

# Causes and effects of nut allergy



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## NUT ALLERGY

### 1. INTRODUCTION:

#### 1. 1 What is an allergy?

When exposed to certain foreign substances, a reaction takes place in our immune system which is referred to as allergy [1]. Population of more than 25% in industrialized countries suffer from allergies [2]. These reactions are exaggerated because these foreign substances are recognized as harmless and no response takes place in non-allergic individuals. Most of the allergies are hypersensitive immune responses to these foreign substances. A substance that causes allergy is known as an ‘allergen’ [1]. Allergens include dust mites, foods, molds, pollens, animal dander, insect stings, medicines, etc. [2, 3]. Allergens may be ingested (swallowed or eaten), inhaled, injected into the body or applied to the skin. Most of the allergens are harmless and so majority of the individuals are not affected by them.

In the modern world allergy is one of the most wide spread diseases. Allergy can vary in many ways like different individuals show various symptoms of allergies which can be moderate (runny nose) to extreme (anaphylaxis) [2].

#### 1. 2 The Immunology of Allergies:

Our body is protected from pathogens and other foreign substances by our immune system which produces a glycoprotein known as immunoglobulin (Ig) or antibodies from B-cells or plasma cells. The antibody involved in allergic reaction is Immunoglobulin E (IgE). There is overproduction of IgE during allergic response [2].

### 1. 3 Food Allergy:

An abnormal response triggered by the body's immune system to a food is known as food allergy [4]. Food allergy is different from food intolerance, toxin mediated reactions and pharmacological reactions [4]. 2. 4-3. 7% of adults are affected by food allergy [5]. Various fruits like peach, apple including peanut and tree nut are the most common foods which elicit a reaction. The most common cause of food allergy is anaphylactic reactions. Different studies have shown that food allergy has various health related issues which has a negative impact on individuals. Food allergy is the major cause of life threatening hypersensitivity reactions [5].

The most common foods that elicit allergy reactions include:

- Fish
- Milk
- Egg
- Soy
- Wheat
- Peanut
- Treenut

To prevent further reactions related to food allergy we need to avoid allergenic foodstuff [6].

### 1. 4 Nut Allergy:

Individuals affected by nut allergy experience a large variation in the intensity of their allergic reactions. Nut allergy is majorly seen in children.

Peanuts and tree nuts mostly cause life threatening food allergic reactions. Life of children and adolescents can be severely compromised by nut allergy. Patients dying from nut anaphylaxis suffered from multiple nut allergies. Symptoms related to nut allergy have specific IgE to more than one nut [5].

#### Types of Tree Nuts:

- Almonds
- Cashew nuts
- Filberts
- Brazil nuts
- Chestnuts
- Walnuts
- Pistachios
- Pecans
- Hickory nuts
- Macadamia nuts
- Hazelnuts [7]

Nut allergy can produce:

- Swelling (angioedema)
- Asthma symptoms
- Vomiting
- Swelling in the throat, causing difficulty in swallowing or breathing
- A tingling feeling in the lips or mouth
- An itchy nettle rash (urticaria, hives)
- Diarrhoea

- Cramping tummy pains
- Unconsciousness and faintness [8]

### 1. 5 PEANUT ALLERGY:

The most common and the leading cause of food allergy in children and adults is Peanut allergy. Peanut is a cheap source of protein. Therefore, peanuts are used mostly in protein rich food products [9]. 1 in 50 children and 1 in 200 adults suffer from this allergy. It is the most likely food to cause death and anaphylaxis [10].

Peanuts are also known as earth nuts, monkey nuts and ground nuts. *Arachis hypogaeae* (the peanut plant) belongs to the botanical family *Leguminosae* [11]. The peanut plants bear pods which contains seeds known as peanuts [11]. The peanut is native of South America, but it is also cultivated in Africa, Europe, North America and India.

Peanuts contain 46% fat, 26% proteins (albumins and globulins) and 13% carbohydrates. Further the globulin proteins are divided into two fractions; arachidonic and non-arachidonic. The native arachin protein has a molecular weight of > 600, 000 Daltons. The albumin consists of lectin-reactive glycoproteins, agglutinins, protease inhibitors, phospholipases and Gk $\alpha$ -amylase inhibitors [11].

#### 1. 5. 1 Symptoms:

Symptoms of peanut allergy include:

- Urticarial (hives)
- Wheezing

- Nausea
- Nasal congestion
- Asthma
- Angioedema (tissue swelling, especially of the face)
- Vomiting
- Allergic conjunctivitis (itchy, watery eyes)
- Anaphylaxis

Direct peanut contact can also cause dermatitis and hives. It has been reported that first allergic reaction related to peanuts commonly occurs at home between 15-24 months of age.

It has also been reported that 50% of the children allergic to peanuts have symptoms in one organ system. 30% show symptoms in two systems, 10-15% show in three systems and 1% in four systems. Organ systems which are affected by peanut allergy are as follows:

- Cardiovascular system (irregular heart rate, cardiac arrest, drop in blood pressure)
- Skin (tissue swelling, hives and reddening)
- Gastrointestinal tract (abdominal pain, vomiting, diarrhoea)
- Respiratory tract (cough, breathing difficulty, wheezing, noisy breathing, throat tightening, nasal congestion) [12].

#### 1. 5. 2 Peanut Allergens:

Several proteins in peanuts have distinct structure. Many of these are allergenic and can lead to IgE antibody production.

The major peanut protein allergens include:

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- Ara h1
- Ara h3
- Ara h5
- Ara h7
- Ara h Agglutinin
- Ara h Oleosin
  
- Ara h2
- Ara h4
- Ara h6
- Ara h8
- Ara h TI
- Ara h LTP

Recent studies showed that Ara h2 is the most frequent allergen and induce a reaction at low concentrations, whereas Ara h3 and Ara h1 are the less frequent allergens that react at higher concentrations than Ara h2.

Therefore, it was concluded that Ara h2 was the most important allergen in case of peanut allergy. Many of these allergens are heat stable and their allergenicity is not lost by processing or heating [12].

### 1. 5. 3 Causes:

Peanut allergy is caused due to an abnormal reaction of the immune system. The exact cause of IgE mediated peanut allergy is still unknown but studies show that it is caused due to genetic factors like:

- Filaggrin mutations show an important risk factor for Immunoglobulin E (IgE) mediated peanut allergy. Filaggrin gene plays an important role

in the epithelial barrier function. This gene encodes for profilaggrin which is an insoluble polyprotein, expressed in granular layer of epidermis and is broken down to monomers of filaggrin in the stratum corneum.

Hence, a mutation in this gene leads to dysfunction of epithelial barrier and hence causes atopic dermatitis which is a significant symptom of peanut allergy [13].

- Work on this topic showed that consumption of peanut during pregnancy can cause high level of peanut sensitization [14].

#### 1. 6 HAZELNUT ALLERGY:

In the group of tree nuts Hazelnut ( *Corylus avellana* ) is one of the food sources that cause allergic reactions related to food allergy. Patients suffering with tree pollen allergy are often allergic to hazelnuts [15].

Hazelnut is extensively used in production of ice-creams, cakes, pastries, cookies, chocolates, bread and breakfast cereals [16]. Hazelnut is also known as filbert or as cob nut [17].

Hazelnuts are widely consumed in Europe. The kernel of the nut is a rich source of plant oils (> 50%), dietary fibre (~10%) and protein (~15%) as well as vitamins, minerals and other flavour components. Hazelnuts are also a source of phenolic antioxidants and a supplement of hazelnut reduces the risk of coronary heart disease by lowering the plasma cholesterol and enhancing plasma antioxidant potential [18].

##### 1. 6. 1 Symptoms:



Symptoms of hazelnut allergy include:

- Runny nose
- Blotching
- Watery eyes
- Hives
- Asthma symptoms
- Cramps
- Vomiting
- Itching
- Diarrhoea and swelling
- Burning of the mouth, throat or face

Severe reaction may also lead to anaphylaxis which affects the entire body and can be harmful if not treated with an injection of epinephrine [19].

#### 1. 6. 2 Hazelnut Allergens:

The major allergen in hazelnut is Cor a 9, also known as corylin. This allergen belongs to 11S legumin-like seed-storage protein family. Cor a 9 is expressed by a gene which encodes a protein which contains 515 amino acids with molecular mass of 59kDa [18].

#### 1. 6. 3 Causes:

Hazelnut allergy is often seen in patients with allergic rhino conjunctivitis and tree pollen allergy. This is mainly caused by ingestion of hazelnuts or its products. This is also called oral ‘ allergy syndrome’ which is caused by the

cross-reactivity between tree pollen allergens, especially alder, birch, hazel pollen and hazelnut proteins [15].

### 1. 7 BRAZIL NUT:

Brazil nut (*Bertholletia excelsa*) is known to be the second common cause of nut allergies after peanut. Brazil nut tree grows mainly in the amazon jungle in South America. The seed is about 6cm long and is found in clusters of 8-25 inside a hard, thick-walled globular pod and weighs up to 2kg. The hard shell of each seed is 3-sided and dark brown in colour. The colour of the kernel is white and is a rich source of oil (70%) and protein (17%) [20]. Brazil nuts have a huge market in North America and Europe [21].

#### 1. 7. 1 Symptoms:

- Diarrhoea
- Vomiting
- Laryngeal oedema
- Urticarial
- Atopic dermatitis and
- Anaphylaxis
- Swelling of mouth
- Low blood pressure [20]

#### 2. IMMUNOPATHOGENESIS:

An immunological reaction against a food allergen is typically IgE mediated; non-IgE mediated i. e. cell mediated or mixed IgE and not IgE mediated. [22].

#### 2. 1 IgE Mediated Reaction:

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IgE mediated allergic reactions are reproducible, immediate and readily diagnosed by detecting food specific IgE. During an allergic response there occurs overproduction of Immunoglobulin E (IgE). On first exposure to an allergen, the individual becomes sensitized and produces allergen specific IgE that binds to the IgE receptors present on basophils (in circulation) and on the mast cells (in tissues). On the second exposure, this specific allergen binds to the antigenic determinant site (Fab) of IgE attached to the basophils and mast cells. For the activation of mast cells, crosslinking that is binding of two or more IgE molecules is required. Activation of mast cells results in the release of chemicals such as serotonin, histamine, serine protease, proteoglycans leukotriene C4 and heparin. This further leads to irritation, inflammation, redness and other allergic symptoms [2].

## 2. 2 Non- IgE Mediated Reaction:

The non- IgE mediated allergic reactions show minority of immunological reactions to nuts and occur in the absence of food specific IgE in the serum or skin. They are not well characterized but occur due to chronic or an acute inflammation in the gastrointestinal tract where T cells and Eosinophil play a major role [22].

## 3. DIAGNOSIS:

Diagnoses of food allergy like nuts are typically made by a positive allergy test or by serum-specific IgE assay. Children suffering from nut allergy are strictly advised to avoid eating nuts and to carry an adrenaline auto-injector as an emergency treatment of anaphylactic reactions [23].

Skin prick test and nut specific IgE (CAP) tests are commonly performed for peanut and other tree nuts like Brazil nut, hazelnut, almond and walnut. Patients suffering from Atopic Eczema Dermatitis Syndrome (AEDS) are commonly allergic to peanuts. A clinical diagnosis of asthma plays an important role as patients with near fatal or fatal anaphylaxis have concomitant asthma. The initial Radio allergosorbent tests (RAST) have largely been replaced by the Enzyme linked immunosorbent assays (ELISA) [24].

#### 4. TREATMENT:

The most important treatment of nut allergies is strict avoidance of nuts. Medicines such as corticosteroids, antihistamines or decongestants are helpful only in treating the symptoms of allergies but do not prevent the onset of allergy [2].

##### 4. 1 Traditional therapies:

In case of inhalant allergies injection immunotherapy has been traditionally employed. But this therapy is associated with serious systemic reactions. Since, traditional immunotherapy is considered to be impractical for treating most of the nut allergies various other novel therapies have been discovered [25].

##### 4. 2 Novel therapies:

Treatment of nut allergies by novel therapies includes:

4. 2. 1 Peptide immunotherapy: This immunotherapy makes use of peptide fragments which contain T cell reactive epitopes instead of complete protein

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molecules. The peptide fragments are not able to crosslink two molecules of IgE which are required for the activation of mast cells but do render T cells. One of the studies showed that pepsin-digested peanut allergen contains T cell epitopes but does not contain IgE binding epitope.

4. 2. 2 Mutated protein immunotherapy: This immunotherapy is achieved through attraction of the primary amino acid sequences of IgE binding allergenic epitopes. This has shown to substantially alter binding of IgE antibody to both peanut and shrimp allergens.

4. 2. 3 DNA immunization: Another novel approach under investigation for the treatment of nut allergy is DNA immunization. This therapy employs subcutaneous injection of a plasmid DNA vector which encodes for a specific allergenic protein [25].

#### 4. 3 Homeopathic remedies:

Natural products and homeopathic remedies such as Pulsatilla, Lycopodium and Sulfur can be used to reduce allergic reactions [2].

#### 4. 4 Chinese Herbal therapies:

Unique combination of herbs such as Zhi Fu Zi (Radix Lateralis Aconiti Carmichaeli praeparata) and Xi Xin (Herba Asari) can also help with the induction of tolerance. In case of peanut allergy these herbs have proved to be very successful. But till now tis therapy has not been tried in humans [22].

### 5. MANAGEMENT:

Management of nut allergy is based mainly on:

1. Educating people about nut allergy and how to avoid foodstuffs that contain nuts.
2. Awareness of early signs of allergic reactions.
3. Educating people about proper use of self-injectable epinephrine (e. g. Twinject or EpiPen auto injectors).
4. People must be instructed to read all ingredient labels while purchasing pre-packaged food.
5. Children should be encouraged to wash their hands after meals and discouraged from sharing food at parties or school.
6. Children suffering from nut allergy should always wear MedicAlert bracelets [6].