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# **RESEARCH ARTICLE**

# Allergic Reaction: Symptoms, Diagnosis, Treatment and Management

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## ABSTRACT

Allergies cause a wide range of symptoms, from the common problems that everyone has heard of such as a runny nose, nasal congestion, sneezing; watery, itchy, red eyes; and itchy ears, to less obvious problems like a tickle in the throat, cough, asthma, wheezing, and shortness of breath, hives, eczema, bee sting reactions, and so forth. Fatigue is also common in allergy season. The older antihistamines which cause drowsiness didn't help with fatigue but now the newer antihistamines generally don't cause drowsiness. People develop allergy problems because of an overactive immune system in which certain gamma globulins are overproduced by the body. Gamma globulins are normally present to fight bacterial infections. In the case of allergies, one of the gamma globulins (called IgE) functions abnormally and views the allergens (e.g. cat dander) as being foreign bacteria - so the IgE attempts to "kill" it. When IgE attaches to the pollen, a barrage of chemicals including histamine are released into the body from cells called Mast cells, and as a result patients are left with allergic symptoms.

Keywords: Allergy, Allergens, Eye Allergy, Food Allergy, Medication.

# INTRODUCTION

Allergy is one of the most widespread diseases of the modern world. More than 25% of the population in industrialized countries suffers from allergies.<sup>1</sup> According to the Asthma and Allergic Foundation of America (2002), allergies are the sixth leading cause of chronic diseases in the U.S,

# Address for correspondence:

Ahmed Elshemy\* Department of Pharmacy, International Islamic University Chittagong, Chittagong, Bangladesh. E-mail: elshemyahmed9@gmail.com and the annual cost of dealing with them is estimated at \$18 Billion. Every individual has his or her own immune system; the stronger the immune system, the healthier will be the person. Allergies, also known as hypersensitive reactions, occur when the immune system overreacts to substances that do not affect most people. These substances, also known as allergens, could be pollen, animal dander, chemicals, fungi, dust mites, or foods such as nuts, eggs, shellfish, fish, and milk.

Different people show different symptoms of allergies, which can be mild (runny nose) to severe (anaphylaxis). Symptoms generally depend upon the part of body contacted by the allergen, e.g., pollens from the air enter the respiratory tract via the nose and cause respiratory symptoms such as cough, itchy and runny nose, and nasal congestion, sneezing, and wheezing.

Food allergy related symptoms include vomiting, nausea, abdominal pain, and diarrhea. Skin allergy symptoms are lesions, rashes, blisters, redness and itchiness, and so on.<sup>2</sup>

# The Immunology of Allergies

The immune system protects our body against pathogens and other foreign substances by producing a kind of glycoprotein known as immunoglobulin (Ig) or antibodies from plasma cells or B-cells (a type of lymphocyte). Antibodies are mainly of five types, each one having a different function; the type involved in allergy is immunoglobulin E (IgE).

Immunoglobulin E (IgE) is overproduced during an allergic response. On the very first exposure to an allergen, an allergic person becomes sensitized by producing allergenspecific IgE that binds with IgE receptors on mast cells (in tissues) and basophils (in circulation). If the sensitized person has another exposure to this specific allergen, then this allergen will bind to the antigenic determinant site (Fab) of

IgE attached to the mast cells and basophils. Binding of two or more IgE molecules to mast cells (crosslinking) is required to activate the mast cells. These activated cells result in the release of certain chemicals, such as histamine, serotonin, proteoglycans, serine protease, leukotriene C4 and heparin, that will further bind with their receptors present in other cells (e.g., histamine receptors of blood vessels) and lead to inflammation, irritation, redness and other allergic symptoms.

The primary function of our immune system is to defend against infection; however, during an allergic reaction the immune system responds against a substance that is harmless to most people. There are two subpopulations of T helper cells, Th1 and Th2. Th1 cells are helpful in protecting against invading microbes and other particles by producing interferons and some cytokines. Th2 cells are responsible for triggering allergies by the overproduction of IgE, and are also involved in the struggle against parasitic worms. Th2 cells produce cytokines like interleukins (such as IL-5) that enhance the production of specific IgE antibodies by B cells and result in hypersensitivity, eosinophil activation, mucus production and IgE secretion.<sup>3</sup>



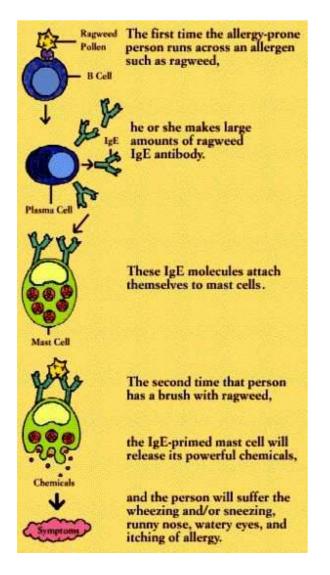


Figure: The Allergic Cascade

# ALLERGIC REACTION CAUSES<sup>4</sup>

Almost anything can trigger an allergic reaction.

- The body's immune system involves the white blood cells, which produce antibodies.
- When the body is exposed to an antigen, a complex set of reactions begins.

- The white blood cells produce an antibody specific to that antigen. This is called "sensitization."
- The job of the antibodies is to detect and help destroy substances that cause disease and sickness. In allergic reactions, the antibody is called immunoglobulin E or IgE.
- This antibody promotes production and release of chemicals and hormones called "mediators."
- Mediators have effects on local tissue and organs in addition to activating more white blood cell defenders. It is these effects that cause the symptoms of the reaction.
- Histamine is one of the better-known mediators produced by the body.
- If the release of the mediators is sudden or extensive, the allergic reaction may also be sudden and severe, and anaphylaxis may occur.
- Allergic reactions are unique for each person. Reaction time to allergens can vary widely. Some people will have an allergic reaction immediately, for others it will take time to develop.
- Most people are aware of their particular allergy triggers and reactions.
- Certain foods such as peanuts, strawberries, shellfish, shrimp, dairy, and wheat.

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- Babies can also have food allergies. There are more than 160 allergenic foods. Common foods that can cause allergic reactions in babies include milk, eggs, nuts, and soy. Talk to your pediatrician if you are concerned about food allergies in your baby.
- Food intolerance is not the same as food allergies. Allergies are an immune system response, while food intolerance is a digestive system response in which a person is unable to properly digest or break down a particular food.
- Vaccines and medications (antibiotics like penicillin, amoxicillin, aspirin, ibuprofen, iodine), general anesthesia and local anesthetics, latex rubber (such as in gloves or condoms), dust, pollen, mold, animal dander, and poison ivy are well-known allergens. Other known allergens can include detergents, hair dyes, and the ink in tattoos.
- Bee stings, fire ant stings, penicillin, and peanuts are known for causing dramatic reactions that can be serious and involve the whole body.
- Minor injuries, hot or cold temperatures, exercise, stress, or emotions may trigger allergic reactions.

- Often, the specific allergen cannot be identified unless you have had a similar reaction in the past.
- Allergies and the tendency to have allergic reactions run in some families.
- Many people who have one trigger tend to have other triggers as well.
- People with certain medical conditions are more likely to have allergic reactions: severe allergic reaction in the past asthma.

# ALLERGIC REACTION SYMPTOMS AND SIGNS <sup>2, 4</sup>

The look and feel of an allergic reaction depends on the body part involved and the severity of the reaction. Some reactions may be localized and limited, while others could involve multiple body systems. Reactions to the same allergen vary among individuals.

- Anaphylaxis is the term for any combination of allergic symptoms that is rapid, or sudden, and potentially lifethreatening. Call an ambulance immediately if you suspect anaphylaxis.
- One sign of anaphylaxis is shock. Shock has a very specific meaning in medicine. The organs of the body are not getting enough blood because of dangerously low blood pressure. Shock may lead rapidly to death. The person in shock may be pale or red,

sweaty or dry, confused, anxious, or unconscious.

- Breathing may be difficult or noisy, or the person may be unable to breathe.
- Shock is caused by sudden dilation of many or large blood vessels. This is brought on by the action of the mediators. If the drop in blood pressure is sudden and drastic, it can lead to unconsciousness, even cardiac arrest and death.
- Symptoms and signs of an allergic reaction include any, some, or many of the following:
- Skin: irritation, redness, itching, swelling, blistering, weeping, crusting, rash, eruptions, or hives (itchy bumps or welts)
- Lungs: wheezing, tightness, cough, or shortness of breath
- Head: swelling or bumps on the face and neck, eyelids, lips, tongue, or throat, hoarseness of voice, headache
- Nose: stuffy nose, runny nose (clear, thin discharge), sneezing
- Eyes: red (bloodshot), itchy, swollen, or watery or swelling of the area around the face and eyes
- Stomach: pain, nausea, vomiting, diarrhea, or bloody diarrhea
- Other: fatigue, sore throat

The tendency to develop allergies is often hereditary, which means it can be passed down through your genes. (Thanks a lot, Mom and Dad!) However, just because a parent or sibling has allergies doesn't mean you will definitely get them, too. A person usually doesn't inherit a particular allergy, just the likelihood of having allergies.

# ALLERGENS 5

Some of the most common allergens are:

**Foods:** Food allergies are most common in infants and often go away as people get older. Although some food allergies can be serious, many simply cause annoying symptoms like an itchy rash, a stuffy nose, and diarrhea. The foods that people are most commonly allergic to are milk and other dairy products, eggs, wheat, soy, peanuts and tree nuts, and seafood.

• **Insect bites and stings.** The venom (poison) in insect bites and stings can cause allergic reactions, and can be severe and even cause an anaphylactic reaction in some people.

• Airborne particles. Often called environmental allergens, these are the most common allergens. Examples of airborne particles that can cause allergies are dust mites (tiny bugs that live in house dust); mold spores; animal dander (flakes of scaly, dried skin, and dried saliva from your pets); and pollen from grass, ragweed, and trees.

• Medicines. Antibiotics — medications used to treat infections — are the most common type of

medicines that cause allergic reactions. Many other medicines, including over-the-counter medications (those you can buy without a prescription), also can cause allergic-type reactions.

• Chemicals. Some cosmetics or laundry detergents can make people break out in an itchy rash (hives). Usually, this is because someone has a reaction to the chemicals in these products. Dyes, household cleaners, and pesticides used on lawns or plants also can cause allergic reactions in some people.

# AVOIDANCE <sup>5</sup>

In some cases, like food allergies, avoiding the allergen is a life-saving necessity. That's because, unlike allergies to airborne particles that can be treated with shots or medications, the only way to treat food allergies is to avoid the allergen entirely. For example, people who are allergic to peanuts should avoid not only peanuts, but also any food that might contain even tiny traces of them.

Avoidance can help protect people against nonfood or chemical allergens, too. In fact, for some people, eliminating exposure to an allergen is enough to prevent allergy symptoms and they don't need to take medicines or go through other allergy treatments.

Here are some things that can help you avoid airborne allergens:

- Keep family pets out of certain rooms, like your bedroom, and bathe them if necessary.
- Remove carpets or rugs from your room (hard floor surfaces don't collect dust as much as carpets do).

• Don't hang heavy drapes and get rid of other items that allow dust to accumulate.

• Clean frequently (if your allergy is severe, you may be able to get someone else to do your dirty work!)

• Use special covers to seal pillows and mattresses if you're allergic to dust mites.

• If you're allergic to pollen, keep windows closed when pollen season's at its peak, change your clothing after being outdoors — and don't mow lawns.

• If you're allergic to mold, avoid damp areas, such as basements, and keep bathrooms and other moldprone areas clean and dry.

# **DEALING WITH ALLERGIES**

So once you know you have allergies, how do you deal with them? First and foremost, try to avoid things you're allergic to!

If you have a food allergy that means avoiding foods that trigger symptoms and learning how to read food labels to make sure you're not consuming even tiny amounts of allergens. People with

environmental allergies should keep their house clean of dust and pet dander and watch the weather for days when pollen is high. Switching to perfume-free and dye-free detergents, cosmetics, and beauty products (you may see non-allergenic ingredients listed as hypoallergenic on product labels) also can help. If you're taking medication, follow the directions carefully and make sure your regular doctor is aware of anything an allergist gives you (like shots or prescriptions).

# EYE ALLERGY 6,7

Eye allergies often are hereditary, and occur due to processes associated with other types of allergic responses. When an allergic reaction takes place, your eyes may be overreacting to a substance perceived as harmful, even though it may not be. These substances are called allergens. For example, dust that is harmless to most people can cause excessive production of tears and mucus in eyes of overly sensitive, allergic individuals. Allergies can trigger other problems, such as conjunctivitis (pink eye) and asthma. Combined nasal and eye allergies create a condition known as rhinoconjunctivitis.

# Allergy Symptoms and Signs

Common signs of allergies include:

- Red, swollen or itchy eyes
- Runny nose
- Sneezing and coughing
- Itchy nose, mouth or throat

Headache from sinus congestion

Beyond more obvious symptoms, you also may feel fatigued and could suffer from lack of sleep.

## **Causes Eye Allergies**

Many allergens are in the air, where they come in contact with your eyes and nose. Airborne allergens include pollen, mold, dust and pet dander. Other causes of allergies, such as certain foods or bee stings, do not typically affect the eyes the way airborne allergens do. Adverse reactions to certain cosmetics or drugs such as antibiotic eye drops also may cause eye allergies. Some people actually are allergic to the preservatives in eye drops such as those used to lubricate dry eyes. In this case, you may need to use a preservative-free brand.

## **Eye Allergy Treatment**

#### Avoidance

The most common "treatment" is to avoid what's causing your eye allergy. Keep your home free of pet dander and dust and keep pets off the furniture. Stay inside with the air conditioner on when a lot of pollen is in the air. Use high quality furnace filters that trap common allergens and replace the filters frequently.

Make sure you wear wraparound sunglasses to help shield your eyes from allergens, and drive with your windows closed during allergy season.

## Medications

If you're not sure what's causing your eye allergies, or you're not having any luck avoiding them, your next step probably will be medication to alleviate the symptoms.

Over-the-counter and prescription medications each have their advantages; for example, over-thecounter products often are less expensive, while prescription ones usually are stronger and may be more effective.

Eye drops are available as simple eye washes, or they may have one or more active ingredients such as antihistamines, decongestants or mast cell stabilizers that inhibit inflammation. Antihistamines relieve many symptoms caused by airborne allergens, such as itchy, watery eyes, runny nose and sneezing. Decongestants help shrink swollen nasal passages for easier breathing.

# **RELIEF FOR WATERY, ITCHY EYES**<sup>6,7</sup>

Common causes of excessively watery eyes are allergies and dry eye syndrome — two very different problems. With allergies, your body's release of histamine causes your eyes to water, just as it may cause your nose to run. It may seem illogical that dry eye syndrome could cause watery eyes. But sometimes an underlying dry eye condition stimulates your tear glands to overproduce the watery component of your eye's tears as a protective response, leading to watery

vasoconstrictors, which make the blood vessels in your eyes smaller, lessening the apparent redness. They treat a symptom but not the cause of eye allergies. In fact, with extended use, the blood vessels can become dependent on the vasoconstrictor When to stay small. you discontinue the eye drops, the vessels actually get bigger than they were in the beginning. This process is called rebound hyperemia, and the result is that your red eyes could worsen over time. Some products have ingredients that act as mast cell stabilizers, which alleviate redness and swelling. Mast cell stabilizers are similar to antihistamines. But while antihistamines are known for their immediate relief, mast cell stabilizers are known for their long-lasting relief. Antihistamines, decongestants and mast cell stabilizers are available in pill form, but pills don't work as quickly as eye drops or gels to bring eye relief. Nonsteroidal antiinflammatory drug (NSAID) eye drops may be prescribed to decrease swelling, inflammation and other symptoms associated with seasonal allergic conjunctivitis, also called hay fever. Prescription corticosteroid eye drops also may provide similar, quick relief. However, steroids have been associated with side effects such as increased inner eye pressure (intraocular pressure) leading to glaucoma and damage to optic nerve. Steroids also have been known to cause the eye's natural lens to become cloudy, producing cataracts Check the

eyes. Decongestants clear up redness. They contain

product label or insert for a list of side effects of over-the-counter medications. For prescription medication, ask your doctor. In some cases, combinations of medications may be used. You may benefit from immunotherapy, in which an allergy specialist injects you with small amounts of the allergen to help you gradually build up immunity.

## **Eye Allergies and Contact Lenses**

> Even if you are generally a successful contact lens wearer, allergy season can make your contacts uncomfortable. Airborne allergens can get on your lenses, causing discomfort. Allergens also can stimulate the excessive production of natural substances in your tears, which can bind to your contacts and cause blur and additional discomfort. Pollen maps can help you determine when allergens are present. Ask your eye doctor about eye drops that can help relieve your symptoms and keep your contact lenses clean. Certain drops can discolor or damage certain lenses, so it makes sense to ask first before trying out a new brand. Another alternative is daily disposable contact lenses, which are discarded nightly. Because you replace them so frequently, these types of lenses are unlikely to develop irritating deposits that can build up over time and cause or heighten allergy-related discomfort.

## When to Seek Medical Care

Because allergic reactions can progress and worsen in minutes causing complications, medical attention is always recommended for all but the most minor and localized symptoms. If the symptoms of your reaction worsen over a few days, or if they do not improve with recommended treatment and removal of the allergen, call your health-care provider. Tell your health-care provider if you have any allergic symptoms after using a drug or other treatment prescribed for you (see Drug Allergy).Allergic reactions can be dangerous. Sudden, severe, widespread reactions require emergency evaluation by a medical professional. Call an ambulance if you or someone around you has any of the following with an allergic reaction:

- sudden, severe, or rapidly worsening symptoms
- exposure to an allergen that previously caused severe or bad reactions
- swelling of the lips, tongue, or throat
- wheezing, chest tightness, loud breathing, trouble breathing, or hoarseness of voice
- confusion, sweating, nausea, or vomiting
- widespread rash or severe hives
- lightheadedness, collapse, or unconsciousness

## **Allergic Reaction Diagnosis**

For typical allergic reactions, your health-care provider will examine you and ask questions about your symptoms and their timing. Blood tests and Xrays are not needed except under unusual circumstances.

In case of severe reactions, you will be evaluated quickly in the emergency department in order to make a diagnosis. The first step for the health-care provider is to judge the severity of the allergic reaction.

- Blood pressure and pulse are checked.
- An examination determines whether you need help breathing.
- Often, an IV line is placed in case you need anti-allergy (antihistamine) medications quickly.
- If you can speak, you will be asked about allergy triggers and previous reactions.

## **Allergic Reaction Treatment**

# Self-Care at Home

Avoid triggers! If you know you have an allergic reaction to peanuts, for example, do not eat them and go out of your way to avoid foods prepared with or around peanuts (see Food Allergy).

Self-care at home is not enough in severe reactions. A severe reaction is a medical emergency. • Do not attempt to treat or "wait out" severe reactions at home. Go immediately to a hospital emergency department.

• If no one is available to drive you right away, call an ambulance for emergency medical transport.

• Use your epinephrine auto-injector (Epi-Pen) if you have been prescribed one by your doctor due to previous allergic reactions (see "prevention" below).

Slight reactions with mild symptoms usually respond to nonprescription allergy medications.

• Oral antihistamines.

• Loratadine (Claritin or Alavert), cetirizine(Zyrtec), and fexofenadine (Allegra) are nonsedating antihistamines that can be taken over the long term.

• Diphenhydramine (Benadryl) can also be taken but may make you too drowsy to drive or operate machinery safely. It can affect concentration and interfere with children's learning in school. These medications should be taken for only a few days.

• For rashes or skin irritations, an antiinflammatory steroid cream such ashydrocortisone can be used.

For small, localized skin reactions, use a cold, wet cloth or ice for relief. Apply a bag of frozen vegetables wrapped in a towel as an ice pack.

## **Allergic Eyes**

Allergic eyes (allergic conjunctivitis) is inflammation of the tissue layers (membranes) that cover the surface of the eyeball and the undersurface of the eyelid. The inflammation occurs as a result of an allergic reaction and may produce the following symptoms:

- Redness under the lids and of the eye overall
- Watery, itchy eyes
- Swelling of the membranes

## Allergic Eczema

Allergic eczema (atopic dermatitis) is an allergic rash that is usually not caused by skin contact with an allergen. This condition is commonly associated with allergic rhinitis or asthma and features the following symptoms:

- Itching, redness, and or dryness of the skin
- Rash on the face, especially children

• Rash around the eyes, in the elbow creases, and behind the knees, especially in older children and adults (rash can be on the trunk of the body)

# Hives

Hives (urticaria) are skin reactions that appear as itchy swellings and can occur on any part of the body. Hives can be caused by an allergic reaction, such as to a food or medication, but they also may occur in non-allergic people. Typical hive symptoms are:

- Raised red welts
- Intense itching

#### Allergic Shock

Allergic shock (anaphylaxis or anaphylactic shock) is a life-threatening allergic reaction that can affect a number of organs at the same time. This response typically occurs when the allergen is eaten (for example, foods) or injected (for example, a bee sting). Some or all of the following symptoms may occur:

- Hives or reddish discoloration of the skin
- Nasal congestion
- Swelling of the throat
- Stomach pain, nausea, vomiting
- Shortness of breath, wheezing
- Low blood pressure or shock

Shock refers to the insufficient circulation of blood to the body's tissues. Shock is most commonly caused by blood loss or an infection. Allergic shock is caused by dilated and "leaky" blood vessels, which result in a drop in blood pressure.

## FOOD ALLERGY<sup>8,9</sup>

It doesn't take much to trigger a reaction in someone with a food allergy — ingesting a tiny piece of peanut or unknowingly eating pasta containing shrimp in a restaurant. In someone with a severe allergy to these items, this can be lifethreatening. It's estimated, based on clinically documented cases, that about 1.8 million Canadians may be affected by food allergies, Health Canada said in a recent release. Some studies show these numbers are increasing, especially among children. Peanuts, tree nuts, sesame seeds, soy, seafood, wheat, eggs, milk, mustard and sulphites are the food allergens most commonly associated with severe allergic reactions in Canada. When someone ingests even a tiny amount of an allergen, a reaction may develop quickly and can become very serious. The most dangerous symptoms include breathing difficulties or a drop in blood pressure with shock, which may result in loss of consciousness, anaphylaxis and even death. There's no cure for food allergies. Avoiding an allergen is the only effective way to prevent allergic reactions. Here are some tips from Health Canada on how to protect yourself if you have a food allergy:

1. Read product labels carefully as manufacturers sometimes change the ingredients used in familiar products.

2. Avoid food products that contain the specific allergens and/or derivatives of the specific allergens to which you are allergic.

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3. Avoid food products that bear a precautionary statement naming an allergen that you are allergic to; for example, precautionary statements like "may contain X" (where "X" is the name of a commonly known allergen).

4. Avoid food products that don't list their ingredients or food products that contain an ingredient you don't recognize.

5. When eating at a friend's or in a restaurant, tells your host/server about your food allergy, and asks specific questions about the food being served.

6. If an allergist prescribes an epinephrine/adrenaline auto-injector, learn how to use it and carry it all the time.

7. Wear a Medic Alert identifier so that, in case of an accident, others know about your allergies and reactions.

8. Look out for allergens listed by other names; food allergens and their derivatives are sometimes found in food under different names.

## **Treatments under Development**

## 1. DNA vaccines

Several types of new allergy treatments are under development. Because they are not proteins and can't translate into proteins to become allergens in allergic persons, DNA vaccines can be used to reduce allergic reactions. DNA vaccines can be

developed by one of three approaches: (i) using the naked DNA of allergens (ii) using hypoallergenic derivatives of allergen DNAs by modification of nucleotides; or (iii) fragmenting allergen DNA and fusing with ubiquitin, as fragmenting the antigen destroys its native structure.

Based on their Th1-promoting properties, DNA vaccines balance Th2-mediated immune reactions, a quality which renders them a promising alternative for immunotherapy against allergies.<sup>10</sup>

# 2. Anti-IgE antibodies

Binding of IgE antibodies to specific high affinity receptors (called Fc epsilon receptors, or FceRI) on basophils and mast cells triggers the release of histamine and other mediators that result in allergy symptoms. Thus developing anti-IgE antibodies against IgE could be a potential therapeutic option for allergy treatment. Various such antibodies have been developed. An anti-IgE monoclonal antibody termed BSW17 peptide has been synthesized that is nonaphylactogenic, predominantly blocks binding of IgE to FceRI, recognizes IgE already bound to FceRI, and interferes with the function of IgE-sensitized basophils and mast cells.<sup>11</sup>

Another such humanized monoclonal antibody is Omalizumab, which not only inhibits the binding of IgE to FccRI but also decreases FccRI expression on mast cells and basophils. It also reduces the synthesis of IgE by B plasma cells and thereby attenuates hypersensitivity reactions.<sup>12</sup> Leung et al.<sup>13</sup> also humanized an IgG1 monoclonal antibody for peanut related allergies called TNX-901 that recognizes and masks an epitope in the IgE responsible for binding to the FccRI on mast cells and basophils. Their results indicate that a dose of 450mg of TNX-901 significantly increases the threshold of sensitivity to peanuts from a level of 178mg (1/2 a peanut) to 2805mg (9 peanuts).

# 3. Modification of the epitopes

Modification of IgE binding sites, i.e. epitopes of allergens, could be another approach to attenuate hypersensitivity reactions. Epitopes of allergens can be created by modifying allergens and their hypoallergic derivatives. Singh and Bhalla<sup>14</sup> have demonstrated that the anaphylactic potential of rye grass pollen can be reduced by introducing a few point mutations in their allergens before using them for immunotherapy. In the shrimp allergen tropomycin, eight IgE epitopes were identified and mutated. These mutations had no effect on their secondary structure (in other words, did not change the basic structure of the IgE) but the allergic response was reduced by 90-98%, so this mutant could be helpful for therapy.<sup>15</sup>

# 4. Target mast cells and basophil cells expressing FccRI

Another possible option to reduce IgE related hypersensitivity reaction is to directly kill the mast

cells and basophils expressing high affinity receptors (FceRI) for IgE. Human originated apoptosis-inducing proteins can be used, as these will be less toxic or less immunogenic than the proteins produced in a different animal or plant. From two human apoptosis-inducing proteins, Bak and Bax, new chimeric proteins termed as Fce-Bak/Bax have been synthesized that induce apoptosis in FceRI-expressing mast cells and basophils.<sup>16</sup> Also, these chimeric proteins do not degranulate mast cells. In birch pollen allergic people, the degranulation of mast cells releases enzymes such as  $\alpha$ -chymase and other serine proteases.<sup>17</sup> Interestingly, the chymase cleaved IgEbinding epitopes of profilin giving profilin no chance to react with IgE and thus attenuated mast cell activation. Destruction of IgE binding epitopes of profilin with chymase could further limit pollen allergic reaction in sensitized individuals.

## 5. Immunotherapy

Immunotherapy (biologic therapy) is indicated for people who are extremely allergic to specific allergens. Immunotherapy is done by gradually exposing the patient to lower doses of allergens to reduce the sensitization. It relies on the progressive production of the blocking antibody IgG and reduction in excessive production of IgE. Li et al.<sup>18</sup> developed a new chimeric peanut protein and coadministered it with adjuvant heat-killed Listeria monocytogenes (HKLM) to mice that were allergic to peanuts. The researchers found that these mice showed lower histamine release and fewer peanut specific IgE antibodies, and that allergic symptoms were reduced. Thus, their results suggest that immunotherapy with peanut protein and HKML could treat peanut allergic patients.

## 6. Harvesting nature

Aqueous extract of the plant bugleweed (Lycopus lucidus) decreases allergic response by reducing histamine, TNF $\alpha$  and interleukin (IL-6) release from mast cells.<sup>19</sup> The same effect was reported by using hop, Humulus lupulus, extracts on rat mast cells of rats and human basophilic cells.<sup>20</sup>

# 7. Reducing the allergenicity of food crops

Scientists are trying to develop methods to reduce plant allergenicity. Generally it is believed that environmental stress to plants due to pollution, fertilizers, pesticides, heavy metals, etc., reduces their vitality and makes them produce various defense molecules (Thi and De Blic, 2005); these defense molecules could be active allergens.<sup>21</sup> Malkov et al.<sup>22</sup> have reported that soil treatment with silicate breaking bacteria (Bacillus oligonitrophilus KU-1) in apples and strawberry plants can attenuate plant allergenic potency. The bioavailability of silicon produced by Β. oligonitrophilus KU-1 increases the vitality of plants and reduces the production of allergens. So soil treatment with B. oligonitrophilus is a simple

and inexpensive method for reducing the allergenic capacity of food crops.

# MEDICATION 23-29

Allergy medications are available as pills, liquids, inhalers, nasal sprays, eye drops, skin creams and shots (injections). Some allergy medications are available over-the-counter, while others are available by prescription only. Here's a summary of the various types of allergy medications and why they're used.

## Corticosteroids

Corticosteroids help prevent the release of symptom-causing chemicals during an allergic reaction. Most corticosteroid medications require a prescription.

- Nasal corticosteroid sprays prevent and relieve signs and symptoms of allergies such as allergic rhinitis (hay fever). These medications can help with nasal stuffiness, sneezing, and itchy, runny nose. Examples include fluticasone (Flonase), mometasone (Nasonex), budesonide (Rhinocort Aqua), triamcinolone (Nasacort AQ) and beclomethasone (Beconase AQ), fluticasone (Veramyst) and ciclesonide (Omnaris). Side effects can include unpleasant smell or taste, nasal irritation and nosebleeds.
- Inhaled corticosteroids are used to relieve symptoms triggered by airborne allergy-

triggering substances (allergens). These medications are generally taken on a daily basis as part of asthma treatment. Examples include fluticasone (Flovent Diskus, Flovent HFA), budesonide (Pulmicort Flexhaler), mometasone (Asmanex Twisthaler), beclomethasone (Qvar) and ciclesonide (Alvesco). Side effects are generally minor and can include mouth and throat irritation and oral yeast infections.

- Corticosteroid eyedrops are used to treat severe eye irritation caused by hay fever and allergic conjunctivitis. Examples include dexamethasone (Maxidex, others), fluorometholone (FML) and prednisolone (Pred Forte, Pred Mild). These medications may cause blurred vision. Prolonged use may increase your risk of eye infections, glaucoma and cataracts.
- Corticosteroid skin creams relieve allergic skin reactions such as scaling and itching. Some low-potency corticosteroid creams are available without a prescription, but talk to your doctor before using a topical corticosteroid for more than a few weeks. Examples include hydrocortisone (Cortaid, others) and triamcinolone (Kenalog, others). Side effects can include skin irritation and discoloration. Long-term use, especially of stronger prescription corticosteroids, thins the top layer of the skin, resulting in easy

bruising where the cream has been applied. Corticosteroids are available in liquid form that can be useful for skin conditions involving the scalp.

✤ Oral corticosteroids (pills and liquids) are used to treat severe symptoms caused by all types of allergic reactions. Examples include prednisone (Prednisone Intensol) and prednisolone (Prelone, others). Because they can cause numerous short- and longterm side effects, oral corticosteroids are usually prescribed for short periods of time. use Long-term can cause cataracts. osteoporosis, muscle weakness, stomach ulcers and delayed growth in children. Oral corticosteroids also can worsen hypertension. In some situations. corticosteroids may be given as a shot (injection) rather than pills.

## Antihistamines

Antihistamines block histamine, a symptomcausing chemical released by your immune system during an allergic reaction.

 Oral antihistamines (pills and liquids) ease symptoms such as swelling, runny nose, itchy or watery eyes, and hives (urticaria). Over-the-counter oral antihistamines include loratadine (Claritin) and cetirizine (Zyrtec). Desloratadine (Clarinex) and levocetirizine (Xyzal) are available by prescription. Fexofenadine (Allegra) is available both over-the-counter and by prescription. Some oral antihistamines may cause dry mouth and drowsiness. Older antihistamines such as diphenhydramine (Benadryl), chlorpheniramine (Chlor-Trimeton) and clemastine (Tavist) are more likely to cause drowsiness and slow your reaction time. These sedating antihistamines shouldn't be taken when driving or doing other potentially dangerous activities.

- ✤ Antihistamine nasal sprays help relieve sneezing, itchy or runny nose, sinus congestion, and postnasal drip. Prescription antihistamine nasal include sprays azelastine (Astelin, Astepro) and olopatadine (Patanase). Side effects of antihistamine nasal sprays may include bitter taste, dizziness, drowsiness or fatigue, dry mouth, headache, nasal burning, nosebleed, nausea, runny nose, sore throat, and sneezing.
- Antihistamine eye drops are often combined with other medications such as mast cell stabilizers or decongestants. Antihistamine eyedrops can ease symptoms such as itching, redness and swollen eyes. You may need to use these medications several times a day, because the effects may last only a few hours. Over-the-counter examples include ketotifen (Zaditor, Alaway, others)

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and pheniramine (Visine-A, Opcon-A, others). Prescription examples include emedastine (Emadine) and olopatadine (Patanol, others). Side effects of these medications can include red eyes, watery eyes, mild stinging or burning and headache. Antihistamine eyedrops increase the risk of eye inflammation when you're wearing contact lenses.

# **Decongestants**

Decongestants are used for quick, temporary relief of nasal and sinus congestion. You may need to avoid decongestants if you're pregnant, if you're an older adult or if you have high blood pressure. Check with your doctor to see which medications are safe for you.

Oral decongestants (pills and liquids) relieve nasal and sinus congestion caused by hay fever. Many decongestants are available over-the-counter. A common example is pseudoephedrine (Sudafed, others). A number of medications contain a decongestant such as pseudoephedrine combined with other medications. Claritin-D, for example, contains pseudoephedrine and an antihistamine. Oral decongestants can cause a number of side effects, including irritability, fast or irregular heartbeat, dizziness, insomnia, headaches, anxiety, tremors, and increased blood pressure.

- Nasal decongestant sprays and drops relieve nasal and sinus congestion. Examples include phenylephrine (Neo-Synephrine, others) and oxymetazoline (Afrin, others). Nasal decongestants can cause dryness, burning or stinging inside the nose, runny nose, and sneezing. Taking too much of a nasal decongestant can cause irritability, fast or irregular heartbeat, dizziness, insomnia, headaches, anxiety, tremors, and increased blood pressure. Don't use a decongestant nasal spray for more than a week or so, or you may develop severe congestion as soon as you stop taking it (rebound congestion).
- Decongestant eyedrops (or combined decongestant-antihistamine eyedrops) can temporarily ease symptoms such as red, itchy eyes. Available over-the-counter, examples include tetrahydrozoline (Visine others) and naphazoline (Clear Eyes, others). Side effects include persistent eye redness and damage to blood vessels in the eye when overused. In rare cases, decongestant eyedrops can cause a type of sudden (acute) glaucoma.

## Other allergy medications

A few other medications work by blocking symptom-causing chemicals released during an allergic reaction.

• Montelukast (Singulair) is a prescription medication that blocks symptom-causing chemicals called leukotrienes. This oral medication relieves allergy signs and symptoms including nasal congestion, runny nose and sneezing. Side effects can include upper respiratory infection in adults, and headache, ear infection and sore throat in children. The Food and Drug Administration (FDA) has warned that in some people, leukotriene-blocking medications could possibly cause psychological symptoms, such as irritability, anxiousness, insomnia, hallucinations, aggression, depression, and suicidal thinking or behavior.

• Cromolyn (Nasalcrom) is an over-the-counter nasal spray. It prevents the release of histamine and other symptom-causing chemicals during an allergic reaction. This medication works best when you take it before your symptoms start. Some people need to use the spray three or four times a day. Side effects may include nasal stinging or sneezing.

• Mast cell stabilizer eyedrops prevent the release of symptom-causing chemicals such as histamine. These prescription medications reduce allergy symptoms such as red, itchy eyes. Examples include cromolyn (Crolom), lodoxamide (Alomide), pemirolast (Alamast) and nedocromil (Alocril). These medications don't usually cause significant side effects.

## Immunotherapy

Immunotherapy injections (allergy shots) may relieve hay fever symptoms or allergic asthma that doesn't improve with medications. Injections may also be an option if you aren't able to take oral allergy medications without having side effects. Over a period of three to five years, you receive regular injections containing allergen extracts. The goal is to stop your body from reacting to specific allergens and decrease or eliminate your need for medications. Immunotherapy may be especially effective if you're allergic to cat dander, dust mites, or pollen produced by trees, grass or weeds. In children with allergic rhinitis, immunotherapy may help prevent the development of asthma. Rarely, immunotherapy injections can cause a lifethreatening allergic reaction (anaphylaxis).

# SEASONAL ALLERGY TREATMENTS <sup>30-36</sup>

Seasonal allergy treatments come in several forms — for example pills, liquids, nasal sprays, eye drops. No known medicine can "cure" allergies. So the goal of allergy treatment is to help relieve symptoms.

What seasonal allergy medication works best for you can often depend on your symptoms and the severity of those symptoms. Your doctor can help

you decide what seasonal allergy treatment is right for you.

## **Different Types of Seasonal Allergy Treatments**

Allergy treatments come in different forms and work in a variety of ways. Here are some examples.

- Antihistamines are one of the most commonly used types of allergy medications. They block histamine, a chemical that is released by the body's immune system. Antihistamines are available in several forms; for example, pills you swallow or as nasal sprays. Some antihistamines may cause drowsiness.
- Decongestants relieve congestion in the nose and sinuses. They work by constricting blood vessels in the nose. However, decongestants may sometimes lead to an increase in blood pressure. For this reason, and others, decongestants should be used with caution in people with certain common medical conditions, including high blood pressure.
- Nasal steroid sprays are used to prevent and treat the inflammation often caused by allergies. They can take up to a week to work. They also have been linked to worsening glaucoma and cataracts.
- Leukotriene blockers treat symptoms by blocking the effects of a chemical that is included in the allergic reaction.

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Immunotherapy, commonly called "allergy shots," may help in cases of persistent seasonal allergic rhinitis. Allergy shots are given regularly over a period of years and contain allergen extracts. The goal is to reduce your sensitivity to specific allergens so that you are less likely to react or to react as strongly to them.

## CONCLUSION

The treatment goal is to relieve symptoms and prevent a severe reaction. Treatment may include: Antihistamines relieve mild symptoms such as rash, hives, and itching Bronchodilators such as albuterol reduce asthma-like symptoms (moderate to wheezing or cough). Corticosteroids applied to the skin, given by mouth, or given intravenously (directly into a vein). Epinephrine by injection to treat anaphylaxis. An allergist has advanced training and experience to properly diagnose your condition and prescribe an allergy treatment and management plan to help you feel better and live better.

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