine, East Anglian Regional Health Authority, Cambridge U.K. Source Dig Dis Sci, 32: 12 Suppl, 1987 Dec, 100S-107S

Total parenteral nutrition or elemental diet can be used to induce remission of Crohn's disease. A randomized study has been conducted of 36 patients to assess the relative efficacy of the two techniques used without pharmacologic support; both were successful, and no significant differences emerged in the number of days to remission or the mean changes in Crohn's disease activity index, erythrocyte sedimentation rate, or serum albumin. The elemental diet is cheaper, simpler and safer. Uncontrolled clinical experience with 77 patients showed that personalized food exclusion diets were associated with an average annual relapse rate of only 11% for the first five years of diet alone; there have been six pregnancies and the longest remission is now 75 months. The use of elemental diet followed by the development of a personal food exclusion diet appears to be an effective long-term therapeutic strategy for Crohn's disease.

Elemental diet improves growth failure in Crohn's disease.

Author Belli DC; Seidman E; Bouthillier L; Weber AM; Roy CC; Pletincx M; Beaulieu M; Morin CL Address Service de Gastroentérologie, Hôpital Sainte-Justine, Québec, Canada. Source Gastroenterology, 94: 3, 1988 Mar, 603-10

Growth failure often complicates Crohn's disease in pediatric patients and is principally due to inadequate caloric intake. To assess whether intermittent courses of an elemental diet could reestablish growth, 8 children (aged 9.8-14.2 yr) with Crohn's disease and growth failure entered into a prospective trial. Each patient was studied during an observation year on standard therapy, then for an experimental year during which they received enteral elemental diet 1 out of 4 mo. An age- and disease-matched control group of 4 patients was treated by conventional medical therapy during both years. Elemental diet therapy was administered nocturnally, at home, by continuous nasogastric
Food Allergy

infusion and increased the daily caloric intake by 25% (p less than 0.01). Anthropometric measurements demonstrated significant height and weight gains in the elemental diet group vs. controls (p less than 0.01). Crohn’s disease activity index and prednisone intake decreased significantly in patients receiving elemental diet therapy when compared with themselves and with controls on conventional medical therapy (p less than 0.05). In contrast, the rate of pubertal development was similar in both groups irrespective of the treatment modality. This study demonstrates that chronic intermittent elemental diet effectively reverses growth arrest, while decreasing prednisone requirements and Crohn's disease activity index in pediatric Crohn's disease patients prior to puberty.

Food protein-induced enterocolitis syndrome

Author Sicherer SH Address Division of Pediatric Allergy and Immunology, Department of Pediatrics, Elliot and Roslyn Jaffe Food Allergy Institute, Mount Sinai School of Medicine, New York, New York 10029-6574, USA. Source J Pediatr Gastroenterol Nutr, 2000, 30 Suppl:, S45-9

Food Protein-Induced Enterocolitis Syndrome (FPIES) is a symptom complex of severe vomiting and diarrhea caused by non-IgE-mediated allergy to cow's milk and/or soy in infants. Symptoms typically begin in the first month of life in association with failure to thrive and may progress to acidemia and methemoglobinemia. Symptoms resolve after the causal protein (usually sensitivity to both cow's milk and soy) is removed from the diet. Symptoms recur approximately 2 hours after reintroduction of the protein along with a coincident elevation of the peripheral blood polymorphonuclear leukocyte count. The sensitivity is usually outgrown by 3 years of age. The purpose of this review is to delineate the characteristic clinical features, diagnosis and management of FPIES. Furthermore, infantile FPIES will be discussed in relation to clinical syndromes that share features with it ("atypical FPIES") and other food-allergic disorders affecting the gastrointestinal tract.

Elemental diets: prophylaxis and therapy for intestinal lesions.

Author Bounous G Address Department of Surgery, Montreal General Hospital, Quebec, Canada. Source Surgery, 105: 5, 1989 May, 571-5

The recognition of potentially noxious physiologic substances in the intestinal milieu prompted the use of an "elemental" semihydrolyzed formula diet in the prophylaxis of experimental acute ischemic enteropathy. Elemental diets have been used in the management of a variety of digestive diseases. An elemental diet protects the intestinal mucosa of rodents from radiation injury and facilitates mucosal healing. Clinical trials have shown the benefits of this form of treatment in the prevention of acute radiation enteropathy and in the therapy for delayed radiation enteropathy and Crohn's disease.
Steroids versus elemental diet in Crohn's disease...

Author O'Keefe SJ; Ogden J; Rund J; Potter P. Address Gastrointestinal Clinic, Groote Schuur Hospital, South Africa. Source JPNJ Parenter Enteral Nutr, 13: 5, 1989 Sep-Oct, 455-60

Recent studies have shown an elemental diet to be as effective as bowel rest plus steroids in the management of acute Crohn's disease. In order to investigate the metabolic and immunological effects of these two therapies, six patients with an acute inflammatory attack of ileal Crohn's disease were randomly assigned to receive steroids or elemental diet for 7 days. Immunological and protein metabolic studies were performed before and after therapy, protein kinetic rates being measured by the method of constant intravenous infusion of 14C-labeled leucine tracer. Clinical and symptomatic improvement was noted in all six patients with significant falls in sedimentation rate and platelet counts and increases in albumin concentrations. Both forms of treatment increased plasma amino acid flux and oxidation rates, whole body protein turnover and rates of incorporation of amino acid into albumin. However, the increased rates of protein metabolism in the patients given steroids were at the expense of body protein stores with a net (average) loss of 58 g of nitrogen over 7 days. While both forms of therapy were associated with suppression of lymphocyte subsets, complement and circulating immune complexes only the steroid regimen was associated with suppression of in vivo IgG synthesis rates. The results indicated that both forms of therapy were associated with clinical improvement, increases in protein turnover and evidence of reduced inflammatory activity. However, the beneficial effects of steroid regimen must be balanced against the deleterious effects on body protein stores; steroids and bowel rest without nutritional support should be avoided in malnourished patients.

Improvement in Crohn's disease by an elemental diet.

Author Sanderson IR; Boulton P; Menzies I; Walker-Smith JA. Address Department of Child Health, St. Bartholomew's Hospital, London. Source Gut, 28: 9, 1987 Sep, 1073-6

Intestinal permeability to sugar has been used as an objective measure of small bowel integrity to assess the efficacy of an elemental diet as the sole treatment or Crohn's disease of the small bowel. Fourteen children aged 11-17 years with active small bowel Crohn's disease were given an elemental diet for six weeks. Investigations with iso-osmolar oral test solutions before and after this treatment showed that all 14 children had abnormally raised lactulose/L-rhamnose permeability ratios, which fell significantly after the elemental diet. This change coincided with marked clinical improvement, as assessed by a disease activity index score.

Clinical remission in Crohn's disease after oligopeptide diet

Author Pfeif AB; Schuster AT; Kemperdick H. Address Department of Pediatrics, University of Düsseldorf, F.R.G. Source J Pediatr Gastroenterol Nutr, 7: 6, 1988 Nov-Dec, 926-30

Abstract A 9.6-year-old patient was treated exclusively with an oligopeptide diet at initial diagnosis and at first relapse of Crohn's ileocolitis. The patient achieved complete remission in both episodes. Control radiologic examinations 14 months after diagnosis revealed complete disappearance of radiologic manifestations of Crohn's disease.
Anti-food antibodies for the diagnosis of food allergy.

Author Johansson SG; Dannaeus A; Lilja G Source Ann Allergy, 1984 Dec, 53:6 Pt 2, 665-72

All individuals are exposed to large amounts of potentially immunogenic food proteins. Most people respond by producing IgG, IgA, or IgM antibodies. The presence of such antibodies in serum is a normal, but not necessarily physiologic phenomenon. In certain groups of individuals, such as young infants, persons with a selective IgA deficiency and patients with inflammatory gastrointestinal disorders, especially high levels of such antibodies are commonly found despite complete tolerance to intake of the food in question. Obviously the finding of IgG, IgA or IgM antibodies to food proteins in serum is of limited clinical relevance. The presence in serum of IgE antibodies to food antigens is not uncommon in some patients with atopic dermatitis, although the clinical relevance of the antibodies for the dermatitis is not always clear. Young, atopic children have low levels of such antibodies as a normal, transient phenomenon. High concentrations of IgE antibodies not only to classical food antigens such as egg, fish, cow's milk, nuts, shellfish, peanuts and cereals but also to less typical allergens such as celery, some spices and other vegetables often indicate a pronounced food allergy that can give rise to a serious reaction upon contact. In contrast to the case with non-IgE antibodies, the presence of IgE antibodies in serum is a non-physiologic state of clinical relevance.

Food allergy and gastrointestinal diseases.

Author Aiuti F; Paganelli R Source Ann Allergy, 1983 Aug, 51:2 Pt 2, 275-80

Several gastrointestinal diseases and symptoms have been attributed to food intolerance, but in only a few cases has the participation of immune mechanisms been confirmed. Acute or chronic gastroenteritis is commonly due to allergic reactions to food proteins, inflammatory diseases and infections, or the presence of immunological defects may induce secondarily a food allergic disorder. This review will focus on the immunopathogenetical importance of the mucosal and systemic defenses, and the absorption of food proteins by the gut.
IgE complexes by allergen challenge in atopic patients.

Author Brostoff J; Carini C; Wraith DG; Johns P Source Lancet, 1979 Jun 16, 1:8129,

Specific IgE complexes and symptoms of asthma and eczema were produced in two allergic patients by oral challenge with food allergen. Both symptoms and IgE complexes could be prevented by pre-treatment with oral sodium cromoglycate. The IgE complexes can fix complement and may therefore provide the vehicle of the "late" responses seen in immediate hypersensitivity. The central role of gut sensitivity is emphasised by the protection afforded by sodium cromoglycate both when given acutely, against the effects of an oral challenge, and when given continuously for asthma and eczema due to food allergy.

selected cytokines in patients with food allergy and chronic gastritis.


Cytokines are produced by many cells and they play a role of mediators in the development of local and systemic inflammatory reaction. The aim of the study was to determine serum concentrations of IL-4, IL-5, IL-8, TNF alpha in patients with chronic gastritis and food allergy, who had been infected with H. pylori. MATERIAL AND METHODS: The study was conducted on patients with atopic diathesis, who were allergic to certain foods. The study group consisted of 71 patients, including 42 females aged 16-54 years (mean age 35.5 years) and 29 males aged 18-60 years (mean age 36.2 years). One control group was formed of 40 non-atopic patients aged 18-56 years (mean age 34.8 years), suffering from chronic gastritis. The other control group consisted of 30 subjects with the diagnosis of functional dyspepsia. Serum levels of selected cytokines were determined with the kits manufactured by ENDOGEN (Cambridge MA, USA) using enzyme immunoassay ELISA. The concentrations of parameters were determined in two tests and they were given as mean value. RESULTS: Mean serum IL-4 level in atopic patients was 27.85 pg/ml, while it was 13.26 pg/ml in non-atopic subjects with chronic gastritis and 4.3 pg/ml in patients with functional dyspepsia. The concentration of IL-5 ranged between 0 and 111.3 pg/ml (mean value: 7.43 pg/ml) in subjects with food allergy. Comparative analysis of IL-4 and IL-5 concentrations in atopic patients and in control subjects showed the presence of statistically significant differences (p < 0.001). The remaining cytokines, i.e. IL-8 and TNF alpha showed a significant increase in serum levels in patients chronic gastritis when compared to the subjects with functional dyspepsia, without inflammatory changes. CONCLUSIONS: Chronic exposure of the patients with food allergy to a given food allergen makes the levels of IL-4 and IL-5 rise. In atopic subjects with chronic gastritis and H. pylori infection, the increase in IL-4, IL-5, IL-8 and TNF alpha levels suggests that both infectious and allergic factors play an important role in the pathogenesis of inflammation.
**Allergy of the nervous system: a review**


Allergies of the nervous system cause diverse behavioral disturbances, including headaches, convulsions, learning disabilities, schizophrenia and depression. Some of the biological mechanisms have been established by research; others remain to be explored. Effective diagnosis and treatment include the elimination diet, followed by dietary rotation and avoidance of offending substances. [References: 159]

**Humoral immune response in children with cow’s milk allergy.**

Author Firer MA; Hoskings CS; Hill DJAddress Department of Chemical Immunology, Weizmann Institute of Science, Rehovot, Israel. Source Int Arch Allergy Appl Immunol, 1987, 84:2, 173-7

In 47 infants and children aged 4-66 months with clinically proven cow's milk allergy and in a group of age-matched controls, serum IgG, IgA and IgM cow's milk-specific antibodies were determined with ELISA assays while IgE cow's milk-specific antibodies were measured with Pharmacia RAST. The patients were divided into three separate groups according to the time of clinical response to a standardized cow's milk challenge protocol. Immediate reactions (less than 45 min after challenge), which were mainly accompanied by urticarial skin eruptions, were associated with elevated IgE milk-specific antibody levels, indicating the involvement of an immediate hypersensitivity mechanism. Alternatively, intermediate reactions (1-20 h after challenge), which were mainly accompanied by vomiting and diarrhea, were not IgE-mediated. In the late reactions (greater than 20 h after challenge) both eczematous and gastrointestinal reactions were seen. Patients with eczematous eruptions also showed elevated IgE milk-specific antibody levels. IgG milk-specific antibody levels were similar in each of the patient groups but all groups were significantly lower than in the controls. Levels of IgA and IgM milk-specific antibodies were similar in patients and controls. The results indicate that different immunopathogenic mechanisms are operative in these subgroups of patients with cow's milk allergy.
Gastrointestinal symptoms in atopic eczema.

Author Caffarelli C; Cavagni G; Deriu FM; Zanotti P; Atherton DJ
Address Clinica Pediatrica, Università di Parma, Italy. Source Arch Dis Child, 1998 Mar, 78:3, 230-4

AIMS: To determine the prevalence of gastrointestinal symptoms in children with eczema and the association of such symptoms with the extent of eczema or skin prick test results.

METHODS: Sixty five children with atopic eczema and a control group matched for age and sex were recruited. Their parents completed a questionnaire about the children's gastrointestinal symptoms. The children's skin was examined; their weight, height, and abdominal circumference were measured; and skin prick tests were carried out.

RESULTS: Gastrointestinal symptoms, especially diarrhea, vomiting, and regurgitation, were more common in the children with eczema. Diarrhea appeared to be associated with the ingestion of specific foods. Gastrointestinal symptoms were related to diffuse eczema and positive skin prick tests to foods. There was no anthropometric differences between the patient and control groups. CONCLUSIONS: A gastrointestinal disorder is common in children with eczema, especially with diffuse distribution. This may be responsible for substantial symptoms and may play a part in the pathogenesis of the disease and in the failure to thrive with which it is sometimes associated.

Hot spices influence permeability of human intestine

Author Jensen Jarolim E; Gajdzik L; Haberl I; Kraft D; Scheiner O;
Address Department of General and Experimental Pathology, University Hospital AKH, Logo, Vienna, Austria. Source J Nutr, 1998 Mar, 128:3, 577-81

Indirect evidence suggests that hot spices may interact with epithelial cells of the gastrointestinal tract to modulate their transport properties. Using HCT-8 cells, a cell line from a human ileocecal carcinoma, we studied the effects of spices on transepithelial electrical resistance (TER), permeability for fluorescein isothiocyanate (FITC)-labeled dextrans with graded molecular weight, and morphological alterations of tight junctions by immunofluorescence using an anti-ZO-1 antibody, a marker for tight junction integrity.

Two different reactivity patterns were observed: paprika and cayenne pepper significantly decreased the TER and increased permeability for 10-, 20- and 40-kDa dextrans but not for 70-kDa dextrans. Simultaneously, tight junctions exhibited a discontinuous pattern. Applying extracts from black or green pepper, bay leaf or nutmeg increased the TER and macromolecular permeability remained low. Immunofluorescence ZO-1 staining was preserved. In accordance with the above findings, capsaicin transiently reduced resistance and piperine increased resistance, making them candidates for causing the effects seen with crude spice extracts. The observation that Solanaceae spices (paprika, cayenne pepper) increase permeability for ions and macromolecules might be of pathophysiological importance, particularly with respect to food allergy and intolerance.
Management of gastrointestinal food allergy in childhood.

Author Walker Smith JA  
Address University Department of Paediatric Gastroenterology, Royal Free Hospital, London, U.K.  
Source Chung Hua Min Kuo Hsiao Erh Ko I Hsueh Hui Tsa Chih, 1998 Jan, 39:1, 12-6

Gastrointestinal food allergy in childhood is characterized by onset of gastrointestinal symptoms following food ingestion where the underlying mechanism is an immunologically mediated reaction within gastrointestinal tract. Presentation may be quick, slow or quick and slow after food ingestion. Diagnosis depends on response to food elimination, response to food challenge and analysis of response to food elimination. Management centres upon an elimination diet, the need for this is temporary. Cow's milk protein hydrolysates or amino acid formulae are preferred to soy formulae.

Current status of digestive intolerance to food protein.

Author Polanco I  
Address Department of Pediatrics, La Paz Children's Hospital, Universidad Autónoma, Madrid, Spain  
Source J Pediatr, 121: 5 Pt 2, 1992 Nov, S108-10

Digestive intolerance to food proteins may occur in childhood as a result of a wide range of etiologic and pathophysiologic mechanisms. Cow milk protein intolerance is the most common form of food intolerance in children. Food allergy and food intolerance may be confused because both produce similar symptoms, especially in young children with clinical manifestations of food allergy localized to the gastrointestinal tract. On the other hand, food-sensitive enteropathy may be defined as the clinical food-related syndromes associated with an abnormal small intestinal mucosa.

Although several foods have been reported to damage the small intestinal mucosa in infancy (soy, rice, fish, chicken meat, egg), cow milk-sensitive enteropathy is the most common cause. Whatever the mechanisms, digestive intolerance to food proteins with or without enteropathy is primarily a temporary condition of infancy, in contrast to most forms of food allergy. In children with these disorders, symptoms usually resolve by 1 to 3 years of age. The variation in prevalence rates of this disorder in different countries can be explained by different diagnostic criteria. The classic food-sensitive enteropathy syndromes with chronic diarrhea and failure to thrive in infancy have become rarer in some European countries, including Spain. Some risk factors for the development of these conditions appear to be early exposure to cow milk feedings, acute infectious diarrhea, and malnutrition. Breast-feeding appears to be at least partially protective.
Eosinophilic gastroenteritis, food allergy and bronchial asthma.

Author Park HS; Kim HS; Jang HJ  Address Department of Allergy and Clinical Immunology, Ajou University School of Medicine, Korea.  Source J Korean Med Sci, 10: 3, 1995 Jun, 216-9

In some patients, eosinophilic gastroenteritis(EG) occurs in those with food allergy. We experienced a non-atopic asthmatic who had an EG associated with food allergy to fish and eggs, and blood eosinophilia. A skin prick test and RAST to causative food allergens showed a negative result. A fiber-optic endoscopic biopsy from the gastric mucosa showed an intense eosinophilic infiltration. We could find symptomatic improvement and a disappearance of eosinophilic infiltration in gastric mucosa after complete avoidance from the causative food and oral corticosteroid. It was suggested that fiber-optic endoscopic biopsy might be needed to identify coexisting EG if an allergic patient with blood eosinophilia complains of severe gastrointestinal symptoms.

Dietary elimination therapy is an effective option for adults with eosinophilic esophagitis.

Wolf WA; Jerath MR; Sperry SL; Shaheen NJ; Dellon ES

BACKGROUND & AIMS: Eosinophilic esophagitis (EoE) is an immune-mediated disorder. Food elimination is an established treatment for children, but data in adults are limited. We aimed to determine the response of adults with EoE to dietary therapy.

METHODS: This was a retrospective cohort study using the University of North Carolina EoE database from 2006 to 2012. Subjects were age 18 and older, had EoE by consensus guidelines, and had undergone dietary therapy either with a targeted elimination diet or a 6-food elimination diet (SFED). Outcomes were symptomatic, endoscopic, and histologic improvement. Demographic, endoscopic, symptomatic, and laboratory predictors of response to dietary therapy were assessed.

RESULTS: Of 31 adults who underwent dietary therapy (mean age, 36 y; 48% male; 90% white; mean baseline eosinophil count, 78 eos/hpf), 22 had a targeted elimination diet and 9 had SFED. Symptoms improved in 71% (68% in targeted, 78% in SFED), and endoscopic appearance improved in 54% (53% in targeted, 56% in SFED). After dietary therapy, the mean eosinophil count decreased to 43 eos/hpf (P = .009). Eleven subjects (39%) responded with fewer than 15 eos/hpf (32% in targeted and 56% in SFED; P = .41). No clinical, endoscopic, or histologic factors predicted response to dietary therapy. Of the 11 responders, 9 underwent food re-introduction to identify trigger(s), and 4 (44%) reacted to dairy, 4 (44%) reacted to eggs, 2 (22%) reacted to wheat, 1 (11%) reacted to shellfish, 1 (11%) reacted to legumes, and 1 (11%) reacted to nuts.

CONCLUSIONS: Dietary elimination is a successful treatment modality for adults with EoE. Further research should emphasize which factors can predict effective dietary therapy.
Chronic constipation as a symptom of cow milk allergy.

Author Iacono G; Carroccio A; Cavataio F; Montalto G; Cantarero MD; Notarbartolo A
Source J Pediatr, 126: 1, 1995 Jan, 34-9

Twenty-seven consecutive infants (mean age, 20.6 months) with chronic "idiopathic" constipation were studied to investigate the possible relation between constipation and cow milk protein allergy (CMPA). The infants were initially observed on an unrestricted diet, and the number of stools per day was recorded. Subsequently the infants were put on a diet free of cow milk protein (CMP) for two periods of 1 month each, separated by two challenges with CMP. During the CMP-free diet, there was a resolution of symptoms in 21 patients; during the two consecutive challenges, constipation reappeared within 48 to 72 hours. In another six patients the CMP-free diet did not lead to improvement of constipation. Only four of the patients who improved on the CMP-free diet had concomitant symptoms of suspected CMPA, but a medical history of CMPA was found in 15 of the 21 patients cured and in only one of the six patients whose condition had not improved (p < 0.05); in addition, in 15 of the 21 cured patients, results of one or more laboratory tests (specific IgE, IgG, anti-beta-lactoglobulin, circulating eosinophils) were positive at the time of diagnosis, indicating hypersensitivity, compared with one of the six patients whose condition did not improve (p < 0.05). The endoscopic and histologic findings at the time of diagnosis showed proctitis with monocytic infiltration in two patients cured with the CMP-free diet; after 1 month on this diet, they were completely normal. We conclude that constipation in infants may have an allergic pathogenesis.

Food sensitive enteropathy: overview and update.


There are two types of food sensitive enteropathy; permanent and temporary. Celiac disease belongs to the former, the temporary food sensitive enteropathies of early childhood to the latter. A food sensitive enteropathy is characterized by an abnormal small intestinal mucosa while having the offending food in the diet; the abnormality is reversed by an elimination diet, only to recur once more on challenge with the relevant food. These disorders are temporary and may follow gastroenteritis. Cow's milk sensitive enteropathy is the most frequent and best known example but soy protein, egg, fish, chicken meat, ground rice and probably gluten may also temporarily damage the small intestinal mucosa in infancy. Treatment is with an elimination diet and protein hydrolysates as a cow's milk substitute.

Gastrointestinal allergy to food: a review.

Author Ahmed T; Fuchs GJ Address Clinical Sciences Division, International Centre for Diarrhoeal Disease Research, Bangladesh. tahmeed@icddrb.org Source J Diarrhoeal Dis Res, 1997 Dec, 15:4, 211-23

Gastrointestinal food allergy still poses a challenge to the clinician because of its variable symptomatology and lack of reliable diagnostic tests. Its prevalence is estimated at 2 approximately 5%, higher in children than in older age-groups. Allergy to food usually diminishes with advancing age. Although a wide variety of foods can cause allergic reactions, cow's milk is the most common cause of food allergy in infants and young children. Depending upon the speed of onset of symptoms, immediate and delayed types
of food allergy have been described. Gastrointestinal symptoms in food allergy have been explained by alterations in transport across the intestinal wall (increased secretory and/or decreased absorptive functions), increased permeability, and motility of the intestine. The exact pathogenesis of food allergy is still not clear. However, immediate type of food allergy is believed to be mediated by type I hypersensitivity reaction, involving mast cells and food-specific IgE antibodies. The diagnosis of food allergy is based upon a favorable response to an elimination diet and a response to a challenge with the suspected food. The condition is treated by eliminating the allergenic food from diet for as long as 9-12 months in case of cow's milk allergy. While exclusive breastfeeding for the initial four months or more reduces the chances of development of food allergy, the role of diet restrictions in the mother in reducing the incidence of food allergy in the infant is controversial. Data on food allergy from developing countries are limited. This may be due to lack of diagnosis or less attention given to the condition relative to other diseases including infectious diarrheas and acute respiratory infections. The role of cow's milk allergy in the pathogenesis of persistent diarrhoea, a major problem in the developing world, remains speculative. Frequent intestinal infections and reduced secretory IgA, which are associated with malnutrition, alter intestinal permeability and result in an increased uptake of food antigens. The increased antigenic load combined with factors such as an atopic predisposition may initiate an abnormal mucosal immune response resulting in chronic enteropathy.

Prevalence of IgE-mediated food allergy among children with atopic dermatitis.

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Source Pediatrics, 1998 Mar, 101:3, E8

Abstract OBJECTIVE: There is a growing body of clinical and laboratory evidence to support the notion that food allergy plays a role in the pathogenesis of atopic dermatitis (AD). However, the incidence of IgE-mediated food allergy in children with AD is not well established. DESIGN: A prospective study to determine the prevalence of IgE-mediated food hypersensitivity among patients referred to a university-based dermatologist for evaluation of AD. SETTING: University hospital pediatric dermatology clinic. PATIENTS: A total of 63 patients with AD were recruited (35 male; 32 white, 24 African-American, 7 Asian). METHODS: Patients were assigned an AD symptom score (SCORAD) and were screened for food-specific serum IgE antibodies to six foods (milk, egg, wheat, soy, peanut, fish) known to be the most allergenic in children. The levels of food-specific serum IgE were determined by the CAP System fluorescein-enzyme immunoassay (CAP); patients with a value >/=0.7 kIUa/L were invited for an additional allergy evaluation. Those with CAP values below the cutoff were considered not food allergic. Patients were considered to be allergic if they met one of the following criteria for at least one food: 1) reaction on food challenge; 2) CAP value more than the 95% confidence interval predictive for a reaction; 3) convincing history of an acute significant (hives, respiratory symptoms) reaction after the isolated ingestion of a food to which there was a positive CAP or prick skin test. RESULTS: A total of 63 patients (median age, 2.8 years; median SCORAD, 41.1) were recruited; 22 had negative CAP values (without a significant difference in age or SCORAD score, compared with the 41 with positive specific IgE values). Further allergy evaluation was offered to the 41 remaining patients; 10 were lost to follow-up and 31 were evaluated further. Of these, 19 underwent a total of 50 food challenges (36 double-blind, placebo-controlled, and 14 open), with 11 patients
experiencing 18 positive challenges (94% with skin reactions). Additionally, 6 patients had a convincing history with a predictive level of IgE; 5 had a convincing history with positive, indeterminate levels of IgE; and 1 had predictive levels of IgE (to egg and peanut) without a history of an acute reaction. Overall, 23/63 (37%; 95% confidence interval, 25% to 50%) had clinically significant IgE-mediated food hypersensitivity without a significant difference in age or symptom score between those with or without food allergy. CONCLUSIONS: Approximately one third of children with refractory, moderate-severe AD have IgE-mediated clinical reactivity to food proteins. The prevalence of food allergy in this population is significantly higher than that in the general population, and an evaluation for food allergy should be considered in these patients.

Cow milk allergy within the spectrum of atopic disorders.

Author Hill DJ; Bannister DG; Hosking CS; Kemp AS Address Department of Allergy, Royal Children's Hospital, Parkville, Australia. Source Clin Exp Allergy, 24: 12, 1994 Dec, 1137-43

Abstract In order to examine the relationship between cow milk allergy (CMA) and atopic disorders in childhood, a consecutive group of 42 infants with IgE mediated CMA was followed for at least 2 years. The incidence of sensitization to common food and inhalant antigens and the development of eczema, asthma, and food allergies was examined for the cohort and compared between patients whose CMA remitted and those with persistent disease. In this cohort the prevalence of eczema was 57%, asthma 69%, egg allergy 67%, peanut allergy 55%, and 83% of infants demonstrated positive skin-prick tests to three or more allergens. At the end of the study CMA had remitted in 13 patients (median age 44 months) whereas in 29 patients it persisted (median age 44 months). Although there was no significant difference in the incidence of eczema or asthma during the study between these two patient groups, the incidence of allergy to egg and peanut butter was significantly greater for children with persistent CMA. Consistent with our hypothesis that children with persistent CMA have a more severe dysregulation of IgE synthesis than those whose disease remits, patients with persistent CMA had a significantly higher incidence of and level of skin sensitivity to inhalant and other dietary allergens. Sensitization to the inhalant allergens Dermatophagoides pteronyssinus, cat dander and rye grass was frequently seen in early infancy and increased during the study period. Thus, children with IgE mediated CMA frequently generate IgE responses to multiple dietary and inhalant allergens in infancy and early childhood and develop immediate hypersensitivity to other foods as well as clinical eczema, and asthma.

Food allergy, coeliac disease and chronic inflammatory bowel disease in man.


It is often stated that the gastrointestinal tract has a limited number of responses to pathogens. Entirely different agents can produce a similar histopathological reaction. However, the expression of the disease in man is very heterogeneous, it varies with the age of the subject and is to a certain extent genetically determined. For example, food allergy is frequent in childhood and not common in adulthood. The intestinal mucosa in the child with cows milk allergy shows a 'flat' mucosa, which may be indistinguishable of that observed in gluten sensitive enteropathy or coeliac disease. Subjects with other forms of food allergy may have a morphologically normal small intestinal mucosa,
occasionally with increased IgE plasma cells and often only characterised by an increased intestinal permeability. An abnormal intestinal permeability is one of the hallmarks of an inflamed gut, however, subjects with a latent form of coeliac disease have an abnormal permeability only without overt signs of inflammation. Recently, it has become clear that what determines the characteristics of the intestinal inflammatory response is dependent on the cytokines involved during the response and this seems to be the same in the stomach, the small intestine and the colon. A so-called Th1 response, with an increased production of IFN-gamma, TNF-alpha and other pro-inflammatory cytokines, occurs in the stomach when infected by Helicobacter pylori, in the small intestine when the subject with coeliac disease consumes normal bread and during the active phases of Crohn's disease. A Th2 response is characteristic of the allergic subject and there is some evidence that it is the predominant response in subjects with ulcerative colitis. We still do not know the fine-tuning of the cytokine response but IL-12 appears to be a key cytokine in polarising the response to a Th1 type. More recently it has become clear that the intestinal mucosa has a unique subset of CD4+ T cells that secrete TGF-beta (Th3 cells) that provide help for IgA. These cells have downregulatory properties for Th1 cells and therefore play an important role in the active suppression of oral tolerance and IgE response. What determines that an individual develops one of these diseases? It is now clear that these different pathological entities are multifactorial. Different environmental factors and a complex genetic predisposition where more than one gene and more than one chromosome are involved. The extent and severity of the inflammatory response depends on the genetic diversity of the bacteria or the amount of the antigen on the one hand and on the genetic constitution of the host on the other. The abnormal immune response in the human gut is predominantly a Th1-like inflammatory response. This can be elicited by bacteria, peptides, possibly the bacterial flora and some viruses. The recent findings in the pathogenesis of the intestinal inflammatory response will probably alter the therapy of the future.

Rice-induced enterocolitis in an infant

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BACKGROUND: Although food allergy is common in children, rice allergy is unusual in Western cultures. OBJECTIVE: To report a case of T-cell-mediated rice intolerance in an 11-month-old girl. METHODS: To evaluate the intolerance to rice in this patient, a graded rice food challenge was performed. To examine the immunologic reactivity to rice, in vitro lymphoproliferative responses and cytokine synthesis of rice-stimulated peripheral blood lymphocytes (PBLs) was performed. Subsequently, skin patch testing to rice and other foods was performed. RESULTS: Allergy skin prick test results were negative for rice and positive for egg, milk, and soy. Specific IgE antibodies to rice, egg, peanut, wheat, walnut, codfish, milk, soybean, corn, shrimp, scallops, and clams were undetectable. Results of a single-blind rice food challenge were positive, manifested by emesis that persisted for more than an hour and required intravenous hydration. In vitro lymphoproliferation by the patient's PBLs to rice stimulation was positive. In addition, cytokine synthesis of interferon-gamma, interleukin 10 (IL-10), tumor necrosis factor a, and IL-5 by the patient's rice-stimulated PBLs was elevated, indicating a TH1/TH2 cell response to rice. Endoscopy revealed normal esophageal, gastric, and duodenal
mucosa; a biopsy specimen revealed mild esophagitis. Duodenal explant T cells were initially established by stimulation with rice and IL-2. After a 2-day rest, the lymphocytes were restimulated with rice for 7 days and revealed increased interferon-gamma and IL-5 synthesis. Twenty billion colony forming units of Lactobacillus GG were added to the patient's diet twice daily. After 6 weeks, rice rechallenge resulted in emesis within 1 hour. Results of patch testing were positive to rice, wheat, and barley but negative to soy, which the patient tolerated on food challenge. CONCLUSIONS: Although this patient did not demonstrate IgE antibody to rice, TH1/TH2 cell-mediated responses to rice were detected, and the patient experienced significant morbidity. Patch testing for gastrointestinal food allergies may be useful when the food specific IgE antibody is negative. Probiotic therapy in this patient did not ameliorate her sensitivity to rice, and food elimination remains the only reliable treatment for TH1/TH2-mediated food hypersensitivity.

Measurements of eosinophil activation before and after food challenges in adults with food hypersensitivity.

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BACKGROUND: Objective assessment of inflammatory reactions in the gastrointestinal tract could be useful in the diagnosis of food hypersensitivity. The aim of the present study was to investigate the involvement of eosinophils and mast cells in the inflammatory response of patients with food hypersensitivity before and after food challenges. METHODS: Eleven patients (4 with IgE-mediated allergy and 7 without) with food hypersensitivity and positive double-blind, placebo-controlled food challenge were subjected to food challenge in a single-blinded fashion. Four subjects with no known food hypersensitivity were recruited as controls. Placebo was given after a 1-week washout period followed by an active dose. Stool, urinary and serum samples were collected and symptoms were recorded in a diary. Fecal samples were analyzed for eosinophil protein X (F-EPX) and tryptase; urinary samples for EPX (U-EPX) and leukotriene E4 (U-LTE4) and serum samples were analyzed for eotaxin and food-specific IgE antibodies.
RESULTS: Patients with IgE-mediated food allergy had increased levels of F-EPX compared to controls and tended to have lower serum levels of eotaxin compared to non-allergic patients and controls. U-LTE4 was significantly higher in allergic patients compared to non-allergic patients after challenge. Moreover, F-EPX correlated to U-LTE4 (p = 0.011). Reported symptoms, abdominal pain, distension, flatulence and nausea were similar in the allergic and non-allergic patients. CONCLUSION: The results strongly indicate that eosinophils are activated in the gastrointestinal tract of food-allergic patients but not in patients with non-allergic food hypersensitivity. Due to the inconsistent pattern of symptoms after placebo and active food challenge, it was not possible to relate the levels of inflammation markers to the recorded symptoms.

Joint complaints and food allergic disorders.
An important problem in investigating food allergic diseases is to adduce evidence that specific diseases of unknown cause may be attributable to food allergy. Polyarthritis is a good example of the difficulties involved in such studies because it is a very heterogeneous disorder and generalizations about aetiology are unlikely to prove correct. We have observed transient synovitis in both children and adults which is caused by food allergy. On the other hand we have not been able to show that food allergy demonstrably contributes to juvenile chronic arthritis or to rheumatoid arthritis in adults. The arthritis associated with inflammatory bowel disease undoubtedly responds to elemental diets and the mechanism of this remission warrants further investigation.

Prevalence and severity of food allergy--need for control.

Abstract Food allergy is an increasingly recognized manifestation of atopy. Patient and public awareness of food allergy is also increasing. Justifiable demands are being made for better medical guidance of the practice of food labelling for industry and catering businesses. Such advice must bear in mind the relative frequency and severity of allergies to certain foods. Some commonly allergenic foods (milk, egg, soya, wheat) are staple components of the diets of populations, used widely in prepared foods. The frequency of the allergies to these foods and their widespread uses means they and their derivatives must be declared on food labels. Less commonly used foods such as fish, shellfish, peanut, and tree nuts demand declaration due to the severity of reactions induced in the admittedly more rare, but increasingly common, sufferers of these allergies. Reactions to more unusual foods are increasingly being identified, and the "minimum" list is likely to be extended in the future.
New insights into allergenicity

Mucosal Immunology (2010) 3, 104–110; doi:10.1038/mi.2009.138; published online 23 December 2009
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Allergic diseases, which have reached epidemic proportions, are caused by inappropriate immune responses to a relatively small number of environmental proteins. The molecular basis for the propensity of specific proteins to promote maladaptive, allergic responses has been difficult to define. Recent data suggest that the ability of such proteins to promote allergic responses in susceptible hosts is a function of their ability to interact with diverse pathways of innate immune recognition and activation at mucosal surfaces. This review highlights recent insights into innate immune activation by allergens—through proteolytic activity, engagement of pattern recognition receptors, molecular mimicry of TLR signaling complex molecules, lipid-binding activity, and oxidant potential—and the role of such activation in inducing allergic disease. A greater understanding of the fundamental origins of allergenicity should help define new preventive and therapeutic targets in allergic disease.

Inflammatory Arthritis

Food Allergy to Wheat

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BACKGROUND: Cereal-associated allergy is particularly considered a serious problem, because cereals are essential in our daily diet. Wheat proteins are classified into albumins, globulins and prolamins (insoluble gliadins and glutenins). OBJECTIVES: Our objectives were to study the involvement in food allergy to wheat of these different protein types by using purified fractions and to identify those binding IgE and IgG antibodies. METHODS: Sera were obtained from 28 patients with food allergy to wheat. Albumins/globulins, gliadins and glutenins were obtained by sequential extraction based on differential solubility; alpha-, beta-, gamma- and omega-gliadins and low molecular weight (LMW) and high molecular weight (HMW) glutenin subunits were purified by chromatography. IgE binding to these extracts and fractions were analysed by radioallergosorbent test (RAST), and immunoblotting; IgG binding was detected by enzyme-linked immunosorbent assay (ELISA). RESULTS: In RAST, 60% of sera were shown to have specific IgE antibodies against alpha-, beta-gliadins and LMW glutenin subunits, 55% to gamma-gliadins, 48% to omega-gliadins and 26% to HMW glutenins. Immunoblotting analysis confirmed results obtained in RAST concerning LMW and HMW glutenin subunits and showed that 67% of patients have IgE antibodies to the albumin/globulin fraction. CONCLUSION: Results obtained in the different tests showed common features and in agreement with other studies indicated the presence of numerous allergens in food allergy to wheat; alpha-, beta-, gamma- and omega-gliadins, LMW glutenin subunits and some water/salt-soluble proteins appeared as major IgE
binding allergens, whereas HMW glutenins were only minor allergens. The same type of antigenic profile against gliadins and glutenins was observed with IgG antibodies. Important sequence or structural homologies between the various gliadins and LMW glutenin subunits could certainly explain similarity of IgE binding to these proteins.

**Diet free of gluten improves rheumatoid arthritis**

The effects on arthritis correlate with a reduction in antibodies to food antigens.

Hafstrom I; Ringertz B; Spangberg A; von Zweigberk L; Brannemark S; Nylander I; Ronnelid J; Laasonen L; Klareskog L 

OBJECTIVE: Whether food intake can modify the course of rheumatoid arthritis (RA) is an issue of continued scientific and public interest. However, data from controlled clinical trials are sparse. We thus decided to study the clinical effects of a vegan diet free of gluten in RA and to quantify the levels of antibodies to key food antigens not present in the vegan diet. METHODS: Sixty-six patients with active RA were randomized to either a vegan diet free of gluten (38 patients) or a well-balanced non-vegan diet (28 patients) for 1 yr. All patients were instructed and followed-up in the same manner. They were analysed at baseline and after 3, 6 and 12 months, according to the response criteria of the American College of Rheumatology (ACR). Furthermore, levels of antibodies against gliadin and beta-lactoglobulin were assessed and radiographs of the hands and feet were performed. RESULTS: Twenty-two patients in the vegan group and 25 patients in the non-vegan diet group completed 9 months or more on the diet regimens. Of these diet completers, 40.5% (nine patients) in the vegan group fulfilled the ACR20 improvement criteria compared with 4% (one patient) in the non-vegan group. Corresponding figures for the intention to treat populations were 34.3 and 3.8%, respectively. The immunoglobulin G (IgG) antibody levels against gliadin and beta-lactoglobulin decreased in the responder subgroup in the vegan diet-treated patients, but not in the other analysed groups. No retardation of radiological destruction was apparent in any of the groups. CONCLUSION: The data provide evidence that dietary modification may be of benefit for certain RA patients, and that this benefit may be related to a reduction in immunoreactivity to food antigens eliminated by the change in diet.

**Fasting & vegetarian diet in arthritis**

Muller H; de Toledo FW; Resch KL. Scand J Rheumatol 2001;30(1):1-10 (ISSN: 0300-9742)

Clinical experience suggests that fasting followed by vegetarian diet may help patients with rheumatoid arthritis (RA). We reviewed the available scientific evidence, because patients frequently ask for dietary advice, and exclusive pharmacological treatment of RA is often not satisfying. Fasting studies in RA were searched in MEDLINE and by checking references in relevant reports. The results of the controlled studies which reported follow-up data for at least three months after fasting were quantitatively pooled. Thirty-one reports of fasting studies in patients with RA were found. Only four controlled studies investigated the effects of fasting and subsequent diets for at least three months. The pooling of these studies showed a statistically and clinically significant beneficial long-term effect. Thus, available evidence suggests that fasting followed by vegetarian diets might be useful in the treatment of RA.
Polyarthritis & celiac disease.

Rheumatol Int 2000 Dec;20(1):29-30  (ISSN: 0172-8172) Bagnato GF; Quattrocchi E; Gulli S; Giacobbe O; Chirico G; Romano C; Purello D'Ambrosio F
This report describes a patient who presented with an unusual polyarthritis accompanied by myalgia, fever and anxiety. After extensive clinical and serological evaluation, duodenal biopsy and serological tests provided evidence for the diagnosis of coeliac disease (CD). The patient was promptly put on a gluten-free diet, which led to an improvement in the clinical abnormalities.

Palindromic rheumatism: dietary manipulation.

Nesher G; Mates M
OBJECTIVE: Evaluation of the contribution of dietary components in triggering the attacks of palindromic rheumatism (PR), and the effect of dietary manipulation on the frequency and severity of PR attacks. METHODS: Sixteen patients (10 males, 6 females) were diagnosed as having PR during 1994-8 in one center. Their mean age was 45 +/- 6, duration of symptoms prior to diagnosis was 4 +/- 1.4 years, and frequency of PR attacks were 3.1 +/- 1.8/month. All patients were instructed to make a list of the food that was consumed daily and to specify the dates of PR episodes. Data were evaluated after a period of 2-4 months in each patient. RESULTS: In 5 patients (31%) there was an association between episodes of PR and certain foods that were consumed within 36 hours prior to PR episodes. These were fish (2 patients), eggs, canned vegetables and processed cheese (each in one case). Elimination of the relevant food from each patient's diet resulted in complete cessation of the PR attacks in two of the cases, while the other three had milder, infrequent attacks. Four patients were rechallenged with the offending food. In all cases it resulted in recurrence of the PR attacks. No association between PR episodes and prior consumption of certain foods could be documented in the other 11 patients. CONCLUSIONS: In some PR patients ingestion of certain foods, specific for each case, can trigger the typical attack.

Modulation of immune function by dietary lectins

Br J Nutr 2000 Mar;83(3):207-17  (ISSN: 0007-1145)
Cordain L; Toohey L; Smith MJ; Hickey MS
Despite the almost universal clinical observation that inflammation of the gut is frequently associated with inflammation of the joints and vice versa, the nature of this relationship remains elusive. In the present review, we provide evidence for how the interaction of dietary lectins with enterocytes and lymphocytes may facilitate the translocation of both dietary and gut-derived pathogenic antigens to peripheral tissues, which in turn causes persistent peripheral antigenic stimulation. In genetically susceptible individuals, this antigenic stimulation may ultimately result in the expression of overt rheumatoid arthritis (RA) via molecular mimicry, a process whereby foreign peptides, similar in structure to endogenous peptides, may cause antibodies or T-lymphocytes to cross-react with both foreign and endogenous peptides and thereby break immunological tolerance. By eliminating dietary elements, particularly lectins, which adversely influence both enterocyte and lymphocyte structure and function, it is proposed that the peripheral antigenic stimulus (both pathogenic and dietary) will be reduced.
Calorie restricted diet in rheumatoid arthritis.


Low-energy diets and fasting have suppressive effects on rheumatoid arthritis. It was reported recently that urine levels of pentosidine (i.e., an advanced glycation end product formed by glycosylation) is associated with the activity of rheumatoid arthritis.

We conducted a regimen of caloric restriction combined with fasting in patients with rheumatoid arthritis, and then evaluated urinary pentosidine levels. Ten patients with rheumatoid arthritis underwent a 54-day caloric restriction program. Urinary pentosidine levels were measured and the Lansbury Index were determined by examining the clinical features, blood biochemistry and the inflammation activity of rheumatoid arthritis on days 0, 25 and 54. On day 0, the mean urinary pentosidine level of patients with rheumatoid arthritis was significantly higher than that of the control subjects. On day 54, the mean body weight had reduced due to caloric restriction. The mean values of the erythrocyte sedimentation rate and the Lansbury Index of patients both significantly decreased during the study. In addition, although the urinary pentosidine levels showed no significant difference between day 0 and 25, it was significantly decreased at the end of the study (day 54).

The study showed that under a low energy diet a reduction of disease activity in rheumatoid arthritis was accompanied with a reduction of the urinary pentosidine.

Mediterranean diet… rheumatoid arthritis


OBJECTIVE: To investigate the efficacy of a Mediterranean diet (MD) versus an ordinary Western diet for suppression of disease activity in patients with rheumatoid arthritis (RA). Patients with well controlled, although active RA of at least two years' duration, who were receiving stable pharmacological treatment, were invited to participate. All patients were randomly allocated to the MD or the control diet (CD). To achieve good compliance with prescribed diets all patients were for the first three weeks served the MD or the CD, respectively, for lunch and dinner at the outpatient clinic's canteen. Clinical examinations were performed at baseline, and again in the 3rd, 6th, and 12th week. A composite disease activity index, a physical function index, a health survey of quality of life, and the daily consumption of non-steroidal anti-inflammatory drugs were used as efficacy variables. From baseline to the end of the study the patients in the MD group (n=26) showed a decrease in DAS28 of 0.56 (p<0.001), in HAQ of 0.15 (p=0.020), and in two dimensions of the SF-36 Health Survey: an increase in "vitality" of 11.3 (p=0.018) and a decrease in "compared with one year earlier" of 0.6 (p=0.016). For the control patients, no significant change was seen at the end of the study. This difference between the two treatment groups was notable only in the second half of the trial. The results indicate that patients with RA, by adopting a Mediterranean diet, did obtain a reduction in inflammatory activity, an increase in physical function, and improved vitality.
Determinants of systemic manifestations of food allergy

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The myriad of systemic manifestations induced by food hypersensitivity responses is testament to the ability of localized exposure to foods in the gastrointestinal tract to result in symptoms in distal target organs. Cow's milk protein, for example, may induce hives (urticaria), atopic dermatitis, isolated gastrointestinal symptoms, or severe generalized anaphylaxis in different individuals or in the same person at different times. These diverse manifestations are the result of complex interactions among the causal food protein, gut, immune system, and target organs. The dynamic state of these interactions is demonstrated by the development of food tolerance in most subjects and by the ability to experience the development of new allergies in some subjects. This review explores the variety of clinical manifestations of food hypersensitivity disorders in the context of the question: What determines the local or systemic expression of food allergy in a given individual at a particular time? Evidence is provided for both systemic and local immune activation. The role of food-protein chemistry, absorption and processing of ingested allergen, immune responses (type, degree, and specificity), and target organ hyperreactivity are considered as determinants in the expression of food allergic disorders.

Corticosteroids vs placebo

Gotzsche PC; Johansen HK Cochrane Database Syst Rev, 2000 01, : 2, CD000189

Abstract BACKGROUND: The effect of low dose corticosteroids, equivalent to 15 mg prednisolone daily or less, in patients with rheumatoid arthritis has been questioned. We therefore performed a systematic review of trials which compared corticosteroids with placebo or non-steroidal, anti-inflammatory drugs. OBJECTIVES: To determine whether short-term (i.e. as recorded within the first month of therapy), oral low-dose corticosteroids (corresponding to a maximum of 15 mg prednisolone daily) is superior to placebo and nonsteroidal, antiinflammatory drugs in patients with rheumatoid arthritis. SEARCH STRATEGY: Medline Silverplatter, The Cochrane Controlled Trials Register, reference lists and a personal archive. SELECTION CRITERIA: All randomised studies comparing an oral corticosteroid (not exceeding an equivalent of 15 mg prednisolone daily) with placebo or a non-steroidal, antiinflammatory drug were eligible if they reported clinical outcomes within one month after start of therapy. DATA. RESULTS: Ten studies, involving 320 patients, were included in the meta-analysis. Prednisolone had a marked effect over placebo on joint tenderness pain and grip strength. Measured in the original units, the differences were 12 tender joints (6 to 18) and 22 mm Hg (5 to 40) for grip strength. Prednisolone also had a greater effect than nonsteroidal, antiinflammatory drugs on joint tenderness and pain whereas the difference in grip strength was not significant. Measured in the original units, the differences were 9 tender joints (5 to 12) and 12 mm Hg (-6 to 31). The risk of adverse effects, also during moderate- and long-
term use, seemed acceptable. REVIEWER'S CONCLUSIONS: Prednisolone in low doses (not exceeding 15 mg daily) may be used intermittently in patients with rheumatoid arthritis, particularly if the disease cannot be controlled by other means. Since prednisolone is highly effective, short-term placebo controlled trials studying the clinical effect of low-dose prednisolone or other oral corticosteroids are no longer necessary.

GI permeability, anti-inflammatory drugs


Non-steroidal anti-inflammatory drugs (NSAIDs) cause gastrointestinal damage both in the upper and lower gastrointestinal tract. New anti-inflammatory drugs have been developed in an attempt to improve their gastrointestinal side effect profile. Our objective was to compare the effect on gastrointestinal permeability of acute equieffective doses of four different NSAIDs; three were designed to reduce gastrointestinal mucosal injury. Healthy volunteers underwent sugar tests in a randomised fashion, 15 days apart, at: (1) baseline; (2) after two days of 75 mg slow release (microspheres) indomethacin; (3) after two days of 7.5 mg oral meloxicam which preferentially inhibits cyclooxygenase 2; and (4) after two days of 750 mg naproxen. A subgroup of subjects was tested after two days of 200 mg celecoxib. In each test, subjects ingested a solution containing sucrose, lactulose, and mannitol and sucralose, to evaluate gastroduodenal, intestinal, and colonic permeability, respectively. RESULTS: Gastric permeability was significantly affected by naproxen (p<0.05) but not by slow release indomethacin, meloxicam, or celecoxib. Intestinal permeability was significantly increased by the first three NSAIDs (p<0.05) but not by celecoxib. Abnormal lactulose/mannitol ratios were observed in 42% of meloxicam treatments, in 62% during indomethacin, and in 75% of subjects treated with naproxen. Finally, colonic permeability, as measured by sucralose, was not significantly increased by any of the four drugs. CONCLUSION: Our study provides evidence that the newly developed NSAIDs reduce gastric mucosal permeability significantly. However, most produced significant alteration of small intestinal permeability. In contrast, our results suggest that celecoxib seems to exhibit the most desirable gastrointestinal side effect profile.
Immune Mechanisms

Allergenicity of food proteins and its possible modification.

Author Coombs RR; McLaughlan P

Source Ann Allergy, 1984 Dec, 53:6 Pt 2, 592-6

All food proteins, taken via the oral route, are likely to be allergenic to some degree, but this usually leads to no untoward effects. Over the last decade excellent immunoassay methods have been developed that are suitable for measuring anti-food protein antibodies of different isotypes. General systemic and local tissue sensitivity to food antigens may also be measured by appropriate methods. All the circumstances (e.g., amount of ingestant, conditions in the gut, selective immunodeficiencies, gut permeability and genetic factors) determining heightened allergic responses are not yet fully understood. Allergic disease "caused by" food allergens may take on a variety of forms depending on the organ(s) bearing the brunt of the reactions: the gut itself, the skin, the lungs, joints or the entire body. Factors governing the severity of disease include the level of sensitization, the antibody isotype, the type of allergic sensitivity and again the extent of antigen absorption from the gut. Among the foods discussed are cow's milk and other formulae based on soya, chicken meat and hydrolysed casein for infant feeding. A test in guinea pigs to screen for potential oral sensitizing capacity of infant feeds is discussed, as is the effect of heat treatment of milks to reduce their sensitizing capacity. The antigenicity of cereal proteins per os in human adults and in laboratory animals is also dealt with.

Nonmurine animal models of food allergy.

Environ Health Perspect 2003 Feb;111(2):239-44 (ISSN: 0091-6765)

Helm RM; Ermel RW; Frick OL

Food allergy can present as immediate hypersensitivity [manifestations mediated by immunoglobulin (Ig)E], delayed-type hypersensitivity (reactions associated with specific T lymphocytes), and inflammatory reactions caused by immune complexes. For reasons of ethics and efficacy, investigations in humans to determine sensitization and allergic responses of IgE production to innocuous food proteins are not feasible. Therefore, animal models are used a) to bypass the innate tendency to develop tolerance to food proteins and induce specific IgE antibody of sufficient avidity/affinity to cause sensitization and upon reexposure to induce an allergic response, b) to predict allergenicity of novel proteins using characteristics of known food allergens, and c) to treat food allergy by using immunotherapeutic strategies to alleviate life-threatening reactions. The predominant hypothesis for IgE-mediated food allergy is that there is an adverse reaction to exogenous food proteins or food protein fragments, which escape lumen hydrolysis, and in a polarized helper T cell subset 2 (Th2) environment, immunoglobulin class switching to allergen-specific IgE is generated in the immune system of the gastrointestinal-associated lymphoid tissues. Traditionally, the immunologic characterization and toxicologic studies of small laboratory animals have provided the basis for development of animal models of food allergy; however, the natural allergic
response in large animals, which closely mimic allergic diseases in humans, can also be useful as models for investigations involving food allergy.

**Stability of food allergens to digestion in vitro.**

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An integral part of the safety assessment of genetically modified plants is consideration of possible human health effects, especially food allergy. Prospective testing for allergenicity of proteins obtained from sources with no prior history of causing allergy has been difficult because of the absence of valid methods and models. Food allergens may share physicochemical properties that distinguish them from nonallergens, properties that may be used as a tool to predict the inherent allergenicity of proteins newly introduced into the food supply by genetic engineering. One candidate property is stability to digestion. We have systematically evaluated the stability of food allergens that are active via the gastrointestinal tract in a simple model of gastric digestion, emphasizing the major allergens of plant-derived foods such as legumes (peanuts and soybean). Important food allergens were stable to digestion in the gastric model (simulated gastric fluid). For example, soybean beta-conglycinin was stable for 60 min. In contrast, nonallergenic food proteins, such as spinach ribulose bis-phosphate carboxylase/oxygenase, were digested in simulated gastric fluid within 15 sec. The data are consistent with the hypothesis that food allergens must exhibit sufficient gastric stability to reach the intestinal mucosa where absorption and sensitization (development of atopy) can occur. Thus, the stability to digestion is a significant and valid parameter that distinguishes food allergens from nonallergens.

**Digestibility of food allergens and nonallergenic proteins**

in simulated gastric fluid and simulated intestinal fluid-a comparative study.

J Agric Food Chem 2002 Nov 20;50(24):7154-60  (ISSN: 0021-8561)
Fu TJ; Abbott UR; Hatzos C U.S. Food and Drug Administration and Illinois Institute of Technology, National Center for Food Safety and Technology

Information on the comparative digestibility of food allergens and nonallergenic proteins is crucial when stability to digestion is to be used as a criterion to assess the allergenic potential of novel proteins. In this work, we compared the digestive stability of a number of food allergens and proteins of unproven allergenicity and examined whether allergens possess a higher stability than nonallergenic proteins of similar cellular functions, and whether there is a correlation between protein digestibility and allergenicity. The stability of groups of storage proteins, plant lectins, contractile proteins, and enzymes, both allergens and proteins with unproven allergenicity, in a standard simulated gastric fluid and a standard simulated intestinal fluid was measured. Food allergens were not necessarily more resistant to digestion than nonallergenic proteins. There was not a clear relationship between digestibility measured in vitro and protein allergenicity.
Antacids inhibit digestion of proteins & causes food allergy

J Allergy Clin Immunol 2003 Sep;112(3):616-23  (ISSN: 0091-6749)

Untersmayr E; Scholl I; Swoboda I; Beil WJ; Forster-Waldl E; Walter F; Riemer A; Kraml G; Kinaciyan T; Spitzauer S; Boltz-Nitulescu G; Scheiner O; Jensen-Jarolim E
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BACKGROUND: Digestible proteins were supposed to be irrelevant for oral sensitization and induction of food allergy. Approximately 10% of the adult population uses antacids for the treatment of dyspeptic disorders, drugs that hinder peptic digestion. In these patients, proteins that are normally degradable might act as food allergens. OBJECTIVE: We aimed to study the influence of antacid intake on the allergenicity of dietary proteins, taking sturgeon caviar and parvalbumin, the major fish allergen, as examples.

METHODS: Caviar proteins and recombinant parvalbumin from carp, rCyp c 1, were applied for intragastric feedings with or without the antacids sucralfate, ranitidine or omeprazole, using a Balb/c mouse model. RESULTS: Both caviar proteins and parvalbumin were rapidly degraded in an in vitro digestion assay at pH 2.0, but not at pH 5.0, imitating the effect of antacids. The groups fed with caviar in combination with ranitidine hydrochloride intramuscularly or sucralfate orally had significant levels of caviar-specific IgE antibodies (P <.01), T-cell reactivity, and elevated counts of gastrointestinal eosinophils and mast cells. Food allergy in these groups was further evidenced by oral provocation tests and positive immediate-type skin reactivity. In contrast, feedings with caviar alone led to antigen-specific T-cell tolerance. None of the groups showed immune reactivity against the daily mouse diet. As a proof of the principle, feeding mice with parvalbumin in combination with ranitidine or omeprazole intramuscularly induced allergen-specific IgE antibodies (P <.05).

The regulation of intestinal hypersensitivity reactions to ovalbumin by omega-3 fatty acid enriched diet.

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Abstract In order to clarify the mechanisms of food-sensitive enteropathy, a food hypersensitive model was generated by feeding ovalbumin to female BALB/c mice after intraperitoneal injection of cyclophosphamide and morphological and immunological changes in the gut mucosa were investigated. Villus atrophy, crypt hyperplasia and increased numbers of intra-epithelial lymphocytes (IEL) were confirmed in this model, as seen in food-sensitive enteropathy in humans. Subpopulations of IEL and lamina propria lymphocytes were enumerated by immunohistochemical observation. CD8-positive cells were increased both in epithelium and lamina propria, whereas CD4-positive cells were decreased in lamina propria. We document here that orally administered food antigen actually induces food-sensitive enteropathy and mucosal damage is generated by lymphocytes that infiltrate the intestinal mucosa. We also investigated the effect of feeding an omega-3 fatty acid-enriched diet in this model and found that it was efficient in attenuating mucosal damage.
Milk proteins, cytokines and intestinal epithelial functions


This paper discusses the relationship between food antigens, lymphocytes and the epithelial properties of the jejunum in children with cow's milk allergy. Experimental results indicate that increased protein permeability is not the primary cause of cow's milk allergy. Rather, results are interpreted as a secondary effect of an abnormal immunological response leading to mucosal inflammation and impairment of the endocytic process by the intestinal epithelial cells. Stimulation by cow's milk proteins caused the lymphocytes from infants with cow's milk allergy to release more tumor necrosis factor-alpha TNF alpha than those from control infants. After appropriate antigenic stimulation, the cytokines released by the activated lymphocytes from these infants perturbed epithelial function, in particular its barrier capacity. Tumor necrosis factor alpha, together with gamma interferon are involved in these adverse effects. It is thought that bovine beta-lactoglobulin present in the intestinal lumen may be responsible for the secretory diarrhea observed in children with cow's milk allergy, as a consequence of stimulation of electrogenic chloride secretion. In addition, luminal foreign protein may stimulate the submucosal cells. As a consequence, the submucosal release of mediators, including lymphokines, might alter the intestinal epithelial barrier. In conclusion, in physiological conditions, the subepithelial tissue that comprises the immune system and many other systemic systems receive information on the antigenic content within the intestinal lumen via the intestinal epithelium.

Analysis of a common inheritable idiotype in IgA-deficient sera

J Immunol 1988 Jun 1;140(11):3880-6 (ISSN: 0022-1767)

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In these studies we describe the production of three mAb raised to an idiotype on an IgG anticasein antibody isolated from the serum of one IgA-deficient blood donor. These are IgM kappa and block the binding of casein Ag to anticasein antibody. Sera of unrelated IgA-deficient donors were tested for the presence of the idiotype; 15 of 56 IgA-deficient sera (25%) contain the anticasein idiotype, whereas 1 of 45 normal sera was positive. Anticasein antibodies as a whole were predominantly of the IgG1 and IgG3 subclass; idiotype-positive anticaseins are predominantly of the IgG1 subclass. For IgA-deficient donors, the relative amount of idiotype-positive anticasein antibody was correlated with the level of anticasein present in the serum. Studies were done to investigate the potential inheritance of the idiotype in families; in three of four families the idiotype was inherited in an apparent autosomal dominant pattern. Our data show that a common cross-reactive idiotype can be detected in the sera of IgA-deficient individuals and their family members. This suggests that V region markers may be conserved in this humoral immunodeficiency disease.
Essential role of Id2 in negative regulation of IgE


Serum concentrations of immunoglobulin E (IgE) in normal circumstances are kept much lower than those of other Ig isotypes to avoid allergic reactions. B cells lacking Id2 have increased E2A activity, which leads to specific enhancement of germline transcription of the immunoglobulin locus. As a consequence, Id2-deficient B cells undergo class switch recombination (CSR) to IgE at a much higher frequency than wild-type B cells. In contrast, Id2 is induced in wild-type B cells by transforming growth factor-β1 (TGF-β1) and suppresses IgE CSR. Our results provide evidence for the inhibitory and selective role of Id2 in IgE CSR in response to TGF-β1. Id2 might act as molecular safeguard to suppress IgE CSR to prevent serious complications such as allergic hypersensitivity during the normal course of immune responses.

Mechanisms in adverse reactions to food

Author Strobel S
Address Division of Cell and Molecular Immunology, Institute of Child Health, London
Source Allergy, 50: 20 Suppl, 1995, 18 - 25
Abstract The intestinal tract is the major immunological organ of the human body. The gut associated lymphoid tissues (GALT) play an important role in the suppression of adverse reactions to foods and in the induction of "Oral Tolerance". Immunologically mediated clinical reactions to foods exist outside the gut environment and can affect virtually all organ systems.

Immunochemistry of food antigens.

Author Gjesing B; Lwenstein H
Source Ann Allergy, 1984 Dec, 53:6 Pt 2, 602-8
The complex mixture of molecules called food contains many types of molecules, some of which cause allergic or pseudo-allergic reactions in some humans. The identification of the antigenic molecules in the various foods and the type of allergic reaction they elicit is important for the satisfactory diagnosis in the individual patient and in the control of modified foods. The study of food antigens by crossed immunoelectrophoresis allows investigations of individual antigens without the interference of other antigens which are present simultaneously. We studied cow's milk electrophoresed into anti-bovine whey and anti-bovine casein. A number of precipitates are described, including albumin, alpha-lactalbumin, beta-lactoglobulin and immunoglobulin. The compositions of different infant milk formulae are compared with cow's milk heated under varying conditions. Albumin and immunoglobulins are the most labile components while beta-lactoglobulin is able to withstand even proteolysis by pepsin for some time. The antigenicity of these proteins in humans is shown by the presence of precipitating antibodies and specific IgE in human sera. Data from hen's egg white and wheat flour are reviewed in the same light. As an
example of a reaction that is very difficult to differentiate from an immune reaction, the possible role of lectins is discussed.

**T-cell mediated immunity in food allergy.**

Author Ferguson A

Source Ann Allergy, 1983 Aug, 51:2 Pt 2, 246-8

Abstract There are many T-cells within the intestinal mucosa, and histopathology, applied to biopsies of intestinal mucosa taken before and after food reintroduction, provides information on possible cell-mediated immunity to foods within the gut. Food sensitive enteropathies occur in man and in domestic animals, particularly in the young. Our hypothesis is that these are related to a relative deficiency of suppressor T-cells. There is no evidence that T-cell-mediated immunity to foods plays a part in severe atopic eczema, even in patients with clinical evidence of associated food allergy and high titres of IgE antibodies to foods.

**Mechanisms in adverse reactions to food. The brain.**

Authors Anderson JA. Institution Division of Allergy & Clinical, Henry Ford Hospital, Detroit, Michigan, USA. Source Allergy. 50(20 Suppl):78-81, 1995.

Abstract Specific chemical mediator release such as histamine and the prostaglandins (PG2a or PGD2) associated with headaches has been found in a few patients who were repeatedly challenged with specific foods, using DBPCFC techniques.

**Mechanisms in adverse reactions to food. The gastrointestinal tract.**

Author Ferguson A Address Dept. of Medicine, Univ. of Edinburgh, Western General Hospital, Scotland. Source Allergy, 50: 20 Suppl, 995, 32-8

Abstract Application of strict diagnostic criteria to celiac disease has led to the realization that there is a wide clinical spectrum within this disease. Normally there are immune reactions to dietary proteins, particularly secretory antibodies of IgA class, low titers of serum antibody and specific down-regulation of IgE and T cell reactivity (oral tolerance). From time to time, abnormal immunity to foods, either as inappropriately high titers of antibodies or qualitatively altered responses, produce disease. Lactase deficiency, with dose-related lactose and milk-intolerance, occurs in 50-90% of most populations. White, western Europeans are the exception.

**A kinin model for food and chemical sensitivities:**

Author Bell IR

Source Ann Allergy, 1975 Oct, 35:4, 206-15

Abstract The plasma peptide hormone bradykinin is hypothesized to be a major mediator of the multiple-system functional symptomatology of adverse food and other chemical reactions. It is postulated that native foods as organic chemicals could act cumulatively with other stresses to mobilize directly the kinin-forming enzyme system.
Skin manifestations in childhood food allergy.

Author Oehling A; Fernández M; Córdoba H; Sanz ML Address Department of Allergology and Clinical Immunology, Faculty of Medicine, University of Navarra, Pamplona, Spain.


Abstract According to Hansen's contact rule, the digestive system should be considered as the main shock organ, yet in food allergy, this is not the case. Very often specific food triggers clinical manifestations not involving the digestive system; that is, reactions are manifested either in the respiratory system, as asthma or rhinitis, or in the skin. In these cases the BALT (broncho-alveolar lymphoid tissue) and GALT (gastrointestinal lymphoid tissue) units play a basic role in the sensitizations. The purpose of this study was to determine the most frequent skin manifestations of food allergy among children, and the most frequently involved foods. We also thought it interesting to evaluate the diagnostic reliability of the different standard immunological parameters utilized by the study team in food allergy. All patients underwent intracutaneous tests with 12 groups of the most frequent food allergens, as well as serum IgE, antigen-specific IgE against foods, and antigen-specific histamine release tests. Antigen-specific IgG4 determination was performed in some cases. The results obtained confirmed previous studies, the most common manifestations being: angioedema (48%), followed by urticaria (31%) and atopic dermatitis (21%). Regarding the frequency of sensitization to different food allergens, in mono- or polysensitization, fish and egg stand out in our environment. Certain food allergens are more frequently responsible for specific skin manifestations. Thus, for fish sensitization, the most frequent skin manifestation is atopic dermatitis (50%); for egg sensitization, angioedema is the most frequent skin manifestation (50%); and for milk, urticaria (50%). Finally, and in agreement with previous works regarding the diagnostic reliability of in vitro techniques, we found that the histamine release test offered the highest percentage of diagnostic reliability. Only for sensitization to milk proteins did antigen-specific IgE demonstrate higher reliability. Once again, we stress that our main problem is the lower reliability of skin tests against food allergens than against inhalant allergens. We emphasize the importance of food as a major factor in the etiopathogenesis of atopic dermatitis, as well as the need to complement the study, when possible, by means of the in vitro techniques described.

Mechanisms in adverse reactions to food. The eye.

Author Bonini S; Bonini S Address Chair of Clinical Immunology and Allergy, Second University of Naples, Instituto di I Clinica Medica, Policlinico Umberto, Rome, Italy.

Source Allergy, 50: 20 Suppl, 1995, 68-73

Direct action of triggers on the target organ may cause vasodilation, exudation, hypersecretion and nerve endings stimulation without participation of mast cells and basophils. Non IgE-mediated release of mediators from mast cells and basophils may explain how triggers other than allergens can induce pseudo-allergic reactions. IgE-mediated triggering of mast cells and basophils is not confined - in the eye too - to an immediate reaction, but represents the starting point for a progression to a late-phase reaction with the participation of a network of several cells and mediators. Inflammatory changes associated with late-phase reaction in the eye represent the pathophysiological basis for a non-specific hyperreactivity to various triggers.
Anaphylaxis. A review of 266 cases.

Author Kemp SF; Lockey RF; Wolf BL; Lieberman P Address Department of Internal Medicine, University of Tennessee College of Medicine, Memphis, USA. Source Arch Intern Med, 155: 16, 1995 Sep 11, 1749-54

A presentation of findings from a large population of anaphylaxis cases. METHODS: Retrospective chart review and follow-up questionnaire provided data on 266 subjects (113 males and 153 females) aged 12 to 75 years (mean age, 38 years) who were referred to a university-affiliated private allergy-immunology practice in Memphis, Tenn, for evaluation and management of anaphylaxis from January 1978 through March 1992. RESULTS: Of 266 subjects, 162 (61%) had three or more anaphylactic episodes, 41 (15%) had two episodes, and 63 (24%) had one episode. Atopy was present in 98 individuals (37%). Physicians thought foods, spices, and food additives caused anaphylaxis in 89 individuals (34%); crustaceans and peanut accounted for about half of these cases. Medications were thought to have caused the anaphylactic episodes in 52 individuals (20%); nonsteroidal anti-inflammatory drugs in about half of these cases. Other probable causes included exercise (n = 19), latex (n = 2), hormonal changes (n = 2), and insect bites (n = 4). A suspected cause could not be determined in 98 individuals (37%). These subjects were diagnosed as having idiopathic anaphylaxis. Of the 266 subjects, 102 responded to a follow-up survey; 68 (67%) of the 102 were thought to have identifiable causes of anaphylaxis (32 of whom [47%] failed to carry epinephrine syringes for self-administration despite instructions to do so). In contrast, of 34 subjects with idiopathic anaphylaxis who responded to the survey, only three (9%) did not carry epinephrine. CONCLUSIONS: (1) Atopy is common in subjects who experience anaphylaxis, regardless of its origin; (2) crustaceans and nonsteroidal anti-inflammatory drugs are the most common food and medication groups, respectively, thought to cause anaphylaxis; (3) causative agents can be identified for two thirds of the subjects, and recurrent attacks are the rule; and (4) subjects with idiopathic anaphylaxis are more likely to carry epinephrine for self-administration than those with identifiable causes.

Food-dependent exercise-induced anaphylaxis.

Author Kidd JM 3d; Cohen SH; Sosman AJ; Fink JN Source J Allergy Clin Immunol, 1983 Apr, 71:4, 407-11

This article describes four cases of exercise-induced anaphylaxis occurring only in temporal relationship to the ingestion of food. One individual developed anaphylaxis if exercise followed the ingestion of any food within 2 hr. Three other individuals had symptoms only if celery was ingested in relation to exercise. Skin reactivity to fresh celery extracts was demonstrated in all three individuals. The episodes were prevented by avoidance of food ingestion in relation to exercise. This syndrome appears to be a variant of exercised-induced anaphylaxis.
Life-threatening, recurrent anaphylaxis caused by allergy to gliadin and exercise.

Author Varjonen E; Vainio E; Kalimo K
Address Department of Dermatology, University Hospital of Helsinki, Finland.
Source Clin Exp Allergy, 1997 Feb, 27:2, 162-6

BACKGROUND: Exercise-induced urticaria or anaphylaxis is regarded as a distinct form of physical allergy. In some patients the symptoms occur only after ingestion of various food products in connection with exercise. We have come across patients with cereal dependent exercise-induced anaphylaxis. OBJECTIVES: The purpose of the present study was to analyse the allergens in cereals responsible for the severe anaphylactic symptoms and to verify the test methods suitable for screening the patients with cereal dependent exercise-induced anaphylaxis. METHODS: The patients underwent skin-prick tests (SPT) with common inhalant and food allergens as well as with various cereal extracts. IgE-immunoblotting was used to identify the allergenic fractions. RESULTS: Five patients found positive in SPT with NaCl wheat suspension had IgE antibodies to wheat, rye, barley and oats, especially directed against the ethanol-soluble protein fractions in immunoblotting. No IgE antibodies were detected against other cereals. The patients had been unaware of any cereal allergy since anaphylaxis occurred only in association with exercise postprandially. The patients were directed to follow a gluten-free diet and have been free from symptoms, being able to continue their outdoor physical activities. CONCLUSION: Wheat gliadin and the corresponding ethanol-soluble proteins of taxonomically closely related cereals were found to be the allergens in cereal-dependent exercise-induced anaphylaxis. Skin-prick testing with NaCl wheat suspension was a simple and practical test to screen patients with this kind of occult, possibly life-threatening, allergy to cereals.

T-cell regulation in allergic reactions.

Author Jansen HM; Kapsenberg ML Address Department of Pulmonology, Academic Medical Center, University of Amsterdam, Netherlands. Source Neth J Med, 45: 6, 1994 Dec, 319-28

Atopy is characterized by an increased tendency to form antibodies to airborne and food proteins. Specific IgE is central to the induction of allergic diseases through its binding of the high-affinity receptor on mast cells and basophils. Cross-linking by allergens of the bound IgE leads to an immediate release of various inflammatory mediators at the local site in the shock organ. Repeated exposure to allergens may lead to the induction of a more chronic inflammatory process where the local influx of T-lymphocytes and eosinophils appears to be an important event. There has been increasing recognition that cytokines, produced by a variety of inflammatory cell subsets, including T-cells, induce this ongoing inflammatory state. Besides, CD4+ T-helper-2 (Th2) cell products like IL-4 play a crucial role in the regulation of the production of specific IgE by B-cells. IL-4 appears to be the immunoregulatory cytokine with a relatively restricted action on reactive cells in this specific immune reaction. The effects of IL-4 are antagonised by IFN-gamma, and vice versa. Proliferation and differentiation of Th2 subsets producing predominantly IL-4 and IL-5 and no IFN-gamma provide an essential signal for isotype switching to IgE in B-cells, on the one hand, and direct the activation and influx of inflammatory effector cells such as eosinophils, on the other hand. In this report the causal relationship between the induction and expression of Th2 cells the IgE production and eosinophilia in atopic allergies is briefly reviewed.
Human epithelial cells trigger dendritic cell–mediated allergic inflammation by producing TSLP


Whether epithelial cells play a role in triggering the immune cascade leading to T helper 2 (TH2)-type allergic inflammation is not known. We show here that human thymic stromal lymphopoietin (TSLP) potently activated CD11c+ dendritic cells (DCs) and induced production of the TH2-attracting chemokines TARC (thymus and activation-regulated chemokine; also known as CCL17) and MDC (macrophage-derived chemokine; CCL22). TSLP-activated DCs primed naïve TH cells to produce the proallergic cytokines interleukin 4 (IL-4), IL-5, IL-13 and tumor necrosis factor-α, while down-regulating IL-10 and interferon-γ. TSLP was highly expressed by epithelial cells, especially keratinocytes from patients with atopic dermatitis. TSLP expression was associated with Langerhans cell migration and activation in situ. These findings shed new light on the function of human TSLP and the role played by epithelial cells and DCs in initiating allergic inflammation.

Hypersensitivity reaction in an infant fed hydrolyzed lactalbumin contained in a semi-elemental formula

Author Heyman MB; Stoker TW; Rudolph CD; Frick OL Address Department of Pediatrics, University of California, San Francisco 94143-0136. Source J Pediatr Gastroenterol Nutr, 10: 2, 1990 Feb, 253-6

Abstract Following introduction of milk protein formula feedings, a 6-month-old male developed profuse, watery diarrhea progressing to shock, requiring cardiopulmonary resuscitation. Reinstitution of enteral feedings with a formula containing hydrolyzed lactalbumin (Travasorb STD) resulted in recurrence of diarrhea with fever. Intestinal and rectal biopsies showed only nonspecific inflammatory changes. He was discharged on an elemental formula (Vivonex). Twenty-three months later, while admitted for evaluation of hypophosphatemic rickets, immunologic testing using the lymphocyte migration inhibition factor (LIF) test demonstrated positive reactions, especially to alpha-lactalbumin (56% inhibition) and whole cow's milk (22%, normal of less than 20% inhibition). Skin tests revealed sensitivity to cow's milk and eggs. Soy formula also produced diarrhea and bloody stools. Protein hydrolysate formulas, touted as hypoallergenic diets, are useful in infants with intolerance to milk protein. This is the first documented case of an immunological reaction to the hydrolyzed whey protein, lactalbumin. Although protein hydrolysate formulas are effective treatment in most infants with milk protein intolerance, allergic reactions are possible. Caution and close observation should be exercised in immunologically sensitized infants rechallenged with any formula.
Cumulative incidence of atopic disorders in high risk infants fed whey hydrolysate, soy, and conventional cow milk formulas.

Author Chandra RK; Hamed A
Address Department of Pediatrics, Memorial University of Newfoundland, St. John's, Canada.
Source Ann Allergy, 67: 2 Pt 1, 1991 Aug, 129-32

Abstract A recent increase in the prevalence of atopic disorders and the enormous costs of management of atopic patients have prompted attempts at prevention. We have examined the effect of exclusive breast feeding and of feeding different infant formulas on incidence of atopic disease in a prospective randomized controlled study. Seventy-two infants were recruited into each of the following groups: cow milk whey hydrolysate formula (NAN/HA) conventional cow milk formula (Similac), soy-based formula (Isomil), and exclusive breast feeding for greater than 4 months. The cumulative incidence of atopic eczema, recurrent wheezing, rhinitis, gastrointestinal symptoms, and colic were noted. Skin prick tests and radioallergosorbent tests for IgE antibodies to milk and soy were performed. At 12 and 18 months of age, the incidence of atopic eczema as also that of all atopic symptoms was significantly lower and similar in the breast-fed and whey hydrolysate groups, compared with the cow milk and soy formula groups. IgE antibodies were detected more often in the cow milk and soy formula groups, especially the former. Among symptomatic infants, fewer skin positive prick tests were seen in the soy group compared with the cow milk group. Our observations show that among infants at high risk of developing atopic disease because of positive family history, exclusive breast feeding or whey hydrolysate formula is associated with a lower incidence and thus a delay in the occurrence of allergic disorders compared with groups fed conventional cow milk or soy formulas.

Follow-up of nutritional status and dietary survey in children with cow's milk allergy.

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Abstract The nutritional status of children with cow's milk allergy was followed during an elimination diet in 19 children (9 boys and 10 girls) beginning at the mean age of two years (range 0.6-4.1 years). The cow's milk allergy had been verified in hospital by a challenge test at a mean age of 0.9 years (range 0.2-1.9 years). Weight, height and laboratory indices to test protein, mineral and vitamin status were measured at three follow-up visits at three-month intervals. In addition to cow's milk allergy all these children had some other food allergies, and six of the 19 children were allergic to soy protein. Only two of the 19 children were given a soy-based formula. In the diets of the other children, cow's milk was replaced by increasing amounts of other foodstuffs and supplementary calcium. At the beginning of the study the relative heights of the children were slightly retarded (-0.6 SD) and remained unchanged during follow-up (-0.8 SD at the end of the study). The relative weights were found to be decreased during follow-up (p less than 0.05). There was a significant reduction in serum prealbumin values; eight of the 19 children showed abnormally low values. Low serum zinc values were seen in 12
children. Serum iron concentration was low in two children and two had high serum alkaline phosphatase values. Seven-day food recording indicated that dietary intake of energy was below the recommendation in some children, but protein intake was high. Some children had low intakes of riboflavin.

**Diet and nutritional status in children with cow's milk allergy.**

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The purpose of this study was to investigate the nutritional status and adequacy of the diet in the children with cow's milk allergy (CMA). DESIGN AND SUBJECTS: 18 children with challenge-proven CMA and 20 healthy children were investigated in the cross-sectional study. The mean (range) age of the children was 2.0 (1.0-3.5) years. The healthy children were matched by age and sex with the allergic children. Food consumption data were collected by the six-day food record method. The weight and height of both groups and laboratory indices of children with CMA were measured to study the nutritional status. RESULTS: Thirteen (72%) of the children with CMA used a formula based on soy or casein hydrolysate. The amounts of these formulas consumed by the allergic children were smaller (371 ml vs 559 ml; P < 0.01) than the amount of milk and milk products consumed by the healthy children. There was no difference in energy intake between the groups. Protein intake by the allergic children was lower (39 g vs 48 g; P < 0.05) and fat intake higher (47 g vs 39 g; P < 0.05) than that of the healthy children. The mean intakes of energy and zinc in both groups, and the intake of iron in the healthy children, were below the RDAs. The diet in the allergic children was supplemented with calcium and in 11 children with vitamins A and D. Fourteen healthy children had vitamin A and D supplement. The height-for-age was lower in the children with CMA (-0.6 vs +0.2 s.d. units; P < 0.05) as compared to healthy children. Serum biochemical measurements were within the reference range in the allergic children, and no nutritional problems were found. CONCLUSIONS: For the eliminated foods children with CMA substituted nutritionally corresponding food items which resulted in adequate mean intakes of nutrients. Specific formulas contributed substantially to the nutrient intake. Children with CMA need intensive nutritional counselling and regular monitoring of growth.
In vitro allergenicity of cows' milk substitutes.

Author Dean TP; Adler BR; Ruge F; Warner JO
Address Department of Child Health, Faculty of Medicine, University of Southampton, U.K.
Source Clin Exp Allergy, 23: 3, 1993 Mar, 205-10
Abstract There are numerous alternatives to cows' milk formula for allergic children. We have investigated the allergenicity of several of these using RAST and RAST inhibition on serum from 16 patients with a known history of cows' milk protein intolerance (CMPI) and 16 atopic controls. A RAST grade of > or = 3 for cows' milk was present in all those with CMPI, whilst all the controls gave RAST of < or = 1. Modified cows' milk formula, goats' infant formula, sheep and goats' milk produced similar results to cows' milk. Only two patients had RAST > or = 3 for soya milk and the soy/beef hydrolysate gave positive results in only three patients. One had positive RAST to Nutramigen and two to Pregestimil. Of the whey hydrolysates investigated, Pepti-junior gave seven positive RASTs whilst we were unable to bind Alfare to the sepharose in sufficient quantities to interpret the results which were negative in all cases. RAST inhibition data on pooled sera from the same patients agreed with the RAST results. The inhibition curves showed high inhibition with goats', sheep, modified cows' milk formula and the casein formula, AL110 (50%). Soy and soy/beef hydrolysate showed a much lower inhibition pattern. Casein hydrolysates showed low inhibition while the whey hydrolysate produced higher inhibition. We have shown that despite claims of low allergenicity, some of these alternative formulae are antigenically recognized in vitro by some cows' milk intolerant patients.

diagnosing allergy by studying eosinophil morphology

Author Nisheva ES; Potikhonova NA; Popova RD
Source Klin Lab Diagn, 2, 1995 Mar-Apr, 29-32
Abstract A total of 107 children with various clinical manifestations of food allergy were examined to investigate the morphological changes of eosinophils under the effect of food allergens. Eosinophil "injury" caused by cow milk allergen was detected in 71.4%, that caused by hen egg white in 82.4%, and that under the effect of fish in 77.8% of the examinees, these data being useful as a laboratory test for the diagnosis of food sensitization. Correlation between the index of eosinophil injury and late reactions to cow milk, as well as increased reactivity to nonspecific stimuli were traced.
Food allergy in cystic fibrosis.

Author Lucarelli S; Quattrucci S; Zingoni AM; Frediani T; Diamanti S; Quintieri F; Barbato M; Cardi E; Antonelli M

Address Istituto di Clinica Pediatrica, Università degli Studi di Roma, La Sapienza.

Source Minerva Pediatr, 46: 12, 1994 Dec, 543-8

Abstract Food allergy was investigated in 20 children with cystic fibrosis (CF), who still suffered from diarrhea and failed to thrive, in spite of adequate diet and enzyme treatment (group A). The study also included two age-matched control groups, comprising 10 CF children without intestinal symptoms and/or failure to thrive (group B), and 20 healthy children (group C). Skin tests were positive and total IgE higher than the mean + 2SD respectively in 14/20 and 11/20 patients of group A, in 3/10 and 2/10 patients in group B and in none in group C. The specific IgE were present in 6/14 children in group A whose skin tests were positive and in none in group B. There was no significant difference between group A and group B (p > 0.05). The levels of specific antibodies IgG, IgA and IgM were overall higher than the mean + 2SD of the normal in 18/20 in group A, in 6/10 in group B and in none in group C. The measurement by ELISA of specific antibodies for cow milk and egg proteins showed a statistically significant difference for casein, beta-lactoglobulin and ovalbumin between the IgG (p < 0.05) and IgA (p < 0.001) levels in group A and the other groups (B and C). Symptoms improved in 90% of CF patients (group A) when the implicated foods were eliminated from the diet and in 78% the oral provocation test resulted positive. The occurrence of food allergy must be considered in CF patients who do not improve with the conventional treatment. In these patients immunological investigations, in particular the measurement of IgG, IgA and IgM specific antibodies, are useful for diagnosis and in selecting an appropriate diet leading to an improvement in nutritional status.

beta-lactoglobulin in hydrolysed protein formulas

Author Mäkinen-Kiljunen S; Sorva R Address University Central Hospital, Department of Allergology, Helsinki, Finland. Source Clin Exp Allergy, 23: 4, 1993 Apr, 287-91

Abstract A bovine milk protein, beta-lactoglobulin (beta LG), was measured by an enzyme-linked immunosorbent assay (ELISA) in seven different infant formulas based on protein hydrolysates from cows' milk whey or casein, and from bovine collagen and soy. beta LG levels in the formulas were 1/100 to 1/4,800,000 lower than in cows' milk (CM). There was a great difference in the beta LG level between the partly and the extensively hydrolysed formulas; the amount of beta LG was 40,000-fold higher in the partial hydrolysates vs the extensively hydrolysed formulas. Residual beta LG may have been responsible for the allergic reactions described in some children with cows' milk allergy (CMA) receiving these formulas.

Interferon-gamma in peanut allergy,

Author Dorion BJ; Burks AW; Harbeck R; Williams LW; Trumble A; Helm RM; Leung DY Address Department of Pediatrics, National Jewish Center for Immunology Denver, CO 80206. Source J Allergy Clin Immunol, 93: 1 Pt 1, 1994 Jan, 93-9
Abstract The current study was undertaken to examine the potential role of T cells in the pathogenesis of peanut allergy. Peripheral blood mononuclear cells (PBMCs) from patients with peanut allergy, patients with asthma, and nonatopic normal control subjects were assessed for proliferation after stimulation with a 17 kd major peanut allergen (Ara h II), ovalbumin, casein, soy, and Candida albicans. We found that Ara h II and C. albicans induced significantly higher levels of proliferation than ovalbumin, casein, and soy. Because interferon-gamma (IFN-gamma) and interleukin-4 (IL-4) play critical roles in IgE regulation, we assessed the production of these cytokines after stimulation with C. albicans and Ara h II. C. albicans stimulated similar levels of IFN-gamma in all three study groups. In contrast, after stimulation with Ara h II, culture supernatants from PBMCs of subjects with peanut allergy contained significantly lower levels of IFN-gamma than did the PBMCs of the two control groups (p = 0.02). More important, there was a significant (p = 0.05) inverse correlation between the serum IgE anti-Ara h II levels and IFN-gamma production by PBMCs from the respective peanut-allergic patients. IL-4 protein was not detected in culture supernatants of PBMCs stimulated with Ara h II. However, amplification of cytokine gene transcripts by polymerase chain reaction did demonstrate IL-4 expression in Ara h II-stimulated PBMCs from both patients with peanut allergy and control subjects. These data suggest that the level of IFN-gamma production in response to Ara h II may be an important factor in determining the development of peanut-specific IgE responses.

patients with milk or soy protein enterocolitis.

Author Burks AW; Casteel HB; Fiedorek SC; Williams LW; Pumphrey CL
Address University of Arkansas for Medical Source Pediatr Allergy Immunol, 5: 1, 1994 Feb, 40-5

Abstract The soybean protein isolate used in powdered soybean formula is hydrolyzed more extensively than the isolate, which is used in liquid soybean formula in most commercial soybean formulas. Previous in vitro studies have shown differences in human antibody response to these soybean protein isolates. Therefore, a prospective clinical study was undertaken to determine if there were differences in adverse reaction rates to these soybean protein isolates. Forty-three patients with possible milk- and/or soy-protein enterocolitis were enrolled in this study. Patients had 3 separate oral food challenges; using milk formula, soybean powder formula and soybean liquid formula. Ten (23%) patients challenged with milk had positive challenges. Fourteen (33%) patients challenged with powdered soy formula had positive challenges while thirteen (30%) challenged with liquid soy formula had positive challenges. In the 10 patients with positive milk challenges, 6 (60%) had a positive soy challenge. In the group with positive soy challenges, 5 reacted to the powdered soy challenge done first, but not the second challenge with the liquid soy formula, and 4 patients reacted to the liquid soy formula challenge done first, but not the second challenge with the powdered soy formula. These results indicate that a significant number of patients with milk protein enterocolitis have soy protein enterocolitis. In addition, an order effect can be demonstrated in the soy challenges because of the tendency to react to the first soy challenge regardless of the type of isolate. These results suggest that a local immune effect caused by the protein may be present.
Food Allergy

**Treatment of delayed food allergy**


This preliminary, descriptive study after extensive clinical experience demonstrates specific IgG food RASTs done in 114 consecutive patients with strong positive histories for delayed food allergy. Elimination of the positive foods was the sole means of treatment. The symptoms leading to the test are detailed, and the method of workup is reviewed. The overall results demonstrated a 71% success rate for all symptoms achieving at least a 75% improvement level. Of particular interest was the group of patients with chronic, disabling symptoms, unresponsive to other intensive treatments. Whereas 70% obtained 75% or more improvement, 20% of these patients obtained 100% relief.

**Cutaneous lymphocyte antigen**


T cells play a pathogenic role in many inflammatory and certain malignant skin diseases, including psoriasis, atopic and allergic contact dermatitis, and cutaneous T-cell lymphoma. Memory T cells that infiltrate the skin express a unique skin-homing receptor called cutaneous lymphocyte-associated antigen (CLA), a carbohydrate epitope that facilitates the targeting of T cells to inflamed skin. CLA is defined by both its reactivity with a unique monoclonal antibody, HECA-452, and its activity as a ligand for E-selectin, but the structure of the protein component of CLA has not previously been defined. Here we report that CLA is an inducible carbohydrate modification of P-selectin glycoprotein ligand-1 (PSGL-1), a known surface glycoprotein that is expressed constitutively on all human peripheral-blood T cells. Cultured peripheral-blood T cells can be differentiated into CLA-bearing cells, which bind both E-selectin and P-selectin, or CLA-negative cells, which bind P-selectin but do not bind E-selectin, suggesting that there is independent regulation of selectin-binding phenotypes. We propose that differential post-translational modification of a single cell-surface receptor, PSGL-1, mediated by fucosyltransferase VII, serves as a mechanism for regulating tissue-specific homing of memory T cells.
**Antigen-specific secretory IgA antibodies** in the gut are decreased in a mouse model of food allergy.

*J Allergy Clin Immunol.* 2004; 114(2):377-82 (ISSN: 0091-6749)

Frossard CP; Hauser C; Eigenmann PA
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**BACKGROUND:** A large body of evidence implicates IgA antibodies in the immune response to pathogens present in the gut. Whether IgA antibodies play a similar role in food allergy remains to be determined. **OBJECTIVE:** We sought to characterize beta-lactoglobulin (BLG)-specific serum and secretory IgA antibody production in the gut and to define the role of antigen-induced cytokines in IgA production in a murine model of food allergy. **METHODS:** BLG-specific IgA antibodies were measured in the sera and feces of mice anaphylactic or tolerant to BLG. The number of antibody-secreting cells in the spleen and Peyer's patches was determined by means of ELISPOT. Mesenteric lymph node cells and Peyer's patch T cells were transferred to naive mice, and antibody production in the sera and feces in recipient mice, as well as antibody-secreting cell numbers, were measured. **RESULTS:** Serum IgA antibody titers were strongly increased in anaphylactic mice. In contrast, BLG-specific IgA antibody titers were increased in feces but not in sera from tolerant mice. These results were correlated with an increased number of BLG-specific IgA-secreting cells in Peyer's patches from tolerant mice. The adoptive transfer of Peyer's patch CD3+ cells from tolerant mice induced an increased number of IgA-secreting cells preferentially in the Peyer's patches of naive recipient mice. Furthermore, an increase of BLG-induced IL-10 and TGF-beta levels was found at IgA production sites. **CONCLUSIONS:** These results suggest a role for secretory IgA in tolerance mechanisms to foods. Peyer's patch CD3+ cells are primarily involved by favoring IgA production through the release of IL-10 and TGF-beta.

**Food Sources and Antigen Identification**

**Threshold doses of food allergens**


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**PURPOSE OF REVIEW:** The purpose of this review is to bring the reader up to date on the importance of assessing a food's lowest observed adverse effect level (LOAEL) with two aims. Firstly, to help industry choose tests with a level of sensitivity capable of detecting food allergens hidden in industrial products. Secondly, to specify protective measures for highly allergic individuals in order to prevent recurrent severe anaphylaxis. The review also seeks to highlight the present issues and unsolved questions. **RECENT FINDINGS:** Thanks to standardized oral-provocation tests (double-blind placebo-controlled food challenges), LOAELs have been identified for many IgE-dependent food allergies. Most studies concern the pediatric population. Data is available for milk, egg, peanut, wheat flour, and sesame. The LOAELs are commonly in the range of 1-2 mg of natural foods, representing a few hundred micrograms of protein. These minimal reactive doses characterize about 1% of people allergic to milk, egg, or peanut. The level at which no observed adverse effect is seen might be a few tens of micrograms of protein for...
peanut. At the present time, allergy to oil seems to be restricted to unrefined cold-pressed oils. SUMMARY: Concerning IgE-dependent food allergies, the threshold dose inducing symptoms is now known to vary a great deal according to the individual. A reactive dose of less than 65 mg characterizes 16 and 18% of patients allergic to egg or peanut. Less than 30 mg of milk proteins characterizes 5% of those allergic to milk. For milk, egg, and peanut, 1% of patients have a very low threshold, about 1 mg. Such data emphasize the necessity of using detection tests with a sensitivity better than 10 parts per million. The modifications of allergenicity undergone by protein ingredients that are now commonly introduced into industrially made products are not yet sufficiently known. A better knowledge of the reactive doses of these proteins is needed.

**Wheat flour allergy**

An entire diagnostic tool for complex allergy.

*Allerg Immunol (Paris).* **2006; 38(2):59-61** (ISSN: 0397-9148)

Battais F; Richard C; Szustakowski G; Denery-Papini S; Moneret-Vautrin DA; Leduc V; Gu?rin L

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Wheat proteins are involved in respiratory allergy, contact allergy and food allergy. Wheat allergens involve in these pathologies are well-known. However, establishment of wheat allergy diagnostic can be sometimes difficult on account of the complex allergenic composition of skin prick test (SPT) solutions of wheat flour. Therefore, we have studied specific IgE reactivity from patient sera with wheat food allergy, and characterized allergenic composition of wheat SPT solutions by specific antibodies directed to wheat allergens. The results showed that 20 of the 25 sera analyzed contained specific IgE to at least one wheat protein fraction. Among positive sera, 75% have specific IgE to water/salt soluble fraction, 85% to native gluten fractions and 65% to wheat isolate fraction. The results showed also that SPT solutions of wheat flour contained major food allergens from each allergenic fraction. These results highlighted the importance of using fractions, which constitute the whole wheat allergenic pattern, during specific IgE reactivity analyses. Moreover, we have observed that wheat isolate extract (results of food industrial process) contained not only modified allergens (neo-allergens) involve of specific food allergy to wheat isolate but also some native allergens involve in wheat food allergy. Thus, these results showed the importance to use, for wheat in vivo diagnosis together wheat SPT solutions (gluten extract and wheat isolate) in order to differentiate wheat food allergy to specific wheat isolate allergy.
The allergenicity of soybean-based products is modified by food technologies.

Int Arch Allergy Immunol 2002 Jul;128(3):212-9 Franck P; Moneret Vautrin DA; Dousset B; Kanny G; Nabet P; Guenard-Bilbaut L; Parisot L

BACKGROUND: Numerous products based on soybean are available and various food technologies are applied for their production. The allergenicity of natural soybean may be modified by these treatments. OBJECTIVES: To compare the allergenicity of native soybean proteins with those of soy milk and texturized protein products. To show additional allergens. METHODS: Three commercial products and two infant formulas were studied: Soybean flour, soy milk, texturized soy proteins, two infant formulas; the first containing total proteins and the second containing a soy protein hydrolysate. Sera from 9 patients allergic to soy protein were tested by immunoblotting (IB). IB inhibition was achieved by incubating sera with protein extract from soybean flour. RESULTS: The SDS-PAGE profile of soybean flour protein and soy milk showed a difference in the proportions of the various protein fractions, with a higher concentration of 37-kD protein in flour and 33-kD protein in milk. Infant formula 1 contained proteins with a molecular weight below 28 kD. The texturized extract contained high proportions of 31- to 34- and 38-kD proteins. Immunoblotting revealed a lack of allergenicity in infant formula. Sera recognizing the 38- and 50-kD proteins in texturized soy protein also recognized the 37- and 49-kD proteins in soybean flour and in soy milk, suggesting a protein glycation by texturization processes. The 30- to 34-kD band in texturized proteins was devoid of any allergenicity. This study seems to indicate that the 30-kD allergen (Gly m Bd 30) disappears during the production of texturized soy protein. CONCLUSION: All technologies applied to soybean-based products induce striking variation in the protein profile and allergenicity. Texturized protein could lack the major allergen Gly m Bd 30. Further studies or texturization might generate modified technologies in order to create hypoallergenic texturized proteins.

Plant food allergens sensitizing via the gastrointestinal tract.

Mills EN; Jenkins JA; Alcocer MJ; Shewry PR

The recently completed genome sequence of the model plant species Arabidopsis has been estimated to encode over 25,000 proteins, which, on the basis of their function, can be classified into structural and metabolic (the vast majority of plant proteins), protective proteins, which defend a plant against invasion by pathogens or feeding by pests, and storage proteins, which proved a nutrient store to support germination in seeds. It is now clear that almost all plant food allergens are either protective or storage proteins. It is also becoming evident that those proteins that trigger the development of an allergic response through the gastrointestinal tract belong primarily to two large protein superfamilies: (1) The cereal prolamin superfamily, comprising three major groups of plant food allergens, the 2S albumins, lipid transfer proteins, and cereal alpha-amylase/trypsin inhibitors, which have related structures, and are stable to thermal processing and proteolysis. They include major allergens from Brazil nut, peanuts, fruits, such as peaches, and cereals, such as rice and wheat; (2) The cupin superfamily, comprising the major globulin storage proteins from a number of plant species. The globulins have been found to be allergens
in plant foods, such as peanuts, soya bean, and walnut; (3) The cysteine protease C1 family, comprising the papain-like proteases from microbes, plants, and animals. This family contains two notable allergens that sensitize via the GI tract, namely actinidin from kiwi fruit and the soybean allergen, Gly m Bd 30k/P34. This study describes the properties, structures, and evolutionary relationships of these protein families, the allergens that belong to them, and discusses them in relation to the role protein structure may play in determining protein allergenicity.

**Immunoglobulin E antibodies in food allergy to crustaceans**

Recombinant tropomyosin from Penaeus aztecus (rPen a 1) for measurement of specific immunoglobulin E antibodies relevant in food allergy to crustaceans and other invertebrates.

*Mol Nutr Food Res.* **2004; 48(5):370-9** (ISSN: 1613-4125)

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Immunoglobulin E (IgE)-mediated food allergy to crustaceans and mollusks is relatively common and affected individuals typically react to a range of different species. The only known major allergen of shrimp was first described over 20 years ago and later identified as the muscle protein tropomyosin. This protein may be useful as a defined and relevant diagnostic marker for allergic sensitization to invertebrate foods. In order to generate an assay reagent suitable for this purpose, tropomyosin from the shrimp Penaeus aztecus (Pen a 1) was produced as a recombinant protein in Escherichia coli and characterized with respect to IgE antibody binding properties in comparison to natural shrimp tropomyosin. Hexahistidine-tagged rPen a 1 accumulated as a predominantly soluble protein in the E. coli expression host and a two-step chromatographic procedure provided a high yield of pure and homogeneous protein. rPen a 1 displayed chromatographic and folding characteristics similar to those of purified natural shrimp tropomyosin. Serum preincubation with serial protein dilutions revealed similar capacity of recombinant and natural tropomyosin to compete with immobilized shrimp extract for IgE binding. rPen a 1 was further shown to extensively and specifically compete for IgE binding to extracts of other crustacean species, house dust mite and German cockroach.

**Molecular properties of food allergens.**


Breiteneder H; Mills EN

Plant food allergens belong to a rather limited number of protein families and are also characterized by a number of biochemical and physicochemical properties, many of which are also shared by food allergens of animal origin. These include thermal stability and resistance to proteolysis, which are enhanced by an ability to bind ligands, such as metal ions, lipids, or steroids. Other types of lipid interaction, including membranes or other lipid structures, represent another feature that might promote the allergenic properties of certain food proteins. A structural feature clearly related to stability is intramolecular disulfide bonds alongside posttranslational modifications, such as N-glycosylation. Some plant food allergens, such as the cereal seed storage prolamins, are
rheomorphic proteins with polypeptide chains that adopt an ensemble of secondary structures resembling unfolded or partially folded proteins. Other plant food allergens are characterized by the presence of repetitive structures, the ability to form oligomers, and the tendency to aggregate. A summary of our current knowledge regarding the molecular properties of food allergens is presented. Although we cannot as yet predict the allergenicity of a given food protein, understanding of the molecular properties that might predispose them to becoming allergens is an important first step and will undoubtedly contribute to the integrative allergic risk assessment process being adopted by regulators.

**A classification of plant food allergens.**

J Allergy Clin Immunol 2004 May;113(5):821-30; quiz 831 (ISSN: 0091-6749)

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Plant food allergens can be classified into families and superfamilies on the basis of their structural and functional properties. The most widespread groups of plant proteins that contain allergens are the cupin and prolamin superfamilies and the protein families of the plant defense system. The cupin superfamily includes allergenic seed storage proteins of the vicilin and legumin type present in soybeans, peanuts, and tree nuts. The prolamin superfamily includes several important types of allergens of legumes, tree nuts, cereals, fruits, and vegetables, such as the 2S albumin seed storage proteins, the nonspecific lipid transfer proteins, and the cereal alpha-amylase and protease inhibitors. Plant food allergens are also found among the various groups of defense proteins that enable plants to resist biotic and abiotic stress, such as the pathogenesis-related proteins, certain proteases, and protease inhibitors. This review focuses on a classification system of plant food allergens that is emerging from the synopsis of allergology and protein evolution.

**Methods for allergen analysis in food**

Food Addit Contam 2004 Jan;21(1):1-31 (ISSN: 0265-203X)

Poms RE; Klein CL; Anklam E
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Food allergies represent an important health problem in industrialized countries. Undeclared allergens as contaminants in food products pose a major risk for sensitized persons. A proposal to amend the European Food Labelling Directive requires that all ingredients intentionally added to food products will have to be included on the label. Reliable detection and quantification methods for food allergens are necessary to ensure compliance with food labelling and to improve consumer protection. Methods available so far are based on protein or DNA detection. This review presents an up-to-date picture of the characteristics of the major food allergens and collects published methods for the determination of food allergens or the presence of potentially allergenic constituents in food products. A summary of the current availability of commercial allergen detection kits is given. One part of the paper describes various methods that have been generally employed in the detection of allergens in food; their advantages and drawbacks are discussed in brief. The main part of this review, however, focuses on specific food
allergens and appropriate methods for their detection in food products. Special emphasis is given to allergenic foods explicitly mentioned in the Amendment to the European Food Labelling Directive that pose a potential risk for allergic individuals, namely celery, cereals containing gluten (including wheat, rye and barley) crustaceans, eggs, fish, peanuts, soybeans, milk and dairy products, mustard, tree-nuts, sesame seeds, and sulphite at concentrations of at least 10 mg kg\(^{-1}\). Sulphites, however, are not discussed.
Peanut agglutinin; soybean trypsin inhibitor; legume allergens

Author  Burks AW; Cockrell G; Connaughton C; Guin J; Allen W; Helm RM
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Source  Int Arch Allergy Immunol, 105: 2, 1994 Oct, 143-9

Peanuts and soybeans are frequent causes of food hypersensitivity reactions in children. Sera from 12 patients with atopic dermatitis and a positive double-blind placebo-controlled food challenge to peanut and sera from 5 patients with atopic dermatitis and a positive double-blind placebo-controlled food challenge to soybean were used to identify and characterize specific legume allergens. Identification of a minor allergen from peanut and a minor allergen from soybean was accomplished using various physicochemical techniques. The peanut fraction, peanut agglutinin, isolated by anion-exchange chromatography and electrolution and confirmed by amino acid sequencing, bound IgE in only 50% of the peanut challenge positive patients. The soybean fraction, soybean trypsin inhibitor, identified by gel filtration and electrolution and confirmed by amino acid sequencing, bound IgE in only 20% of the soy challenge positive patients. The identification of these two known legume proteins as minor allergens should allow further immunologic and structural investigations to compare the major and minor legume allergens.

Rhinitis and Asthma

Association between peanut allergy and asthma morbidity.

Simpson AB; Yousef E; Hossain J. J Pediatr. 2010; 156(5):777-81, 781.e1 (ISSN: 1097-6833)

To evaluate the relationship between peanut allergy and asthma morbidity in school-age children, the study involved a medical chart review to assess the association of peanut allergy with asthma morbidity in children beyond age 3 years. Peanut allergy was assessed by specific and validated criteria. A Poisson regression model was used to compare the frequency of systemic steroid use and of hospitalization for asthma beyond age 3 years in children with asthma with and without peanut allergy. RESULTS: Children with peanut allergy had a 2.32-times greater rate of hospitalization (P = .03) and a 1.59-times greater rate of systemic steroid use (P <.001) after controlling for covariates. CONCLUSIONS: Peanut allergy serves as an early marker for asthma morbidity. Early prevention and intervention can improve quality of care.

Food allergy and asthma


Food allergy and asthma commonly co-exist in the same patient with approximately one-third of children with food allergy having asthma. When both atopic conditions are present a food allergic patient is placed at greater risk of having a fatal reaction from food allergen exposure. For this reason asthma should be diligently managed in a food allergic
Food Allergy

patient and these patients should be carefully instructed on allergen avoidance and the proper use of self-injectable epinephrine. This review summarises the available literature regarding patients with both food allergy and asthma specifically looking at disease prevalence, IgE-mediated effects on the lower respiratory tract secondary to foods, the interplay of food additives and asthma, and food allergy as a risk factor for asthma morbidity with practical applications for clinicians.

Clinical aspects of infantile asthma.

Author Brasher GW Source Ann Allergy, 1975 Oct, 35:4, 216-20

Infantile asthma presents a major therapeutic challenge to the practicing physician. The typical infant with asthma is a 14-month-old boy with recurrent episodes of wheezing since the age of seven months. Nasal eosinophilia is found less often than in older allergic children; however, 47 percent of infants with asthma will have either peripheral blood or nasal secretion eosinophilia to aid in the recognition of their atopic diathesis. The younger the infant (both at age of onset and at age of evaluation) the more likely are foods to be important factors in his allergic respiratory disease. His disease is unlikely to interfere with growth during infancy but may do so later in life. Hyposensitization is more likely to be required later in childhood if he does not respond to dietary manipulation. Despite appropriate therapy, wheezing may continue to be a problem during childhood and this is significantly correlated with the presence of a positive nasal smear at the time of initial allergy evaluation.

Respiratory diseases and food allergy.

Author Heiner DC Source Ann Allergy, 1984 Dec, 53:6 Pt 2, 657-64

Both upper and lower respiratory tracts can be affected by food allergy. Manifestations in either may be exclusively due to food allergy (common in infants) or may result from the combined effects of food allergy plus another defect such as gastroesophageal reflux, a congenital defect of the heart or tracheo-bronchial tree, an immunodeficiency syndrome such as isolated IgA or IgG4 deficiency, or a concomitant inhalant allergy. Chronic rhinitis is the most common respiratory tract manifestation of food allergy. When it occurs in conjunction with lung disease, it may be a helpful indicator of activity of the allergic lung disease and of the patient's compliance in following a specific diet. Recurrent serous otitis media may be solely or partially due to food allergy. Large tonsillar and adenoid tissues, sometimes with upper airway obstruction, may be caused, or aggravated by, food allergies. Lower respiratory tract disease manifested by chronic coughing, wheezing, pulmonary infiltrates, or alveolar bleeding may also occur. Lower respiratory tract involvement is generally associated with a greater delay in onset of symptoms and with a larger quantity of allergen ingestion than chronic rhinitis. Food allergy should be considered when there is a history of prior intolerance to a food in childhood or of symptoms beginning soon after a particular food was introduced into the diet. It is an important consideration in patients who have chronic respiratory tract disease which does not respond adequately to the usual therapeutic measures and is otherwise unexplained.

Common respiratory manifestations of food allergy

Previous investigations have established the pathogenic role of food allergy in respiratory tract symptoms, which rarely occur in isolation. Specific foods have been implicated in these reactions. Food-induced asthma is more common in young pediatric patients, especially those with atopic dermatitis. Asthma induced by food allergy is considered a risk factor for fatal and near-fatal anaphylactic reactions. Moreover, food allergy can elicit airway hyperreactivity and asthmatic responses. Therefore, evaluation for food allergy should be considered among patients with recalcitrant or otherwise unexplained acute severe asthma exacerbations; asthma triggered by ingestion of particular foods; and asthma and other manifestations of food allergy (eg, anaphylaxis, moderate to severe atopic dermatitis).

Relevance of inhalational exposure to food allergens.

Roberts G; Lack G Paediatric Respiratory Medicine, Royal London Hospital, Whitechapel, London.

PURPOSE OF REVIEW: This review discusses the inhalational route as a clinically important route of exposure to food allergens.RECENT FINDINGS: In childhood, we have recently demonstrated that food allergens can induce both early and late phase bronchial reactions within blinded, placebo-controlled challenges. Additionally, clinically important levels of food allergens have been measured in environmental air samples. SUMMARY: It is well known that the ingestion of food allergens frequently causes respiratory symptoms and that the mechanism of death in fatal anaphylaxis is usually profound bronchospasm. The mechanism by which ingested food allergens induce bronchial reactions is unclear. There are many case reports of bronchial reactions to aerosolized food allergens. Within the food industry the problems have been examined more systematically. From such work it is possible to gain an impression of the potential prevalence of the problem. With 10% of adult asthma being occupational and 10% of occupational asthma being induced by aerosolized food, inhalational exposure to food allergens plays a major role in at least 1% of adult asthma. For a patient with co-existent food allergy and asthma it is important that both dietary and environmental avoidance be practised. The similar pathophysiology of allergic and occupational asthma and the ability of inhaled food allergens to cause the latter raises the question as to whether aerosolized food could play a role in the pathogenesis of childhood asthma.

Mechanisms in adverse reactions to food. The lung.

Author Bousquet J Address Clinique des Maladies Respiratoires, Hôpital Arnaud de Villeneuve, Centre Hospitalier Universitaire, Montpellier, France. Source Allergy, 50: 20 Suppl, 1995, 52-5
Abstract A positive food challenge doesn't imply that there is an IgE mediated allergy but implies the patient is intolerant to certain foods. If specific IgE and/or prick test to a specific food-stuff is positive, an IgE-mediated mechanism is likely to be involved but a proportion of patients with IgE to foods do not present any symptom when ingesting the food

Asthma nutritional, environmental, and genetic risk factors.
Author Greene LS  Address Department of Anthropology, University of Massachusetts/Boston 02125-3393, USA. Source J Am Coll Nutr, 14: 4, 1995 Aug, 317-24

Abstract A considerable body of evidence suggests that oxidant stress results in inflammation and tissue damage in the respiratory system, and later in immune damage, and that individuals with lowered cellular reducing capacity are at increased risk to develop asthma. Reducing capacity in the erythrocyte is generated through the pentose phosphate pathway and this pathway also generates a major portion of the reducing capacity in all cells of the body. Therefore, dietary, environmental, and genetic factors which diminish cellular reducing capacity will increase tissue vulnerability to oxidant stress and are likely to increase asthma risk. Dietary selenium deficiency lowers red cell glutathione peroxidase activity and is associated with an increased risk for asthma, and low dietary intakes of vitamins C and E also appear to increase asthma risk. High body iron stores increase free radical production and may also elevate asthma risk. Environmental lead exposure depresses the activities of a several enzyme systems that influence cellular reducing capacity (glucose-6-phosphate dehydrogenase, NAD synthetase, glutathione peroxidase, superoxide dismutase, catalase) and consequently may increase asthma risk. Genetically-determined low activity of glucose-6-phosphate dehydrogenase lowers cellular reducing capacity and may also heighten asthma risk. Simple dietary and environmental interventions may significantly reduce oxidant stress and prevent or minimize the development of asthmatic symptoms and should prove to be a cost effective approach to asthma management in addition to current pharmacological strategies.

Children with allergic rhinitis, asthma treated with elimination diet.

Author Ogle KA; Bullock JD Source Ann Allergy, 1977 Jul, 39:1, 8-11

Abstract 169 of 188 (90%) of infants with allergic rhinitis and/or bronchial asthma improved on a hypo-allergenic diet.

Comparison of immunologic tests in the diagnosis of occupational asthma and rhinitis.

Author Räsänen L; Kuusisto P; Penttilä M; Nieminen M; Savolainen J; Lehto M Source Allergy, 49: 5, 1994 May, 342-7

Abstract In this study, three immunologic tests, skin prick test, RAST, and basophil histamine-release test (BHRT), were compared by provocation in the diagnosis of occupational asthma and rhinitis. Twenty-three positive bronchial or nasal challenges were performed on 16 patients (six farmers, six bakery workers, and four food industry workers) and asthma or rhinitis was diagnosed as caused by cereal flour or grain, cow epithelium, storage mites, garlic, or soy dust. A control group consisted of 12 patients, of whom four (two bakery workers, one food industry worker, and one farmer) were challenge-negative, and the rest suffered from pollen allergy and seasonal rhinitis and were not challenged. The sensitivity and specificity of the prick test, RAST, BHRT, and a panel of them
Food allergy and asthma.

Author Businco L; Falconieri P; Giampietro P; Bellioni B
Address Department of Pediatrics, University La Sapienza, Rome, Italy.

Abstract Food allergy (FA) is one of the causes of atopic dermatitis (AD), of acute urticaria, of reactions of the gastrointestinal tract, and of acute systemic anaphylaxis, but its role in asthma appears to be less clear. The prevalence and incidence of subjects with food-induced wheezing have not been well studied. In addition, the number of subjects with proven food-induced wheezing by double-blind, placebo-controlled oral food challenge (DBPCOCFC) has been small. At the moment wheezing is considered unusual in food-hypersensitive subjects, and wheezing as the unique symptom of FA is rare. Furthermore, most cases of food-induced asthma have been observed in children. Food allergy may trigger allergic respiratory symptoms through two main routes: ingestion or inhalation. Children with asthma, who are allergic to foods, present some particular features such as AD and a related significantly elevated total serum IgE level. Alternatively, FA may occur in patients who are "high IgE responder" and more prone to become sensitive to many allergens, including foods. Therefore, children with asthma and a history of AD and/or elevated total serum IgE level should be carefully assessed for FA. We have shown that a significant proportion of children with IgE-mediated cow's milk allergy experienced asthma following DBPCOCFC with cow's milk.

Food allergy risk life-threatening asthma in childhood

J Allergy Clin Immunol 2003 Jul;112(1):168-74 (ISSN: 0091-6749)

Roberts G; Patel N; Levi-Schaffer F; Habibi P; Lack G
Department of Paediatric Allergy and Clinical Immunology, St Mary's Hospital, London.

BACKGROUND: No objective clinical risk factors exist for pediatric life-threatening asthma. OBJECTIVES: In this study, we address whether persistent food allergy and degree of atopy are risk factors for life-threatening asthma. METHODS: By use of a case-controlled design, children (1-16 years) ventilated for an exacerbation of asthma were enrolled. Each case was matched by sex, age, and ethnicity, with 2 controls who had attended with a non-life-threatening exacerbation. All subjects were assessed by means of a questionnaire, spirometry, and skin prick or RAST testing. The data were analyzed by conditional logistic regression. RESULTS: Nineteen cases and 38 controls were enrolled. Compared with controls, cases were found to have the following risk factors: food allergy (odds ratio, 8.58; 95% CI, 1.85-39.71), multiple allergic diagnoses (4.42; 1.17-16.71), early onset of asthma (6.48; 1.36-30.85), and frequent admissions (14.2; 1.77-113.59). After regression analysis, only frequent admission with asthma (9.85; 1.04-93.27) and food allergy (5.89; 1.06-32.61) were independently associated with life-threatening asthma. Half the cases had food allergy compared with only 10% of controls. CONCLUSION: This study demonstrates that poorly controlled asthma and food allergy are significant risk factors for life-threatening asthma. More intensive management of this high-risk group of children might help to reduce future morbidity and mortality.
**Bronchial asthma induced by hypersensitivity to legumes.**

Author García Ortiz JC; López-Asunsolo A; Cosmes P; Duran AM
Source Allergol Immunopathol (Madr), 23:1, 1995 Jan-Feb, 38-40
Abstract We report the case of a 54-year-old female patient, diagnosed of nasal polyposis and intrinsic corticodependent bronchial asthma, who since a year has developed episodes of asthma when exposed to vapours from cooking some kinds of legumes (peas, chick-peas, beans, lentils) and an oral allergy syndrome with peanuts. We prepared extract with these legumes. The skin tests were clearly positive for legumes but negative for pneumoallergens. Specific IgE by CAP was strongly positive for legumes. CAP inhibition was preformed and the results show the presence of cross-reactivity among legumes.

**Immediate-type reactions in patients with allergic bronchopulmonary aspergillosis.**

Author Ricketti AJ; Greenberger PA; Patterson R Source J Allergy Clin Immunol, 1983 Jun, 71:6, 541-5
Abstract Allergic features of 38 patients with allergic bronchopulmonary aspergillosis (ABPA) were reviewed. These features included skin reactivity to other inhalant antigens and to molds other than Aspergillus fumigatus (Af) plus clinical manifestations of rhinitis, conjunctivitis, asthma, eczema, urticaria, anaphylaxis, food allergy, and drug allergy. ABPA patients have a high degree of allergic reactivity in all these clinical features, in particular, clearly documented food allergy. These findings differ from those previously reported in ABPA patients in England, where it was noted that patients with ABPA whose asthma began after age 30 had few manifestations of other allergic diseases. By contrast, our patients in the same age group (onset of asthma after age 30) had the same multiple allergic manifestations as younger patients. These results show that ABPA patients are a subset of atopic individuals with a greater predisposition for the development of a wide spectrum of allergic diseases, despite the lack of manifestations of other major immunologic disease patterns.

**Comparison of immunologic tests in the diagnosis of occupational asthma and rhinitis.**

Author Räsänen L; Kuusisto P; Penttilä M; Nieminen M; Savolainen J; Lehto M Source Allergy, 49:5, 1994 May, 342-7
Abstract In this study, three immunologic tests, skin prick test, RAST, and basophil histamine-release test (BHRT), were compared by provocation in the diagnosis of occupational asthma and rhinitis. Twenty-three positive bronchial or nasal challenges were performed on 16 patients (six farmers, six bakery workers, and four food industry workers) and asthma or rhinitis was diagnosed as caused by cereal flour or grain, cow epithelium, storage mites, garlic, or soy dust. A control group consisted of 12 patients, of whom four (two bakery workers, one food industry worker, and one farmer) were challenge-negative, and the rest suffered from pollen allergy and seasonal rhinitis and were not challenged. The
Food Allergy

sensitivity and specificity of the prick test, RAST, BHRT, and a panel of them were as follows: 74 and 89%, 57 and 86%, 78 and 93%, and 91 and 71%, respectively. The overall concordance among these three type I allergy tests or between immunologic tests and challenge was relatively good.

Food-induced and occupational asthma due to barley flour.

Author Vidal C; González-Quintela A  Address Allergy Unit, Complejo
Source Ann Allergy Asthma Immunol, 75: 2, 1995 Aug, 121-4

Occupational exposure to inhalant allergens may induce asthma but the presence of asthma after the ingestion of the allergen is rarely reported. OBJECTIVE: To clarify the clinical relevance of every identified allergen in a patient with respiratory symptoms after exposure to feeding stuffs and cereal flours in his work environment and after ingestion of beverages made of these cereal grains. METHODS: Case report. Skin prick tests and serum-specific IgE (CAP-FEIA-fluoroenzymeimunoassay) were used in order to identify specific IgE antibodies. Bronchial provocation tests were performed as an aid in determination of clinical relevance of occupational exposure to the patient's asthma. RESULTS: A 50-year-old man developed bronchial asthma both after exposure to feeding stuffs and flours and after ingestion of beverages made of cereal flours. Allergy to barley and corn flours were demonstrated by skin testing and serum-specific IgE. Bronchial challenge tests with every allergen showed no response except for an immediate response to barley flour. The most relevant clinical feature was an immediate asthmatic response developed after oral provocation with either barley-made beer or barley flour itself which indicates IgE-mediated, food-induced bronchial asthma (sulfite sensitivity was ruled out). CONCLUSION: In some particular cases, barley flour may induce bronchial asthma through inhalational and oral routes due to an IgE-mediated mechanism.

Eosinophilic gastroenteritis, food allergy and bronchial asthma

Author Park HS; Kim HS; Jang HJ  Address Department of Allergy and Clinical Immunology, Ajou University School of Medicine, Korea. Source J Korean Med Sci, 10: 3, 1995 Jun, 216-9

In some patients, eosinophilic gastroenteritis(EG) occurs in those with food allergy. We experienced a non-atopic asthmatic who had an EG associated with food allergy to fish and eggs, and blood eosinophilia. A skin prick test and RAST to causative food allergens showed a negative result. A fiber-optic endoscopic biopsy from the gastric mucosa showed an intense eosinophilic infiltration. We could find symptomatic improvement and a disappearance of eosinophilic infiltration in gastric mucosa after complete avoidance from the causative food and oral corticosteroid. It was suggested that fiber-optic endoscopic biopsy might be needed to identify coexisting EG if an allergic patient with blood eosinophilia complains of severe gastrointestinal symptoms.

Nutritional triggers in asthma.

Author Nékám KL
Food Allergy

Address Department of Allergology and Clinical Immunology, National Institute of Rheumatology, Budapest, Hungary.


Food and food additive triggers play an important role in approximately 5-8% of all asthma cases. Exact epidemiological data are lacking, partly because the etiological link is not always obvious, the diagnosis of food hypersensitivity is often complicated and ambiguous, food triggers usually act in concert with other trigger(s), and intraspecies and intrabotanic cross-reactivities between inhalant and nutritional allergens can make the time-course of the symptoms confusing. The participation of airway symptoms in food allergy goes up to 40%. Relevant diagnosis can only be established by the combination of procedures used for both food allergy and asthma. In the therapy avoidance measures are of great importance besides usual asthma therapy, and probably in combination with the reduction of gut permeability.

Long-lasting sensitization to food during the first two years precedes allergic airway disease.

Author Kulig M; Bergmann R; Tacke U; Wahn U; Guggenmoos-Holzmann I


The purpose of the study was to investigate whether the duration of sensitization to food allergens during early childhood is related to later development of IgE mediated hypersensitivity to inhalant allergens and of allergic rhinitis and asthma in 5-year-old children and whether long-lasting food-sensitization may be used to predict subsequent allergic airway diseases. Five hundred and eight children of a prospective birth cohort study with available serum samples at one and two years of age were included and followed up until five years of age. Specific sensitization to food and inhalant allergens and the occurrence of subsequent allergic airway diseases were determined. Children with a long-lasting sensitization to food allergens (persistently sensitized for more than one year) produced significantly higher total IgE and specific IgE levels than children who were only transiently food-sensitized by two years of age. Children persistently sensitized to food had a 3.4 fold higher risk of developing allergic rhinitis and a 5.5 fold higher risk of developing asthma than infants who were only transiently food sensitized. Persistent food sensitization in combination with a positive atopic family history was a strong predictor for the development of allergic rhinitis and asthma at five years of age. The risks for these children are up to 50%, and 67% respectively. Persistently detectable sensitization to food over more than one year in early childhood is a strong prognostic factor for subsequent allergic airway disease. Persistently food-sensitized children especially in atopic families have to be regarded as a high-risk group and should be considered for preventive measures against respiratory atopy.

Role of new allergens in the increased incidence of food sensitizations in France.

Author André F; André C; Colin L; Cacaraci F; Cavagna S Address Laboratoire d'Immunopathologie Digestive, INSERM, Centre Hospitalier Lyon-Sud, Pierre Bénite, France. Source Toxicology, 93: 1, 1994 Sep 22, 77-83

Abstract Food allergy is a group of distinct clinico-pathological entities that have an immunological basis in common, and in which an abnormal or exaggerated
immunological response to a specific food leads to disease. Some clinical pictures involving multiple organ system (anaphylaxis) are potentially fatal. The data on the incidence, prevalence, mortality rate and food products involved in food-induced anaphylaxis and the evolution of food sensitization compared with changes in eating habits are not very reliable. In the present study we analysed, over a period of 9 years (1984-1992), a group of 580 patients with pathological reactions to foods, 60 of which presented severe, near-fatal reactions. We sought the etiologic components and food sensitization in comparison with the principal tendencies of food consumption in France. Food products most frequently incriminated in anaphylactic reactions are not of a primary nutritional importance: celery (30%), crustaceans (17%), fish (13%), peanuts (12%), mango (6%), mustard (3%), but they are often hidden allergens in commercial foods. The sensitization to food products in the group of 580 patients reveals, in decreasing order of frequency: wheat (39%), peanuts (37%), crab (34%), celery (30%), soy (30%). Compared with previous data, the frequency of sensitization to different foods has changed; for instance, the sensitizations to wheat, soy, peanuts, celery, mustard, rice, are definitely increasing. The increased consumption and more attentive clinical research may be the reasons for this evolution. For products such as egg and pork, the data are stable and parallel with consumption, whilst for other products like milk and other dairy products, the increased consumption is accompanied by a decrease of the incidence of sensitization. The reactivity to some allergens may be affected by the way of preparing the food.

Respiratory manifestations of food allergy.

Pediatrics. 2003; 111(6 Pt 3):1625-30 (ISSN: 1098-4275)

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Food allergy may present with a variety of respiratory tract symptoms that generally involve immunoglobulin E antibody-mediated responses. Exposure is typically through ingestion, but in some cases, inhalation of airborne food particles may trigger these reactions. Upper and lower respiratory tract reactions are often a significant component of multisystem, anaphylactic reactions. It is important to recognize that food allergy in early childhood is a marker indicating an increased risk to develop respiratory allergy. Asthmatic responses to food additives can occur but are uncommon. Studies using blinded oral food challenges have demonstrated that foods can elicit airway hyperreactivity and asthmatic responses. Therefore, an evaluation for food allergy should be considered in patients who are at risk, including those with recalcitrant or otherwise unexplained acute, severe asthma exacerbations, asthma triggered after ingestion of particular foods, and asthma that is accompanied by other manifestations of food allergy (e.g., anaphylaxis, moderate to severe atopic dermatitis).

Wheat Allergy and Celiac Disease

Systemic Autoimmune Disorders in Celiac Disease

Celiac disease is an immune-mediated disorder clinically characterized by a multitude of symptoms and complications. The comorbidity between celiac disease and other autoimmune disorders has been clearly established.

Recent Findings: Two main theories have been postulated to explain this comorbidity: (1) linkage disequilibrium between the genes responsible for celiac disease and those responsible for the coexpressed autoimmune diseases or (2) untreated celiac disease leading to the onset of other autoimmune diseases. This article reviews the current literature supporting either theory and places the current knowledge in the field within the context of the most recent data on the pathogenesis of celiac disease.

Summary: The current literature did not clearly establish which of the two theories explain the comorbidity between celiac disease and other autoimmune disorders. There is, however, growing evidence that the loss of the intestinal barrier function typical of celiac disease could be responsible of the onset of other autoimmune disease. This concept implies that the autoimmune response can be theoretically stopped and perhaps reversed if the interplay between autoimmune predisposing genes and trigger(s) is prevented or eliminated by a prompt diagnosis and treatment.

Gender and clinical presentation in adult celiac disease.

Author Ciacci C; Cirillo M; Sollazzo R; Savino G; Sabbatini F; Mazzacca G
Address Gastrointestinal Unit, Medical School, University Federico II of Naples, Italy.
Source Scand J Gastroenterol, 1995 Nov, 30:11, 1077-81

Abstract BACKGROUND: Celiac disease may present in various forms. This study aimed to investigate whether gender affects the clinical presentation of the disease in adult celiac patients from the Mediterranean area. METHODS: This study retrospectively analyzes data collected in all adult patients with celiac disease (n = 195) seen during the past 13 years at the Gastrointestinal Unit of the Federico II University of Naples, Italy. RESULTS: In these series of patients the ratio of women to men was 3.33. Age at diagnosis was lower in women that in men (p < 0.05). Except for asthenia, all signs and symptoms were more frequent in women than in men. Hypochromic anemia was the most commonest finding in women and was 40% more frequent in women than in men (p < 0.001). Dyspepsia was twice as frequent in women as in men (p < 0.05); genital disorders were reported by 44% of women and by no men. Recent weight loss or low body mass index was the commonest finding in men. About 60% of men and women reported diarrhea; among patients without diarrhea, the prevalence of hypochromic anemia differed between sexes (p < 0.05), occurring in about 80% of women. CONCLUSION: This study shows that the clinical presentation of celiac disease is not the same in men and women. The disease is not only more frequent in women than in men but is also more severe and more rapid. The data also suggest the need to look for celiac disease in patients with unexplained hypochromic anemia.

High prevalence of undiagnosed coeliac disease in 5280 Italian students screened by antigliadin antibodies.

Author Catassi C; RÂatsch IM; Fabiani E; Ricci S. Acta Pediatr, 1995 Jun, 84:6, 672-6
Abstract

Many cases of coeliac disease are currently undiagnosed. We carried out a pilot study on screening for coeliac disease in a school population. The screening protocol consisted of three parts: (1) IgG and IgA antigliadin antibody (AGA) assay; (2) antiendomysium antibody and total serum IgA determinations; (3) jejunal biopsy. A total of 5280 students aged 11-15 years (71.7% of the eligible population) underwent the first evaluation; 113 subjects performed the second tests and 35 of these needed the third investigation. Coeliac disease was diagnosed in 23 cases, most of which were atypical or silent forms. The prevalence of undiagnosed coeliac disease was 4.36 per 1000 screened subjects (95% CI 2.58-6.14) and 5.03 per 1000 (95% CI 3.41-6.65) in the general population. The ratio of known to undiagnosed cases was 1 to 6.4. This high prevalence of undiagnosed coeliac disease raises a number of problems that require further evaluation.

Prevalence and diagnosis of celiac disease in IgA-deficient children.

Author
Meini A; Pillan NM; Villanacci V; Monafo V; Ugazio AG; Plebani.

Abstract
BACKGROUND: Reported frequencies of celiac disease in selective IgA deficiency in childhood vary widely and this is probably due to the different characteristics of the patients studied and to the different criteria used for intestinal biopsy: all patients or only those with symptoms of malabsorption. Diagnosis of celiac disease is of considerable importance in IgA deficiency because of its increased frequency and also because avoidance of dietary gluten permits elimination of the symptoms and complications of celiac disease. OBJECTIVES: To obtain a more reliable estimate of the incidence of celiac disease in childhood IgA deficiency jejunal biopsies were performed in 65 consecutively diagnosed IgA-deficient children whose parents consented. Some clinical and laboratory parameters including IgA-antigliadin and IgG-antigliadin antibodies were evaluated to predict their usefulness in selecting IgA-deficient patients for intestinal biopsy. METHODS: All IgA-deficient patients had serum IgA levels below 5 mg/dL and salivary IgA below 0.5 mg/dL. Jejunal biopsy was performed using a peroral Watson capsule and IgA-antigliadin and IgG-antigliadin antibodies were performed by an ELISA assay. RESULTS: Biopsy findings of severe villous atrophy permitted diagnosis of celiac disease in 7.7% (5/65 children). IgG-antigliadin antibody levels, elevated in 16 patients including all five celiacs, were the best parameter for predicting celiac disease and gave no false negatives. CONCLUSIONS: The 7.7% frequency of celiac disease observed in these IgA-deficient children is about 20 times higher than in the general Italian population, and the lowest among the studies biopsying all patients; this is probably attributable to the presence of a substantial proportion of healthy children (20/65) and very few (2/65) with autoimmune disorders. The elevated sensitivity and negative-predictive value of IgG-antigliadin antibodies lead us to suggest that positive IgG-antigliadin antibodies can be used to select IgA-deficient children for jejunal biopsy with a very low probability of missing celiac disease while allowing a drastic reduction in the number of biopsies performed.

Food Allergy to Wheat

Identification of immunoglobulin E and immunoglobulin G-binding proteins with sequential extracts and purified proteins from wheat flour.
BACKGROUND: Cereal-associated allergy is particularly considered a serious problem, because cereals are essential in our daily diet. Wheat proteins are classified into albumins, globulins and prolamins (insoluble gliadins and glutenins). OBJECTIVES: Our objectives were to study the involvement in food allergy to wheat of these different protein types by using purified fractions and to identify those binding IgE and IgG antibodies. METHODS: Sera were obtained from 28 patients with food allergy to wheat. Albumins/globulins, gliadins and glutenins were obtained by sequential extraction based on differential solubility; alpha-, beta-, gamma- and omega-gliadins and low molecular weight (LMW) and high molecular weight (HMW) glutenin subunits were purified by chromatography. IgE binding to these extracts and fractions were analysed by radioallergosorbent test (RAST), and immunoblotting; IgG binding was detected by enzyme-linked immunosorbent assay (ELISA). RESULTS: In RAST, 60% of sera were shown to have specific IgE antibodies against alpha-, beta-gliadins and LMW glutenin subunits, 55% to gamma-gliadins, 48% to omega-gliadins and 26% to HMW glutenins. Immunoblotting analysis confirmed results obtained in RAST concerning LMW and HMW glutenin subunits and showed that 67% of patients have IgE antibodies to the albumin/globulin fraction. CONCLUSION: Results obtained in the different tests showed common features and in agreement with other studies indicated the presence of numerous allergens in food allergy to wheat; alpha-, beta-, gamma- and omega-gliadins, LMW glutenin subunits and some water/salt-soluble proteins appeared as major IgE binding allergens, whereas HMW glutenins were only minor allergens. The same type of antigenic profile against gliadins and glutenins was observed with IgG antibodies. Important sequence or structural homologies between the various gliadins and LMW glutenin subunits could certainly explain similarity of IgE binding to these proteins.
Is celiac disease a lifelong disorder?


Abstract That celiac disease is a lifelong disorder was suggested by clinical case records and was considered to have been demonstrated through the widespread use of intestinal biopsies by the end of the 1950s. It was clear that the mucosal lesions observed in children and adults were identical and responded similarly to gluten withdrawal. In fact, in 1970 the European Society for Paediatric Gastroenterology and Nutrition instituted the practice of a challenge after diagnosis. A relapse of clinical symptoms and of the intestinal lesions after gluten was reintroduced into the diet demonstrated the "permanent" nature of sensitivity to gluten in children with celiac disease. Twenty-five years later, the permanence of the sensitivity of the intestinal mucosa to gluten is again a matter of debate. Several lines of evidence, gathered during recent years, show that celiac disease is not always a lifelong condition. First, the long-term follow-up of children with proven celiac disease shows that 10% to 20% of them become "tolerant" (defined on clinical, biological and histologic grounds) to gluten during adolescence. Second, it has also been shown, in individual cases, that the mucosal lesions typical of the disease may appear during adulthood. Our increasing knowledge of the long-term evolution of the disease suggests that celiac disease develops and, in some cases, fades in a predisposed group of people with intestinal sensitivity to gluten, which is probably a common condition. The factors leading to the appearance or disappearance of the disease, however, are still unknown.

Allergy to cereals and dairy products in adult, asthma: an epidemiological survey.

Author May KL Source Allergol Immunopathol (Madr), 1980 Nov-Dec, 8:6, 643-50

Abstract From a representative group from the adult population (34,958) of a town of 77,384 inhabitants, 99 persons were selected who: a) claimed to be periodically dyspneic independently with respect to respiratory tract infections. b) had normal chest x-rays and normal PE flow values. Approximately one year later, a history of atopic diseases was taken from 79 of them, and intradermal skin tests were performed with some inhalants and food allergens. At this time, 15 persons failed to report their previous complaints of dyspnea. Only 5 persons reported that various vegetables and pickles were responsible for their urticaria or eczema. Only 2 persons admitted various gastrointestinal symptoms, but none mentioned milk, eggs or cereals as possible causative agents of their bronchial, nasal, skin or circulatory symptoms. Distinctly positive immediate type skin reactions to the mixed milk and egg allergen were recorded in 19 patients (24%), and to cereals in 11 persons (14%). They all reacted strongly also to the house dust allergen, but they did not differ from all the remaining subjects in the intensity of their skin response to the control solution of histamine. People with positive skin reactions to cereals or dairy products complained of chronic or recurrent rhinitis much more often than the others (73% and 63% compared with 35%). Forty-five (47%) of them had a positive personal history of urticaria or eczema. These "food reactors" did not differ from "non reactors" in the frequency of the elevated serum IgE level that was raised in 66% of the whole group (of 79). The results suggest that allergy to cereals and dairy products may often be underestimated in adult asthmatics especially when positive reactions to inhalants are also present. The problems of reliability of the skin tests and history taking in food allergy are briefly discussed.
Celiac disease is a lifelong disorder.

Author Chartrand LJ; Seidman EG

Abstract Celiac disease has always been considered a permanent condition. A relapse, defined on the basis of mucosal changes, occurring within 2 years of reintroducing gluten to a patient's diet (challenge) has been taken as confirmation of the permanence of the disease. Some observers have questioned whether the disease is permanent, since long periods of unexplained clinical remission occur, mainly among adolescents. However, the presence or absence of symptoms has no correlation with the histologic activity of the disease or with the results of serologic tests. With very few exceptions, patients in whom celiac disease is diagnosed during their childhood eventually have a relapse. However, in some cases, many years may elapse before a relapse; therefore, the 2-year limitation is no longer considered valid. On the other hand, there have been anecdotal observations that some patients eating a normal diet containing gluten appear to have experienced a "natural recovery." This recovery is partial and probably temporary, since there is evidence that celiac disease can be present in a latent form. Long-term randomized studies, in which morphometric and ultrastructural measurements are taken, that show villous integrity, the absence of abnormal inflammation and a lack of long-term complications of a diet containing gluten are needed before the current "zero-gluten" approach to celiac disease is altered. The individual variation in the extent and time course of celiac disease does not contradict the evidence that the disease persists throughout life, actively, silently or latently. Currently, there is no justification for recommending long-term consumption of gluten for either children or adults with celiac disease.

Lymphocytic gastritis and permeability in patients with celiac disease.

Author Vogelsang H; Oberhuber G; Wyatt J Source Gastroenterology, 1996 Jul, 111:1, 73-7

Abstract Lymphocytic gastritis is associated with celiac disease. Gastric permeability can now be assessed by a sucrose test, and intestinal permeability measured by a lactulose/mannitol test is increased in untreated celiac patients. The aim of this study was to prospectively compare gastric and intestinal permeability with histological changes of the stomach and small bowel in patients with celiac disease. METHODS: Gastric and intestinal permeability were measured by oral or duodenal (during endoscopy) administration of a triple sugar solution containing 20 g sucrose, 10 g lactulose, and 5 g mannitol in 100 mL water in 43 adult patients with celiac disease (28 without diet) and in 30 healthy controls. Endoscopic biopsy specimens were taken from the antrum and distal duodenum and investigated for intraepithelial lymphocyte counts. RESULTS: Urinary sucrose excretion decreased after duodenal administration (n = 8) as opposed to oral administration and thus measured gastric permeability in celiac disease. Gastric permeability was elevated in 60% of the celiac patients and correlated with antral intraepithelial lymphocyte counts. Intestinal permeability (measured by a lactulose/mannitol test) was also elevated in 69% of the celiac patients and correlated with duodenal intraepithelial counts. CONCLUSIONS: There is a high prevalence of lymphocytic gastritis in untreated celiac disease associated with elevated gastric permeability. Celiac disease seems to be a general disorder of the gastrointestinal tract associated with disturbed permeability.
Gut permeability to human alpha-lactalbumin, beta-lactoglobulin, mannitol, and lactulose in celiac disease.

Author Kuitunen M; Savilahti E
Address Children's Hospital, University of Helsinki, Finland.
Abstract Our objective was to examine the permeability of the gut to protein macromolecules and sugar probes and their possible association in celiac disease patients. We studied the permeability to human alpha-lactalbumin, beta-lactoglobulin, mannitol, and lactulose on 46 occasions in 33 celiac disease patients in various phases of the disease; in addition, mannitol and lactulose permeability was studied in 18 healthy controls. Lactalbumin absorption was detected in 19 of 42 patients tested, more often in celiac disease patients with villous atrophy than in those with normal jejunal biopsy (p = 0.01). Higher absorption of lactalbumin was found in patients with subtotal villous atrophy than in those with normal biopsy (p = 0.02). beta-lactoglobulin was found in four of 42 patients tested. Less mannitol was absorbed by patients with either subtotal or partial villous atrophy than by those with normal histology (p = 0.001 and 0.006, respectively). Lactulose recovery was higher in newly diagnosed patients and patients with subtotal villous atrophy than in controls (p = 0.007 and 0.03, respectively). The lactulose/mannitol ratio was higher in newly diagnosed patients and patients with villous atrophy than in controls (p = 0.002 and 0.002, respectively). The correlation between permeability to lactalbumin and mannitol and lactulose was poor. We conclude that permeability to proteins and sugar molecules is abnormal in celiac disease patients with mucosal damage and that they probably reflect different mechanisms of penetration.

Migraine

The clinical features of migraine as a manifestation of allergic disease.

Authors Wilson CW. Kirker JG. Warnes H. O'Malley M.
Abstract: Patients with a clinical history of migraine were evaluated psychiatrically, and by electroencephalography. They were challenged with food antigens by skin-prick test, and abdominal symptoms were evaluated following oral ingestion of food allergens. A significant correlation was found between challenge with specific food allergens and the development of migraine headaches, the appearance of abdominal symptoms and the occurrence of positive skin reactions. Psychiatric abnormalities and EEG alterations were associated with the occurrence of headaches and allergic clinical features. It is suggested that the clinical features of migraine can be explained as a result of release of chemical mediators following antigen-antibody reactions in the brain and other tissues where specific antibodies are localized. The continuous ingestion of the responsible food allergens would account for the raised tissue concentrations of noradrenaline, histamine and other mediators to which the clinical features of migraine are attributed.

Neurogenic vascular headaches, food and chemical triggers.
Food Allergy

**Authors** Trotsky MB. Institution University of Nebraska College of Medicine, Lincoln.

Abstract Recent evidence has demonstrated that neurogenic vascular headaches are a combination of neurological primary events and secondary vasomotor changes. The neurological events involve the hypothalamus and sensory cortex with sympathetic hypofunction and noradrenergic abnormalities. A platelet theory has been proposed but has not really been confirmed as a legitimate cause of the neurogenic vascular headaches. Food and chemicals in foods can act as a precipitating factor in the food-sensitive neurogenic vascular headache patient. In these patients evidence is now being demonstrated to confirm this, but larger patient studies are needed. The food-sensitive migraine patient and cluster headache patient must give a good history and food diary to go along with active challenges and provocative testing in order to determine the causative foods. Any concomitant allergies of inhalants or environmentals must also be treated. The treatment modalities of elimination and rotation diets or provocation neutralization may successfully control the headaches without the need for continuous medications.

**T cells expressing IL-2 receptor in migraine**

Authors Martelletti P. Institution Centro Cefalee, Universita La Sapienza, Roma, Italia.

Abstract We studied a group of migraine patients for circulating immune complexes, lymphocyte subpopulations, IgG4 and anti-IgG antibodies, before, after 4 hours and after 72 hours a specific challenge test. We found an increased incidence of circulating immune complexes. Total T cells showed a marked increase after challenge test. The most important finding was the presence of T-activated cells. Also K and NK cells showed an early increase after the challenge. In commenting the outcomes of this investigation, it must be stressed that the evidence of an early lymphocyte activation after the challenge test indicates an involvement of interleukin-2 related receptor in food-induced migraine. The results have reinforced the idea of immune mechanism involvement in food-induced migraine, but it seems to be localized at different step from that until now hypothesized, with the involvement of the complex cytokines network.

[References: 54]

**Food allergy in migraine. Study of dietary exclusion and RAST.**

Author Monro J; Brostoff J; Carini C; Zilkha K Source Lancet, 1980 Jul 5, 2:8184, 1-4

Abstract Two-thirds of severe migraineurs were allergic to certain foods, shown by dietary exclusion and subsequent challenge. Radioallergosorbent test confirmed the relevance of these foods. Oral sodium cromoglycate protected these patients from food challenges. The initial specific allergic reaction in the gut may result in increased mucosal permeability, which allows food antigens, complexes, or mediators to be absorbed and cause symptoms.
Oligoantigenic diet treatment of children with epilepsy and migraine

Author Egger J; Carter CM; Soothill JF; Wilson J Address Department of Neurology, Hospital for Sick Children, London. Source J Pediatr, 1989 Jan, 114:1, 51-8

Abstract We studied the role of oligoantigenic diets in 63 children with epilepsy; 45 children had epilepsy with migraine, hyperkinetic behavior, or both, and 18 had epilepsy alone. Of the 45 children who had epilepsy with recurrent headaches, abdominal symptoms, or hyperkinetic behavior, 25 ceased to have seizures and 11 had fewer seizures during diet therapy. Headaches, abdominal pains, and hyperkinetic behavior ceased in all those whose seizures ceased, and in some of those whose seizures did not cease. Foods provoking symptoms were identified by systematic reintroduction of foods, one by one; symptoms recurred with 42 foods, and seizures recurred with 31; most children reacted to several foods. Of 24 children with generalized epilepsy, 18 recovered or improved (including 4 of 7 with myoclonic seizures and all with petit mal), as did 18 of 21 children with partial epilepsy. In double-blind, placebo-controlled provocation studies, symptoms recurred in 15 of 16 children, including seizures in eight; none recurred when placebo was given. Eighteen other children, who had epilepsy alone, were similarly treated with an oligoantigenic diet; none improved.


Author Egger J; Carter CM; Wilson J; Turner MW; Soothill JF Source Lancet, 1983 Oct 15, 2:8355, 865-9

Abstract 93% of 88 children with severe frequent migraine recovered on oligoantigenic diets; the causative foods were identified by sequential reintroduction, and the role of the foods provoking migraine was established by a double-blind controlled trial in 40 of the children. Most patients responded to several foods. Many foods were involved, suggesting an allergic rather than an idiosyncratic (metabolic) pathogenesis. Associated symptoms which improved in addition to headache included abdominal pain, behaviour disorder, fits, asthma, and eczema. In most of the patients in whom migraine was provoked by non-specific factors, such as blows to the head, exercise, and flashing lights, this provocation no longer occurred while they were on the diet.

Effect of diet treatment on enuresis in children with migraine or hyperkinetic behavior.

Author Egger J; Carter CH; Soothill JF; Wilson J Clin Pediatr, 1992 May, 31:5, 302-7

Abstract Twenty-one children with migraine and/or hyperkinetic behavior disorder which was successfully treated with an oligoantigenic (few-foods) diet also suffered from nocturnal and/or diurnal enuresis. On diet, the enuresis stopped in 12 of these children and improved in an additional four. Identification of provoking foods was by sequential reintroduction of the foods that were avoided on the oligoantigenic diet. In eight of the 12 children who recovered on the oligoantigenic diet and in the four who improved, reintroduction of one or more foods provoked a reproducible relapse of the enuresis. Nine children were subjected to a placebo-controlled, double blind reintroduction of provoking
foods. Six children relapsed during testing with incriminated foods; none reacted to placebo. Enuresis in food-induced migraine and/or behavior disorder seems to respond, in some patients, to avoidance of provoking foods.

**Food allergies and migraine**

Authors Grant EC  

Abstract 60 migraine patients completed elimination diets after a 5-day period of withdrawal from their normal diet. 52 (87%) of these patients had been using oral contraceptive steroids, tobacco, and/or ergotamine for an average of 3 years, 22 years, and 7.4 years respectively. The commonest foods causing reactions were wheat (78%), orange (65%), eggs (45%), tea and coffee (40% each), chocolate and milk (37% each), beef (35%), and corn, cane sugar, and yeast (33% each). When an average of ten common foods were avoided there was a dramatic fall in the number of headaches per month, 85% of patients becoming headache-free. The 25% of patients with hypertension became normotensive. Chemicals in the home environment can make this testing difficult for outpatients. Both immunological and non-immunological mechanisms may play a part in the pathogenesis of migraine caused by food intolerance.

**Migraine: nutritionally supported fast - a diagnostic test for food causes**


Abstract A diagnostic procedure during a nutritionally supported fast week followed by conventional food sensitivity management achieved major improvement for 80% of a migraine panel. This procedure gave a reliable (0.8 correlation coefficient) prognosis on the substantial value of this approach for selection of the treatment of migraine. The study gave two lines of evidence which indicate that migraine has an etiology of food sensitivity.

**Migraine is a food-allergic disease.**

Author Monro J; Carini C; Brostoff J  
Source Lancet, 1984 Sep 29, 2:8405, 719-21

Abstract Foods which provoked migraine in 9 patients with severe migraine refractory to drug therapy were identified. The patients were then given either sodium cromoglycate or placebo orally in a double-blind manner, with foods previously identified as provocants. Sodium cromoglycate exerted a protective effect, thus confirming that it can prevent a hypersensitivity mechanism as well as the symptoms of migraine. Immune complexes were not produced in those patients who were protected by sodium cromoglycate. These observations confirm that a food-allergic reaction is the cause of migraine in this group of patients.
Nephritis

Do food antigens play a role in the pathogenesis of glomerulonephritis?

Author van der Woude FJ; Hoedemaeker PJ; van der Giessen M; de Graeff PA; de Monchy J; The TH; van der Hem GK Source Clin Exp Immunol, 1983 Mar, 51:3, 587-94

Abstract Circulating immune complexes after a test meal were measured with three methods (PEG precipitation, Clq-ELISA and the indirect granulocyte phagocytosis test) in 10 controls, two symptomless persons with selective IgA deficiency and 14 patients with various types of glomerulonephritis, of which two patients (with idiopathic membranous glomerulopathy and local focal glomerulonephritis) also had selective IgA deficiency. The PEG and Clq-ELISA test did not show significant differences between the groups. In the two symptomless persons with selective IgA deficiency and in the patient with local focal glomerulonephritis and selective IgA deficiency the indirect granulocyte phagocytosis test (IGFT) showed a reproducible increase in IgG, IgM and complement containing immune complexes. In the last patient multiple food antigens were probably responsible for this phenomenon, a rapid amelioration of kidney function could be induced three times by giving an antigen free diet.

Food antigens, IgA-immune complexes and IgA mesangial nephropathy.

Author Fornasieri A; Sinico RA; Maldifassi P; Paterna L; Benuzzi S; Address Division of Nephrology, San Carlo Hospital, Milano, Italy. Source Nephrol Dial Transplant,'88, 3:6, 738-43

Abstract To investigate whether patients with IgA nephropathy have an exaggerated serum IgA response to ubiquitous food antigens we measured serum IgA antibodies to gliadin, ovalbumin, bovine serum albumin (BSA), beta-lactoglobulin and casein in 120 patients and 53 normal controls, using ELISA.Nine patients but no controls had an association of two or more IgA antibodies to dietary antigens. Sixty-six per cent of these patients (vs 24% in the remaining population) had IgA CIC, suggesting a possible involvement of these antibodies in the constitution of IgA CIC. Analysis of sera by HPLC revealed that both monomeric and higher molecular forms of IgA antibodies were present, the latter being coincident with the peak of IgA CIC. Preincubation of sera with serial concentrations of the specific antigen decreased significantly IgA CIC, suggesting that in this subgroup of patients IgA antibodies to food antigens (mainly BSA) are involved in the formation of IgA CIC. BSA-containing IgA CIC were in fact demonstrated by ELISA using rabbit IgG anti-BSA coated plates and peroxidase-conjugated anti-human IgA. The role of these CIC in the pathogenesis of IgA nephropathy needs to be further elucidated.
**Circulating immune complexes following food in glomerulonephritis.**

Author Cairns SA; London A; Mallick NP  Source J Clin Lab Immunol, 1981 Sep, 6:2, 121-6

Abstract Following a meal containing a variety of animal and vegetable proteins circulating immune complexes (CIC) have been found in sera from eight normal subjects. Levels of CIC rose to significantly higher levels in ten patients with idiopathic immune complex glomerulonephritis and return to fasting levels was significantly delayed. The type of CIC detected bore no relation to those in renal biopsy material. The CIC which accumulated in GN were small (MW similar to or approximately 350,000), and plasma exchange did not influence the extent or duration of CIC rise following the meal. An immunological defect manifested by impaired clearance of frequently encountered antigens may exist in subjects who develop GN. The CIC detected in the serum of these patients may be markers of this state and cannot be assumed to be the pathogenic agents in the disease.

**Immune complexes in IgA nephropathy:**

Author Sancho J; Egido J; Rivera F; Hernando Clin Exp Immunol, 1983 Oct, 54:1, 194-202

Abstract Several features suggest that IgA nephropathy is an immune complex (IC)-mediated disease. The source of antigen(s) is unknown but the predominant involvement of IgA suggest that it is associated in some way with the gut or respiratory tract. Taking into account the specific hepatobiliary transport by polymeric IgA of circulating antigens entering through the mucosal surfaces we examined the possible involvement of antibodies against food antigens in the circulating IC and the existence of a defect in their blood clearance in patients with IgA nephropathy. A rise in multimeric IgA-IC (Raji assay) occurred in three of seven control subjects with a peak at 2-4 h after food ingestion. The amount of multimeric IgA-IC present at fasting in four out of six patients, diminished 2-4 h after food challenge, reaching a new peak around 6 h. At fasting, three out of six patients had IC containing antibodies against diet antigens (e.g. ovalbumin). These IC paralleled, both in patients and controls, the levels of multimeric IgA-IC. In patients small multimeric IgA-IC predominated at fasting and 24 h after food ingestion, while larger IC were detected at 2-4 h of food challenge. The specific polymeric IgA-IC showed in controls a maximal peak with similar distribution to that of multimeric IgA-IC, but with a quicker disappearance from the circulation. By contrast, polymeric IgA-IC remained elevated 24 h after food ingestion in most patients. These results suggest that antibodies against common antigens are within circulating IC and that a defect in the hepatic clearance of circulating polymeric IgA-IC exists in patients with IgA nephropathy.
Circulating immune complexes… cow’s milk… IgA nephropathy.

**Author** Sato M; Takayama K; Wakasa M; Koshikawa S  
**Source** Nephron, 1987, 47:1, 43-8

**Abstract** We recently reported on an experimentally induced model of IgA nephropathy in mice by long-term oral immunization under the reticuloendothelial dysfunction, which was found to be effectively inhibited by the administration of the antiallergic agent sodium cromoglycate (SCG). On the basis of these findings, we investigated the participation of food antigens in patients with IgA nephropathy. We studied 24 patients with IgA nephropathy, 11 patients with primary glomerulonephritis (PGN) except IgA nephropathy and 11 healthy controls. Serum levels of immunoglobulins (IgG, IgA, IgE) and circulating immune complexes containing IgG (IgG-CIC) or IgA (IgA-CIC) were measured in the fasting state and 30, 60, 120 or 180 min after oral challenging with cow's milk (400 ml). After the oral challenge IgA-CIC levels remained within the normal range in healthy controls and in patients with PGN, while 3 out of the 24 patients with IgA nephropathy showed a transient elevation and 2 cases showed a significant rise of IgA-CIC levels. The levels of IgG, IgA, IgE and IgG-CIC remained uninfluenced by the challenge test in all subjects. In addition, we carried out the same challenge test under SCG administration. These cases indicating an oral-challenge-induced IgA-CIC elevation demonstrated an inhibition of this elevation, and in 3 out 7 patients who showed hyper-IgA-CICemia before and after oral challenge IgA-CIC levels returned to the normal range through SCG administration. These results suggest that food antigens participate strongly in the pathogenesis of some patients with IgA nephropathy, and that SCG is an effective agent for such patients.

Immune complex glomerulopathy in a child with food hypersensitivity.

**Author** McCrory WW; Becker CG; Cunningham-Rundles C; Klein RF; Mouradian J; Reisman L  
**Source** Kidney Int, 1986 Oct, 30:4, 592-8

**Abstract** This report describes the occurrence of immune complex glomerulonephritis in a patient with eosinophilic gastroenteritis and food hypersensitivity. A coincident allergen injection may have been a contributing factor in the sudden development of the nephrotic syndrome. Markedly elevated levels of circulating immune complexes (greater than 6400 mg/dl) were found containing kappa-casein and bovine serum albumin (BSA), the latter predominating. Markedly elevated serum BSA hemagglutinating titers were also present (1:40,960). Cross-reacting precipitating antibodies to BSA, beef, and pork were demonstrated, but not to flounder or ovalbumin. Renal biopsy revealed immune complex glomerulonephritis with BSA, immunoglobulins M and G and complement deposited focally in the glomerular basement membrane. With strict dietary limitation of identified causative antigens and prednisone therapy, CIC levels decreased to 16,000 micrograms/dl and serum BSA antibody hemagglutinating titer fell 32-fold over a period of 15 months. There was prompt symptomatic relief and amelioration of signs of nephritis. The patient was able to consume a diet normal in protein and caloric content, and statural catch-up growth occurred. Recognition of food antigens to which the patient was hypersensitive provided a rationale for the relief of the gastrointestinal disturbance, growth stunting, and renal disease.
IgA-containing immune complexes; food antigens; IgA nephropathy

Author Jackson S; Moldoveanu Z; Kirk KA; Julian BA; Patterson TF; Mullins AL; Jilling T; Mestecky J; Galla JH

Address Department of Microbiology, University of Alabama, Birmingham 35294.


Abstract The possibility that patients with IgA nephropathy (IgAN) might have abnormal IgA immune responses to immunogens commonly encountered at mucosal surfaces, resulting in the formation of circulating immune complexes (CIC), was examined. Since it is generally held that such increased IgA responses are characterized by detectable aberrancies in handling of IgA-containing CIC, IgAN patients and controls were given a large volume of bovine milk (after dietary deprivation of bovine antigens) and immune complex levels were measured over a period of 12 h. An assay based on binding of CIC containing C3 to solid-phase anti-C3 and subsequent development with isotype-specific antibody revealed no differences in responses of patients and controls with respect to IgG- and IgM-containing CIC. Although IgAN patients tended to have higher levels of IgA-containing CIC, there were no differences in response patterns when IgA CIC levels after ingestion of the milk stimulus were related to baseline levels. Polymorphonuclear leucocytes (PMNC), which bear surface receptors for IgA, were isolated from some subjects at the same times as the samples for CIC levels and examined by two-colour immunofluorescence for the coincident presence of IgA and milk antigens. In contrast to the data obtained in the CIC assays, these experiments revealed the simultaneous presence of IgA and two of three milk proteins in PMNC of IgAN patients but not controls. Follow-up experiments designed to assess more quantitatively the coincidental presence of IgA and milk antigens indicated no significant differences between patients and controls. However, milk proteins seemed to be more commonly associated with IgA in PMNC of IgAN patients, suggesting the presence of non-complement-fixing IgA/antigen CIC after mucosal challenge of some IgAN patients.
Low-antigen-content diet in the treatment of patients with IgA nephropathy.

**Author** Ferri C; Puccini R; Longombardo G; Paleologo G; Migliorini P; Moriconi L; Pasero G; Cioni L

**Source** Nephrol Dial Transplant, 1993, 8:11, 1193-8

**Abstract** Since dietary macromolecular antigens can be involved in the pathogenesis of IgA nephropathy (IgAN), the effect of a low-antigen-content diet was evaluated in 21 patients (10 women, 11 men, mean age 27.7 +/- 10 years) with immunohistochemical findings of active IgAN. The diet was followed for a 14-24-week period (mean 18.8 +/- 6); in all cases the effects of the treatment were evaluated by clinical and serological parameters, and in 11 patients also by repeat renal biopsy. After dietetic therapy a significant reduction of urinary proteins was recorded present in 12 cases during the 6 months preceding the treatment, was markedly reduced or disappeared in 11. At post-treatment control biopsy mesangial and parietal deposits of immunoglobulins, complement C5 fraction and fibrinogen were significantly reduced. The improvement of the objective parameters such as heavy proteinuria, a strong predictor of a poor prognosis, and of immunohistochemical alterations indicate that a low-antigen diet can positively affect patients with IgAN. These results could be ascribed to a reduction of nephritogenic food antigen input and to a putative functional restoration of the mononuclear phagocytic system.

**IgA antibodies to dietary antigens; lectin-binding IgA; nephropathy patients**

**Author** Coppo R; Amore A; Roccatello D; Gianoglio B; Molino A; Piccoli G; Clarkson AR; Woodroffe AJ; Sakai H; Tomino Y **Source** Am J Kidney Dis, 1991 Apr, 17:4, 480-7

**Abstract** We studied serum IgA as antibodies to dietary antigens (Ag), as lectin-binding molecules, and as conglutinin-binding immune complexes (IgAIC) in people from geographical areas in which IgA nephropathy (IgAGN) is particularly frequent. Sera from 63 Italian, 21 Australian, and 25 Japanese patients affected by IgAGN and 24 Italian, 20 Australian, and 40 Japanese healthy controls were studied. Increased values of IgAIC were detected in 42.8% of Italian patients, while only in 23.8% and 8% of Australian and Japanese patients, respectively. Mean values were significantly increased only in Italian patients (P less than 0.0001). Positive values of IgA antibodies against dietary Ag had variable prevalences, but again Italian patients showed the highest frequency, from 19% to 28.5% versus 0 to 38% in Australians and 0 to 16% in Japanese. Mean values of these antibodies were not significantly increased in any patient groups in comparison to the corresponding healthy populations. However, patients with elevated values of IgAIC had significantly higher serum concentrations of antibodies to alimentary components and a linear correlation was found between IgAIC and some IgA antibodies to food components. The relationship between these two series of data was particularly evident for Italian and Australian IgAGN patients. Moreover, the patients with positive data tended to have a cluster of increased levels of IgA antibodies against several alimentary Ag at the same time. A linear correlation was evident between values of IgA antibodies to gluten fractions and to heterologous albumins. None of these correlations was evident among healthy controls.
Permeability and Immune Complexes

Do surface-active lipids in food increase the intestinal permeability to toxic substances and allergenic agents?

Med Hypotheses 2004;63(4):724-30 (ISSN: 0306-9877)
Ilback NG; Nyblom M; Carlfors J; Fagerlund-Aspenstrom B; Tavelin S; Glynn AW

The incidence of many common diseases has increased during the last decades. High fat intake is a risk factor for many diseases. We propose that some of the negative effects of fat are caused by lipid-induced damage of the gastrointestinal epithelium, thus compromising the epithelial function as a barrier for passage of toxic substances and allergenic agents to the circulatory system. Monoglycerides (MGs), phospholipids and fatty acids (FAs) are surface-active molecules that in pharmaceutical studies act as permeability enhancers for hydrophilic drugs with low absorption. Three possible mechanisms were proposed: (a) lipid-induced alterations in intracellular events may cause destabilization of tight junctions between the GI epithelial cells, (b) lipids may destabilize cell membranes, (c) lipids cause intestinal cell damage, which increase the permeability of the GI epithelium. These "side effects" of lipids may partly explain the association between fat intake and disease observed in epidemiological studies.

Presentation of allergen affects the allergic reaction.

Clin Exp Allergy 2003 Nov;33(11):1581-5 (ISSN: 0954-7894)
Grimshaw KE; King RM; Nordlee JA; Hefle SL; Warner JO; Hourihane JO
BACKGROUND: Characterization of fatal and non-fatal reactions to food indicates that the majority of reactions are due to the ingestion of prepared foods rather than the non-processed allergen. In an ongoing study that used a double-blind placebo-controlled food challenge to investigate peanut allergy and clinical symptoms, the observed reaction severity in four of the first six subjects was greater than anticipated. We hypothesized that this was due to differences in the composition of the challenge vehicle. OBJECTIVE: The aim was to investigate whether the severity of observed challenge reactions would be repeated on re-challenge with a lower fat challenge vehicle. METHODS: Peanut-allergic subjects were re-challenged with a lower fat recipe after reacting more severely than was anticipated to an initial peanut challenge. Similar challenge vehicle recipes were used, the only difference being the lower fat content (22.9% compared with 31.5%). The peanut content of the two recipes was analysed using RAST inhibition studies and ELISA tests. RESULTS: Three of four subjects reacted to much smaller doses of peanut protein on re-challenge (mean dose equivalence - 23 times less peanut) with the lower fat recipe. RAST inhibition showed that neither recipe altered epitope recognition. The higher fat recipe required twice as much peanut to cause 50% inhibition. ELISA detected far lower levels of peanut in the higher fat recipe (220 000 parts per million (p.p.m.)) than in the lower fat recipe (990 000 p.p.m.). CONCLUSION: The fat content of a challenge vehicle has a profound effect on the reaction experienced after allergen ingestion. This is another factor to be considered in assessing the risk of certain foods to food-allergic consumers and adds another dimension to clinical, research and regulatory practice.
Hot spices influence permeability of human intestinal epithelia

Jensen Jarolim E; Gajdzik L; Haberl I; Kraft D; Scheiner O; Graf J
Address Department of General and Experimental Pathology, University Hospital AKH, Logo, Vienna, Austria. Source J Nutr, 1998 Mar, 128:3, 577-81
Abstract Indirect evidence suggests that hot spices may interact with epithelial cells of the gastrointestinal tract to modulate their transport properties. Using HCT-8 cells, a cell line from a human ileocecal carcinoma, we studied the effects of spices on transepithelial electrical resistance (TER), permeability for fluorescein isothiocyanate (FITC)-labeled dextrans with graded molecular weight, and morphological alterations of tight junctions by immunofluorescence using an anti-ZO-1 antibody, a marker for tight junction integrity. Two different reactivity patterns were observed: paprika and cayenne pepper significantly decreased the TER and increased permeability for 10-, 20- and 40-kDa dextrans but not for 70-kDa dextrans. Simultaneously, tight junctions exhibited a discontinuous pattern. Applying extracts from black or green pepper, bay leaf or nutmeg increased the TER and macromolecular permeability remained low. Immunofluorescence ZO-1 staining was preserved. In accordance with the above findings, capsaicin transiently reduced resistance and piperine increased resistance, making them candidates for causing the effects seen with crude spice extracts. The observation that Solanaceae spices (paprika, cayenne pepper) increase permeability for ions and macromolecules might be of pathophysiological importance, particularly with respect to food allergy and intolerance.

Intestinal permeability in patients with eczema and food allergy.

Author Jackson PG; Lessof MH; Baker RW; Ferrett J; MacDonald DM
Source Lancet, 1981 Jun 13, 1:8233, 1285-6
Abstract Polyethylene glycol (PEG) was used as a probe molecule to investigate intestinal absorption in eight patients with eczema and evidence of food allergy and ten with eczema alone. In both groups absorption of molecules of larger molecular weight was greater than in normal subjects but absorption of molecules of low molecular weight was normal. There was no difference in absorption between eczema patients with or without food allergy. These results suggest that there is an intestinal mucosal defect in eczema which exists whether or not there is coexistent food allergy. Half the patients with eczema alone and two of the eight with food allergy had more of the large molecular weight PEG recovered in their urine in the second 12 h after ingestion than in the first 12 h. This could be the result of abnormal permeability in the more distal small bowel or even in the colon.

Low doses of drugs able to alter intestinal mucosal permeability to food antigens...

Author Bazzi C; Sinico RA; Petrini C; Rizza V; Torpia R; Arrigo G; Ragni A; D'Amico G
Address Nephrology and Dialysis Division, San Carlo Borromeo Hospital, Milan, Italy.
Source Nephron, 1992, 61:2, 192-5
Abstract In an uncontrolled trial, patients with IgA nephropathy (IgAN) were treated with drugs that can alter the intestinal mucosal permeability to food antigens. These drugs are
known to ameliorate urinary abnormalities and histological lesions of IgAN associated with ulcerative colitis or Crohn's disease [5-aminosalicylic acid (5-ASA)] or to prevent, in mice, the induction of IgAN-like disease by oral immunization [disodium cromoglycate (SCG)]. Nine patients [serum creatinine (s-Cr) less than 2 mg/dl; 24-hour proteinuria higher than 1.5 g, but not nephrotic] were treated with 5-ASA (2.4 g/day for 6 months); 9 similar patients were treated with SCG (400 mg/day for 6 months); the follow-up extended to 6 months after stopping therapy. The 5-ASA group showed a slight but not significant decrease in s-Cr, 24-hour/proteinuria, IgA circulating immune complexes (IgA-CIC) and IgA rheumatoid factor (IgA-RF); serum beta 2-microglobulin and serum IgA were unchanged; 2 of 9 treated patients showed, after 6 months of therapy, a reduction in proteinuria of more than 50% that lasted for the subsequent 18 months. The SCG-treated group showed a slight but not significant increase in 24-hour proteinuria and a significant decrease in serum IgA; unchanged were s-Cr, IgA-CIC, IgA-RF, serum beta 2-microglobulin; no patient treated with SCG showed a reduction in proteinuria of more than 50%. At the dosages and for the periods used, 5-ASA and SCG did not show a significant influence on clinical and laboratory parameters of disease in IgAN; other trials with increased dosages are warranted to definitely ascertain the possible therapeutic role of these drugs in IgAN.

**Intestinal permeability in healthy and allergic children before and after sodium-cromoglycate treatment** …

Author Fälth-Magnusson K; Kjellman Nl; Magnusson KE; Sundqvist T

Source Clin Allergy, 1984 May, 14:3, 277-86

Abstract Gastrointestinal permeability was investigated in twenty-two children on two occasions, before and after treatment with sodium cromoglycate. The children were between 8 and 10 years old; half of them were classified as allergic according to history and laboratory tests, and half of them as healthy. The 6-hr urinary recovery of different-sized polyethyleneglycols (PEG 400 and PEG 1000) in combination with a mathematical model was used to assess the intestinal permeability barrier. No significant differences were seen in the first PEG test between healthy and allergic children, although those with gastrointestinal allergy showed a slightly lower, and those with other allergies a slightly higher recovery of the smaller PEGs than seen in the healthy individuals. After treatment with sodium cromoglycate, however, there was a significant decrease in uptake by allergic children, which could indicate that the permeability properties had returned to normal. The PEG method offers a simple, harmless and reproducible method to measure intestinal permeability properties. The change in permeability observed after sodium cromoglycate corresponds well with the clinical experience of usefulness of the drug in some children with food allergy.
Skin Allergy

Skin disorders caused by food allergy.

Author Atherton DJ  Source  Ann Allergy, 1984 Dec, 53:6 Pt 2, 623-8

A major aetiologic role for foods has been demonstrated in urticaria, atopic eczema and dermatitis herpetiformis. In some patients with urticaria, whealing occurs within minutes of the ingestion of a particular food. In most, but not necessarily all cases, this appears to be a consequence of IgE-mediated cutaneous mast cell degranulation, i.e. a classical type I hypersensitivity response. In other patients with recurrent urticaria, the whealing may be provoked by foods by a much slower and more insidious reaction. This type of reaction has been established in the case of several common food additives, notably azo dyes, but other foods may be able to cause urticaria in a similar fashion. Foods appear to play an important provocative role in many patients with atopic eczema. The reaction in such cases appears to be slow and insidious, almost always unrecognized by the patient and not detected by skin testing or tests for IgE antibodies. There can be no real doubt that dietary gluten is responsible for most, if not all dermatitis herpetiformis, though this relationship was revealed only by the finding of concurrent and usually asymptomatic jejunal villous atrophy in affected individuals. The mechanisms responsible for the slow food reactions in urticaria, atopic eczema and dermatitis herpetiformis remain largely unknown, but are likely to be different in each case.

Contact allergy to food.

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Contact allergies to foods, spices, and food additives can occur to individuals in the workplace or at home. Seven different reaction types have been described. These include irritant contact dermatitis, allergic contact dermatitis, contact urticaria, protein contact dermatitis, phototoxic contact dermatitis, photo-allergic contact dermatitis, and systemic contact dermatitis. The causes of each of these are reviewed and an approach to the diagnosis and management of contact allergy to foods, spices, and food additives is formulated.
Skin manifestations and immunological parameters in childhood food allergy.

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According to Hansen's contact rule, the digestive system should be considered as the main shock organ; yet in food allergy, this is not the case. Very often specific food triggers clinical manifestations not involving the digestive system; that is, reactions are manifested either in the respiratory system, as asthma or rhinitis, or in the skin. In these cases the BALT (broncho-alveolar lymphoid tissue) and GALT (gastrointestinal lymphoid tissue) units play a basic role in the sensitizations. The purpose of this study was to determine the most frequent skin manifestations of food allergy among children, and the most frequently involved foods. We also thought it interesting to evaluate the diagnostic reliability of the different standard immunological parameters utilized by the study team in food allergy. All patients underwent intracutaneous tests with 12 groups of the most frequent food allergens, as well as serum IgE, antigen-specific IgE against foods, and antigen-specific histamine release tests. Antigen-specific IgG4 determination was performed in some cases. The results obtained confirmed previous studies, the most common manifestations being: angioedema (48%), followed by urticaria (31%) and atopic dermatitis (21%). Regarding the frequency of sensitization to different food allergens, in mono- or polysensitization, fish and egg stand out in our environment. Certain food allergens are more frequently responsible for specific skin manifestations. Thus, for fish sensitization, the most frequent skin manifestation is atopic dermatitis (50%); for egg sensitization, angioedema is the most frequent skin manifestation (50%); and for milk, urticaria (50%). Finally, and in agreement with previous works regarding the diagnostic reliability of in vitro techniques, we found that the histamine release test offered the highest percentage of diagnostic reliability. Only for sensitization to milk proteins did antigen-specific IgE demonstrate higher reliability. Once again, we stress that our main problem is the lower reliability of skin tests against food allergens than against inhalant allergens. We emphasize the importance of food as a major factor in the etiopathogenesis of atopic dermatitis, as well as the need to complement the study, when possible, by means of the in vitro techniques described.

Oral food challenges in atopic eczema dermatitis syndrome.

Allergy 2004 Aug:59 Suppl 78:32-4  Niggemann B

The diagnosis of food allergy in infants and children is still a challenging task for the pediatrician. While immediate-type allergic reactions to foods can be diagnosed quite easily, late-phase reactions, e.g. in atopic dermatitis, often represent a diagnostic challenge. Once classical diagnostic procedures such as history, skin prick tests, atopy patch test, and specific immunoglobulin E in serum have been exhausted, double-blind, placebo-controlled food challenges represent the state of the art. After an oligo-allergenic diet, suspected foods or placebo are given in a titrated manner until a clear clinical reaction or the highest dose. The observation period should be 48 h in the case of atopic dermatitis. Constant clinical monitoring is mandatory. Dietetic recommendations are given for 12 months. The effort involved in such a procedure is justified because it can help to avoid clinically relevant food allergens in some cases and in others can prevent children from being exposed unnecessarily to diets that may be harmful to them.
Epicutaneous exposure to protein antigen and food allergy.

Clin Exp Allergy 2003 Aug;33(8):1067-75  (ISSN: 0954-7894)
Hsieh KY; Tsai CC; Wu CH; Lin RH

BACKGROUND: The aetiology of food allergy remains unclear. Although failure to develop or breakdown in oral tolerance has been proposed, the existence of physiologic sensitization routes other than the gastrointestinal tract cannot be excluded. OBJECTIVE: The purpose of this study is to clarify whether or not exposure to allergen through the skin can promote food allergy. METHODS: BALB/c mice were shaved on the back, and a patch impregnated with 100 micro g of ovalbumin (OVA) was applied to the dorsal skin for a 1-week period and then removed. After three courses of sensitization, OVA-specific antibodies in sera were measured, and then mice were orally challenged with 50 mg of OVA. Anaphylactic symptoms, plasma histamine levels, and histology of intestines and lungs after oral challenge were examined. RESULTS: Epicutaneous (EC) sensitization of mice to OVA induced a high level of OVA-specific IgE. Subsequent oral challenge with OVA resulted in symptoms of systemic anaphylaxis with elevated levels of plasma histamine as well as histological changes in both intestines and lungs. In the presence of anti-IL-4 antibodies, EC sensitization failed to provoke an IgE response, but still induced a Th2-predominant cellular immune response in lungs after oral challenge. CONCLUSION: We demonstrated for the first time that food allergy can be induced by allergen exposure through the skin. Our results identify a novel role of EC sensitization in the pathogenesis of food allergy.

Mechanisms in adverse reactions to food. The skin.

Author Sampson HA Address Department of Pediatrics, Johns Hopkins University School of Medicine, Baltimore, MD 21205, USA. Source Allergy, 50: 20 Suppl, 1995, 46-51

Ingested food antigens rapidly cross the gastrointestinal barrier and reach pro-inflammatory cells in the skin. Food allergy provokes urticaria/angioedema by classical, Type I, IgE-mediated hypersensitivity. Food-induced atopic dermatitis is the result of non-classical, IgE-directed hypersensitivity involving resident mast cells, Langerhans cells, CD4+, TH2 lymphocytes and monocytes. A form of gluten sensitivity provokes a characteristic eczematous-like rash and enteropathy (Dermatitis herpetiformis).

Precipitins to dietary proteins in atopic eczema.

Author Barnetson RS; Drummond H; Ferguson A Source Br J Dermatol, 1983 Dec 109:6, 653-5

Precipitating antibodies to foods have been assayed in three groups of patients with atopy. Forty-five per cent of patients with atopic eczema and IgE-mediated food allergy had precipitins to foods in their serum compared with only 15% of patients with atopic eczema without evidence of food allergy, and 16% of patients with atopic asthma and/or rhinitis. It is likely that this results from increased intestinal permeability in the group with eczema and food allergy.
Effects of sodium cromoglycate in asthma and urticaria due to foods.

Author Harries MG; O'Brien IM; Burge PS Source Clin Allergy, 1978 Sep, 8:5, 423-7

Out of twenty patients with a history of asthma or urticaria attributed to food substances, ten reacted on oral challenge: seven with asthma, one with asthma and urticaria and two with urticaria alone. In five of the eight asthmatic reactors, the symptoms developed within a few sec and there was no associated rise in free venous plasma histamine. In those remaining, two with asthma, two with urticaria and one with both, the symptoms developed only after 20-30 min. A rise in free plasma histamine occurred only in the two subjects with urticaria alone. The third with urticaria and asthma did not have blood estimations performed. Sodium cromoglycate in a dosage of 800 mg a day for 1 week, or a single dose of 1.0 g by mouth, did not block any of the reactions. By inhalation it blocked the asthmatic reactions which developed within a few sec of challenge.

Differences in lymphocyte proliferative responses to food antigens

Author Iida S; Kondo N; Agata H; Shinoda S; Shinbara M; Nishida T; Fukutomi O; Orii T Address Department of Pediatrics, Gifu University School of Medicine, Japan. Source Ann Allergy Asthma Immunol, 74: 4, 1995 Apr, 334-40

Abstract BACKGROUND: Clinical symptoms of patients with food-sensitive atopic dermatitis often improve with increasing age. OBJECTIVE: To investigate this tendency and the underlying mechanism. METHODS: We selected and divided 194 food-sensitive atopic dermatitis patients into three age groups. The proliferative responses of peripheral blood mononuclear cells (PBMCs) to food antigens and specific IgE antibodies to foods then were evaluated with respect to age. We also followed up 55 food-sensitive patients with atopic dermatitis and examined their improvement ratio after 1 year. Further, we investigated changes in lymphocyte proliferative responses to food antigens and specific IgE antibodies to foods in food-sensitive patients with atopic dermatitis during elimination diets. RESULTS: Proliferative responses of PBMCs to ovalbumin of patients in the over 6-years-old group were significantly (P < .05) lower than those of the less than 1-year-old group. Proliferative responses of PBMCs to bovine serum albumin of patients in the over 6-years-old group were significantly (P < .05) lower than those in the 1 to 5-year-old group and in the less than 1-year-old group. RAST values for hen egg in the over 6-years-old group were significantly (P < .05) lower than those for the less than 1-year-old group. Improvement was shown by 13 of the 33 hen egg-sensitive patients with atopic dermatitis, an improvement ratio of 39%, and by 9 of the 22 cow milk-sensitive patients with atopic dermatitis, an improvement ratio of 41%. Proliferative responses of PBMCs to food antigens in food-sensitive patients with atopic dermatitis decreased rapidly after patients were placed on elimination diets. CONCLUSION: The PBMC proliferative responses to food antigens and RAST values were higher for young children and lower for older ones who suffered from food-sensitive atopic dermatitis. Oral tolerance, in addition to the development of digestive and absorptive functions, may be responsible for these immunologic changes.
Experimental food allergen-induced cutaneous reactions.

Prescott VE; Forbes E; Foster PS; Matthaei K; Hogan SP

Individuals with food allergy often present with urticaria and atopic dermatitis. Indeed, susceptibility to food allergy may predispose to the development of these cutaneous allergic disorders. Recently, we developed a model of food allergy, whereby oral consumption of food [pea Pisum sativum L.; expressing alpha-amylase inhibitor-1 (alphaAI) from the common bean Phaseolus vulgaris L. cv Tendergreen (pea-alphaAI)] promotes a T helper cell type 2 (Th2) inflammatory response and predisposes to cutaneous allergic reactions following subsequent food allergen (alphaAI) exposure. To delineate the kinetics of food allergen-induced cutaneous reactions and examine the inflammatory mechanisms involved in this allergic reaction, we used interleukin (IL)-13-, IL-4 receptor alpha-, and eotaxin-1-deficient mice and performed serum transfer and CD4+ T cell depletion studies. We demonstrate that consumption of pea-alphaAI promotes an alphaAI-specific immunoglobulin G1 (IgG1) and IgE antibody response. Furthermore, we show that subsequent food allergen (alphaAI) challenge in the skin induced an early (3 h)- and late-phase (24 h) cutaneous allergic reaction. The early-phase response was associated with mast cell degranulation and the presence of Ig, whereas the late-phase response was characterized by a lymphoid and eosinophilic infiltrate, which was critically regulated by CD4+ T cells, IL-13, and eotaxin-1. Collectively, these studies demonstrate that food allergy can predispose to cutaneous inflammatory reactions, and these processes are critically regulated by Th2 immune factors.
Food allergy in children: diagnosis and treatment with sodium cromoglycate.

Author Businco L; Cantani A AddressDepartment of Pediatrics, University of Rome La Sapienza Medical School, Italy. Source Allergol Immunopathol (Madr), 1990 Nov-Dec, 18:6, 339-48

Abstract Food allergy (FA) is a very important problem affecting numbers of infants and children with protean manifestations which are frequent challenges to the pediatrician and other specialists working with children. Adverse reactions to food are very complex, frequently mediated by IgE mechanisms, and often by other mechanisms. To make the correct diagnosis and to arrive at a proper therapeutic approach requires all the skill a physician can gather. Only an extensive knowledge of the various mechanisms and pharmacologic agents that can be used to prevent or treat these adverse reactions will allow the physician to approach the problem scientifically and come to a reasonable solution for the patient. The role of dietary factors in atopic dermatitis (AD) has long been a subject of controversies. However, it has been shown that FA plays a role in some children with AD. Therefore, the management of this multifaceted disorder is a challenge for pediatricians, dermatologists, and allergists. SCG, which is the salt of a bis-chromone carboxylic acid, has been shown to be of proven efficacy in the prophylaxis of bronchial asthma, allergic rhinitis, and of other disorders associated with mast cell degranulation. The drug has different modes of action, such as inhibition of rat passive cutaneous anaphylaxis, and the antigen-induced histamine release from passively sensitized peritoneal cells. Recently, clinical studies indicated that SCG has a direct effect on inflammatory cells, inhibiting either various leukocyte functions (membrane receptor expression, cytotoxic capacity), or "in vitro" activation of human neutrophils, eosinophils and monocytes.

Although SCG has been widely used for the management of respiratory allergy, conflicting results of FA treatment have been reported by several authors. We have reviewed 18 papers on the use of SCG in the management of children with FA, which included 341 children aged 0.5-15 years. In this paper we discuss 12 studies reporting 281 children affected with AD.
**Eosinophils in the pathogenesis of skin lesions food-sensitive atopic dermatitis.**

Author Magnarin M; Knowles A; Ventura A; Vita F; Fanti L; Zabucchi G Address Institute of General Pathology, University of Trieste, Italy. Source J Allergy Clin Immunol, 96: 2, 1995 Aug, 200-8

Abstract Atopic dermatitis is associated with skin and blood eosinophilia, but the role of eosinophils in the pathogenesis of the skin lesions is poorly understood. METHODS: To determine whether eosinophils play a role in the pathogenesis of the skin lesions in atopic dermatitis, we studied the relationship between the severity of the disease and both the number and the extent of activation of eosinophils in 15 patients with food-sensitive atopic dermatitis. Furthermore, this relationship was re-evaluated in eight of these patients who, after a period of elemental diet or total parenteral nutrition, showed significant clinical improvement. RESULTS: A clear relationship was found between the number of light-density eosinophils and the severity of the disease both during the active disease and after clinical improvement. Furthermore, we describe an adhesion-stimulating activity for eosinophils in patients’ plasma, which does not change after recovery. CONCLUSIONS: Taken together, these observations strongly indicate that eosinophils play a pivotal role in the pathogenesis of the skin lesions in atopic dermatitis. In particular, the light-density phenotype seems to be an essential feature of eosinophils involved in this process. The adhesion-promoting activity that we observed in the patients’ plasma could be important in the recruitment of eosinophils from the blood into the skin.

**IgE-binding; wheat, rye, barley and oats... adult atopic dermatitis patients.**

Author Varjonen E; Savolainen J; Mattila L; Kalimo K Address Department of Dermatology, Helsinki University Central Hospital, Finland. Source Clin Exp Allergy, 1994 May, 24:5, 481-9

Abstract The allergen extracts of wheat, rye, barley and oats flours were characterized by IgE-immunoblotting with serum samples from 40 adult patients; 35 patients with atopic dermatitis, one with rhinitis and four with urticaria. All these patients had been positive when skin-prick testing was carried out with one or more of the four flour extracts or displayed one or more positive cereal RAST results. Acidic and neutral protein extracts of wheat, rye, barley and oats flours were processed for the immunoblotting experiments and 35 patients appeared positive in IgE immunoblotting with wheat and rye, 32 with barley and 33 with oats. The IgE immunoblots showed polyspecific binding patterns; wheat exhibited 36 IgE stained bands, rye 35, barley 33 and oats 10. Eighteen of the IgE stained bands could be classified as intermediate allergens for wheat, 23 for rye and 15 for barley. The 66 kDa protein in oats was visualized by 28 out of 33 sera (84%), however, there was evident non-specific binding to this region and thus it may also represent lectin-like binding. The most frequent staining with wheat extract was seen in the 26 kDa protein region (15/35, 43%), with rye in the 40 kDa (16/35, 46%) and with barley in the 26 and 46 kDa protein bands (14/32, 44%). Simultaneous staining with wheat, rye and barley extracts were observed with 16 bands suggesting crossreactivity between these cereals.
Children with atopic eczema

Author Sloper KS; Wadsworth J; Brostoff J  Address Department of Immunology, University College and Middlesex Hospital School of Medicine, London. Source Q J Med, 1991 Aug, 80:292, 695-705

Abstract A group of 91 children with atopic eczema entered a study where clinical and immunological features were compared before and after a food elimination diet, and after double blind randomized food challenges in which a food was given for several days at a time. Eczema improved significantly during the diet and became worse on food challenges. The clinical outcome of food elimination could not be predicted by the initial skin prick test results, serum immunoglobulins, total or food-specific IgE, or complexed IgG or IgE. There was a tendency for patients whose eczema did not improve after food elimination to have higher initial serum IgG levels, without a corresponding increase in skin infections. The radioallergosorbent test to soy gave a higher result in those who improved on diet. No significant changes in serum or complexed immunoglobulins occurred over the period of food elimination or subsequent food challenge. Results of food challenges could not be predicted by initial serum immunoglobulin levels. A history of spring/summer exacerbations of eczema correlated with positive skin prick tests to silver birch pollen, but not to grass pollen. Serological tests did not help in planning food diets in atopic eczema, and the immunological studies did not delineate any particular mechanism by which foods might exacerbate eczema.

CD4+ cells proliferate after peanut-extract-specific and CD8+ cells proliferate after polyclonal stimulation of PBMC of children with atopic dermatitis

Author Laan MP; Tibbe GJ; Oranje AP; Bosmans EP; Neijens HJ; Savelkoul HF Address Department of Immunology, Erasmus University Rotterdam, The Netherlands. Source Clin Exp Allergy, 1998 Jan, 28:1, 35-44

Abstract  Few studies describe in vitro food-allergen induced proliferative responses and cytokine production of PBMC of children with atopic dermatitis. This is especially true for peanut-allergen. OBJECTIVES: To analyse the specificity of the T cell in proliferative responses, in children with atopic dermatitis with or without peanut allergy and healthy age-matched children. METHODS: Proliferative responses were measured by [3H]-thymidine incorporation and by expression of the intracellular Ki67-antigen using flow cytometry after antigen-specific stimulation of PBMC with peanut-extract (day 7) or polyclonal stimulation with Phorbol-12myristate-13acetate and Ca-ionophore (day 3). Cytokine mRNA (Interferon-gamma (IFN gamma), IL-4) was detected by semiquantitative RT-PCR. Cytokine production (IL-4, IFN gamma) was measured by ELISA. RESULTS: Peanut-extract induced proliferative responses of PBMC from children with atopic dermatitis and peanut allergy (AD+PA+) were significantly higher as compared with the other groups studied. Ki67-antigen double staining revealed that 80-100% of the proliferating cells were CD4+. These proliferative responses correlated significantly with the increase in IL-4 mRNA expression after peanut-extract specific stimulation. After polyclonal stimulation, however, CD8+ cells preferentially proliferated. The degree of proliferation after polyclonal stimulation correlated inversely with the ratio of IL-4/IFN gamma production. CONCLUSIONS: The principal responding population of T cells in proliferative responses is different after peanut-extract specific and polyclonal stimulation of PBMC from AD+PA+ patients. Furthermore, we found indirect evidence
that the PBMC fraction of AD+PA+ children contains increased frequencies of peanut-specific T helper-2 cells.
Children with atopic eczema response to food elimination

Author Sloper KS; Wadsworth J; Brostoff J
Address Department of Immunology, University College and Middlesex Hospital School of Medicine, London.

Abstract The role of foods in the exacerbation of atopic eczema was studied by offering a food elimination diet and subsequent random order, double-blind food challenges to 91 eczematous patients, [49 males and 42 females, median age 4.5 years (range 0.5-15)]. Eczema improved in 49 of 66 (74 per cent) (skin score fall greater than or equal to 3) after stopping cows’ milk, eggs and various other foods, with significant decreases in erythema, excoriation, lichenification and extent of eczema. One hundred and ninety-four food challenges were given to 64 patients who had shown objective or subjective improvement. Eczema and associated symptoms were significantly worse after cows’ milk and tomato compared with placebo. Egg did not worsen eczema, but 48 per cent of 44 challenges were incomplete, mainly due to hypersensitivity reactions and challenge refusal. The longer a food had been avoided, the less likely was the chance of a positive food reaction. Clinical history did not predict response to dietary manipulation. A standard elimination diet avoiding cows’ milk, egg, tomatoes and possibly colours and preservatives should help up to three-quarters of patients, and is easy to implement with the help of a dietician. This diet may be considered in all children with moderate or severe eczema.

Food contact hypersensitivity and elimination diet in young children

Author Oranje AP; Aarsen RS; Mulder PG; van Toorenbergen AW; Liefaard G; Dieges PH
Address Department of Dermato-Venereology, Erasmus University, Rotterdam, The Netherlands.
Source Acta Derm Venereol Suppl (Stockh), 176:1992, 41-4

Abstract In atopic dermatitis [AD], not only food consumption, but direct skin-contact too can provoke hypersensitivity reactions. We imitated food immediate-contact hypersensitivity [FICH] to cow’s milk, egg, peanut or soy by a skin provocation test. This skin application food test [SAFT] was applied in 91 patients aged up to 5 years and suffering from AD, and in 16 healthy controls (all SAFT-negative). In the SAFT-positive patients (n = 61), FICH to egg was observed in 72%, to cow's milk in 47%, to peanut in 34% and soy in only 1 patient. SAFT and RAST scores correlated weakly. Nevertheless, many discrepancies between SAFT and RAST results were found. In 20 of the 61 (33%) patients with FICH, a flare-up in AD was noted at SAFT testing. Upon introducing dietary restrictions, AD improved impressively in 9 of 23 patients who could be followed up. FICH is an important symptom in children with AD and food allergy.
Effect of age on antibodies to food antigens in elderly Swiss people.

Author Brüssow H; Sidoti J; Blondel-Lubrano A; Borel Y; Michel JP; Dirren H; Decarli B

Abstract Serum antibody concentrations to two viral, five bacterial, and two food antigens were investigated in 307 elderly Swiss subjects, and the hypothesis of whether serum antibody titers decreased with age was tested. The cross-sectional part of the study consisted of 216 unselected consecutive patients hospitalized in one geriatric hospital. The patients were divided into two age groups (65 to 84 and 85 to 102 years old), and their antibody titers were compared. No age-related decreases in antibody titers were observed. The members of the two age groups were well matched for medical diagnosis and nutritional and inflammatory status. The prospective part of the study consisted of 91 healthy elderly subjects living in the community; they were 71 to 76 years old when they were enrolled in the study. Their serum antibody status was measured at the beginning of the study and 4 years later. We observed a significant decrease in diphtheria antitoxin levels and a significant increase in antibody titer to the capsular polysaccharide of Streptococcus pneumoniae. No change in antibody titer to rotavirus, respiratory syncytial virus, lipopolysaccharide of Escherichia coli, C polysaccharide of S. pneumoniae, or the polyribosyl-ribitol phosphate of Haemophilus influenzae was observed. Thus, no signs of B-cell immunosenescence were seen in these two groups of elderly Swiss people.

Radioimmunoassay for detection of circulating food protein antigens

Author Paganelli R; Levinsky RJ Source J Immunol Methods, 1980, 37:3-4, 333-41

Abstract A two site solid phase radioimmunoassay for detection of common food antigens is described. Bovine serum albumin, beta-lactoglobulin and ovalbumin can be detected in normal human serum at levels ranging from 0.1 to > 1000 ng/ml; sensitivity is not impaired by the presence of low levels of antibodies. Thirty min to 3 h after oral intake of milk, beta-lactoglobulin could be detected in the sera of 3 normal individuals, at a concentration of 0.1-3 ng/ml. This assay should prove useful in assessing the importance of macromolecular absorption in food allergy and in other gastrointestinal diseases.

Influence of dietary manipulation on atopic disease in infants

Author Bardare M; Vaccari A; Allievi E; Brunelli L; Coco F; de Gaspari GC; Flauto U
Address Pediatric Clinic I, University of Milan. Source Ann Allergy, 71: 4, 1993 Oct, 366-71

Abstract Of 5,500 newborn infants whose family histories were screened, 900 were found to have anamnestic risk. Cord-blood IgE was evaluable in 4,677 of these newborns, of which 394 had levels > or = 1 IU/mL; 84 infants had both anamnestic risk and elevated cord-blood IgE levels. Parents of infants with anamnestic risk were informed of their child's risk of atopy. Additionally, for 391 infants at two of the three participating hospitals, a preventive diet was prescribed that recommended breastfeeding for the first 6 months of life, with maternal diet restricted to no more than 200 dL of cow milk per day, no more than one egg per week, and no tomato, fish, shellfish, nuts, or foods allergic to the mother. Only soy formula was recommended, and introduction of solid foods was also carefully prescribed. Furthermore, doctors recommended against exposure to tobacco
smoke, animal allergens, and early entrance into daycare. Evaluable infants whose parents complied with the prescribed diet were found to have a lower incidence of atopy during the first year of life (13.3%, n = 158) than infants whose parents had ignored the prescribed diet (54.7%, n = 86) or infants whose parents were offered no dietary recommendations (28.9%, n = 218). Differences between the compliant group and the two groups with unrestricted diets were significant, indicating that this prescribed diet may protect against or delay onset of food allergies during the first year of life.

Milk-induced eczema is associated with the expansion of T cells

Author Abernathy-Carver KJ; Sampson HA; Picker LJ; Leung DY Address Department of Pediatrics, National Jewish Center for Immunology and Respiratory Medicine, Denver, Colorado 80206. Source J Clin Invest, 95: 2, 1995 Feb, 913-8

Abstract The extravasation of T cells at sites of inflammation is critically dependent on the activity of homing receptors (HR) involved in endothelial cell recognition and binding. Two such HR (the cutaneous lymphocyte antigen [CLA] and L-selectin) have been shown to be selectively involved in T cell migration to skin and peripheral lymph nodes, respectively. This study was designed to assess the relationship between the organ specificity of an allergic reaction to food and the expression of HR on T cells activated in vitro by the relevant food allergen. Peripheral blood mononuclear cells were isolated from seven milk allergic children with a history of eczema when exposed to milk. All patients had a positive prick skin test and double-blind placebo-controlled food challenge to milk. 10 children with either allergic eosinophilic gastroenteritis or milk-induced enterocolitis and 8 nonatopic adults served as controls. Five-parameter flow cytometry using monoclonal antibodies was used for detection of the specific HR on freshly isolated T cells versus T cell blasts induced by a 6-d incubation with casein, as compared with Candida albicans. After in vitro stimulation with casein, but not C. albicans, patients with milk allergy and atopic dermatitis had a significantly greater percentage of CLA+ T cells (P < 0.01) than controls with milk-induced enterocolitis, allergic eosinophilic gastroenteritis, or nonatopic healthy controls. In contrast, the percentage of L-selectin-expressing T cells did not differ significantly between these groups. These data suggest that after casein stimulation allergic patients with milk-induced skin disease have an expanded population of CLA+ T cells, as compared with nonatopics or allergic patients without skin involvement. We postulate that heterogeneity in the regulation of HR expression on antigen-specific T cells may play a role in determining sites of involvement in tissue-directed allergic responses.
Differences in lymphocyte proliferative responses to food antigens

Author: Iida S; Kondo N; Agata H; Shinoda S; Shinbara M; Nishida T; Fukutomi O; Orii T
Address: Department of Pediatrics, Gifu University School of Medicine, Japan. Source: Ann Allergy Asthma Immunol, 74: 4, 1995 Apr, 334-40

Abstract: Clinical symptoms of patients with food-sensitive atopic dermatitis often improve with increasing age. OBJECTIVE: To investigate this tendency and the underlying mechanism. METHODS: We selected and divided 194 food-sensitive atopic dermatitis patients into three age groups. The proliferative responses of peripheral blood mononuclear cells (PBMCs) to food antigens and specific IgE antibodies to foods then were evaluated with respect to age. We also followed up 55 food-sensitive patients with atopic dermatitis and examined their improvement ratio after 1 year. Further, we investigated changes in lymphocyte proliferative responses to food antigens and specific IgE antibodies to foods in food-sensitive patients with atopic dermatitis during elimination diets. RESULTS: Proliferative responses of PBMCs to ovalbumin of patients in the over 6-years-old group were significantly (P < .05) lower than those of the less than 1-year-old group. Proliferative responses of PBMCs to bovine serum albumin of patients in the over 6-years-old group were significantly (P < .05) lower than those in the 1 to 5-year-old group and in the less than 1-year-old group. RAST values for hen egg in the over 6-years-old group were significantly (P < .05) lower than those for the less than 1-year-old group. Improvement was shown by 13 of the 33 hen egg-sensitive patients with atopic dermatitis, an improvement ratio of 39%, and by 9 of the 22 cow milk-sensitive patients with atopic dermatitis, an improvement ratio of 41%. Proliferative responses of PBMCs to food antigens in food-sensitive patients with atopic dermatitis decreased rapidly after patients were placed on elimination diets. CONCLUSION: The PBMC proliferative responses to food antigens and RAST values were higher for young children and lower for older ones who suffered from food-sensitive atopic dermatitis. Oral tolerance, in addition to the development of digestive and absorptive functions, may be responsible for these immunologic changes.

Food-induced contact urticaria syndrome (CUS) in atopic dermatitis:

Author: Oranje AP; Van Gysel D; Mulder PG; Dieges PH
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Abstract: IgE-mediated contact urticaria syndrome (CUS) is one of the manifestations of allergy in childhood atopic dermatitis (AD). Allergens such as foods and animal products penetrate the skin easily. They can then cause urticarial reactions in sensitized individuals. A provocation test system for foods, called the skin application food test (SAFT), has been developed. Over more than 5 years, a group of 175 patients with AD was built-up and investigated in a prospective follow-up study with SAFT. SAFT was more frequently positive in AD children aged 0-2 years than in older children. In several children of this population (Group 1), we repeated SAFT within a period of 1 year. In another unrelated group of children (Group 2-1), we compared the results of ‘original’ SAFT and SAFT using square chambers (Van der Bend) or Silver patches. In the 3rd group (Group 2-2) we compared ‘original’ SAFT with SAFT using big Finn Chambers. The agreement between the tests was high: in Group 1, we observed 88 to 93% concordant scores, and in Group 2, the scores were 96% to 100%. Statistically, the kappa coefficient ranged from 0.71-0.87 in Group 1, and from 0.83-1.00 in Group 2. SAFT is therefore
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highly reproducible. Agreement was at least $\geq 88\%$ between the scores (the lowest kappa value observed was at least 0.71).

**Problem foods using food and symptom diaries.**

Author Kueper T; Martinelli D; Konetzki W; Stamerjohn RW; Magill JB Address Wisconsin Data Laboratory, Ltd, Waukesha. Source Otolaryngol Head Neck Surg, 112: 3, 1995 Mar, 415-20

Abstract Food and symptom diaries were used to identify problem foods for each of 164 patients with chronic medical problems such as headache, fatigue, congestion, abdominal pain, and sinus problems. A statistical analysis related the total load of 90 biologic families, as well as caffeine, alcohol, and lactose, to changes in symptom intensity during a 2-week diary. The results helped 75% of the patients when used as a guide for elimination diets. Open challenges confirmed 47% of the identified food components. This study required a database and software to estimate recipe components for an average of 243 foods per patient. The analysis of each patient's diary produces a main report that lists suspect food components for each symptom. The report lists components in decreasing order of statistical confidence and gives lag times between food ingestion and symptom change. This report also shows that initial direction of the symptom change as a direct or masking effect. Foods that appear "safe" or unrelated to the symptoms are also listed. A second report lists the patient's food sources for each of the suspected food components. The report shows the percentage contribution of source foods and is useful for patient education and the design of elimination diets.

**Cow milk allergy .... atopic disorders.**

Author Hill DJ; Bannister DG; Hosking CS; Kemp AS Address Department of Allergy, Royal Children's Hospital, Parkville, Australia. Source Clin Exp Allergy, 24: 12, 1994 Dec, 1137-43

Abstract In order to examine the relationship between cow milk allergy (CMA) and atopic disorders in childhood, a consecutive group of 42 infants with IgE mediated CMA was followed for at least 2 years. The incidence of sensitization to common food and inhalant antigens and the development of eczema, asthma, and food allergies was examined for the cohort and compared between patients whose CMA remitted and those with persistent disease. In this cohort the prevalence of eczema was 57%, asthma 69%, egg allergy 67%, peanut allergy 55%, and 83% of infants demonstrated positive skin-prick tests to three or more allergens. At the end of the study CMA had remitted in 13 patients (median age 44 months) whereas in 29 patients it persisted (median age 44 months). Although there was no significant difference in the incidence of eczema or asthma during the study between these two patient groups, the incidence of allergy to egg and peanut butter was significantly greater for children with persistent CMA. Consistent with our hypothesis that children with persistent CMA have a more severe dysregulation of IgE synthesis than those whose disease remits, patients with persistent CMA had a significantly higher incidence of and level of skin sensitivity to inhalant and other dietary allergens. Sensitization to the inhalant allergens Dermatophagoides pteronyssinus, cat dander and ryegrass was frequently seen in early infancy and increased during the study period. Thus, children with IgE mediated CMA frequently generate IgE responses to
multiple dietary and inhalant allergens in infancy and early childhood and develop immediate hypersensitivity to other foods as well as clinical eczema, and asthma.
Atopic dermatitis and food hypersensitivity reactions.

Author Burks AW; James JM; Hiegel A; Wilson G; Wheeler JG; Jones SM; Zuerlein N
Address Department of Pediatrics, University of Arkansas for Medical Sciences, Little Rock, Source J Pediatr, 1998 Jan, 132:1, 132-6

Abstract To determine the role of food hypersensitivity in atopic dermatitis and to determine whether patients with atopic dermatitis who had food hypersensitivity could be identified by screening prick skin tests using a limited number of food allergens. STUDY DESIGN: Patients with atopic dermatitis attending the Arkansas Children's Hospital Pediatric Allergy Clinic underwent allergy prick skin testing to a battery of food antigens. Patients with positive prick skin tests underwent double-blind, placebo-controlled food challenges. RESULTS: One-hundred sixty-five patients were enrolled and completed the study. Patients ranged in age from 4 months to 21.9 years (mean 48.9 months). Ninety-eight (60%) patients had at least one positive prick skin test. A total of 266 double-blind, placebo-controlled food challenges were performed. Sixty-four patients (38.7% of total) were interpreted as having a positive challenge. Seven foods (milk, egg, peanut, soy, wheat, cod/catfish, cashew) accounted for 89% of the positive challenges. By use of screening prick skin tests for these seven foods we could identify 99% of the food allergic patients correctly. CONCLUSIONS: This study confirms that most children with atopic dermatitis have food allergy that can be diagnosed by a prick skin test for the seven foods.

Skin disorders caused by food allergy.

Author Atherton DJ
Source Ann Allergy, 1984 Dec, 53:6 Pt 2, 623-8

Abstract A major aetiologic role for foods has been demonstrated in urticaria, atopic eczema and dermatitis herpetiformis. In some patients with urticaria, whealing occurs within minutes of the ingestion of a particular food. In most, but not necessarily all cases, this appears to be a consequence of IgE-mediated cutaneous mast cell degranulation, i.e. a classical type I hypersensitivity response. In other patients with recurrent urticaria, the whealing may be provoked by foods by a much slower and more insidious reaction. This type of reaction has been established in the case of several common food additives, notably azo dyes, but other foods may be able to cause urticaria in a similar fashion. Foods appear to play an important provocative role in many patients with atopic eczema. The reaction in such cases appears to be slow and insidious, almost always unrecognized by the patient and not detected by skin
testing or tests for IgE antibodies. There can be no real doubt that dietary gluten is responsible for most, if not all dermatitis herpetiformis, though this relationship was revealed only by the finding of concurrent and usually asymptomatic jejunal villous atrophy in affected individuals. The mechanisms responsible for the slow food reactions in urticaria, atopic eczema and dermatitis herpetiformis remain largely unknown, but are likely to be different in each case.

**Skin manifestations of food allergy.**

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The pediatrician is faced with evaluating a panoply of skin rashes, a subset of which may be induced by food allergy. Acute urticaria is a common manifestation of an allergic skin response to food. Approximately one third of infants/children with moderate to severe atopic dermatitis have food allergy. Although diagnosis of acute urticaria provoked by a food may be evident from a straightforward history and confirmed by diagnostic tests to detect food-specific IgE antibody, determination of the role of food allergy in patients with atopic dermatitis is more difficult and may require additional diagnostic maneuvers, including elimination diets and oral food challenges. The immunopathologic basis of food-allergic disorders that affect the skin and a rational approach to diagnosis and treatment are discussed. Additional disorders that are caused by or mimic ones caused by food allergy are reviewed.
CONCEPTS OF IMMUNE-MEDIATED DISEASE

FOOD ORIGIN OF ANTIGENS

The Concept of delayed pattern or Type 3, 4 "FOOD ALLERGY"

Important References To 1984

Laroche, G., Richet, C. (Fils) and Saint-Girons, F., Alimentary anaphylaxis (Gastrointestinal Food Allergy) Translated by Rowe, M.P., and Rowe, A.H., (Eds.). Berkley: University of California Press, 1930.


Kraehenbuehl, J.P., and Champiche, M.A., Early stages of intestinal absorption of specific antibodies in the newborn: An ultrastructural,
Clinical and immunological aspects of food allergy in childhood Estimation of IgG, IgA and IgE antibodies to food antigens in children with food allergy and atopic dermatitis. Acta Paediatrica Scandinavia,
66, 31.

Geha, R.S. (1977) Circulating immune complexes and activation of the complement sequence in acute allergic bronchopulmonary aspergillosis. Journal of Allergy and Clinical Immunology. 60, 357.


Zweiman, B., A new therapeutic strategy in systemic vasculitis? New
McLaughlan, P., and Coombs, R.R.A., Latent anaphylactic sensitivity of
Alpha Education Book List

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Alpha Nutrition Program

Dr. Stephen Gislason invented "diet revision therapy" in 1983 and has in subsequent years written a series of books on nutritional therapy. His method of diet revision evolved over the next 15 years as the "Core Program" and has been tested by thousands of people. In 1998, the venerable Core Program was incorporated into Alpha Nutrition as the Alpha Nutrition Program.

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The recipes are gluten-free, milk-free, egg-free and follow a progressive path from Phase 1 foods (a strict hypoallergenic diet) to a more expanded food list in Phase 3.