Archives of Immunology and Allergy

ISSN: 2639-1848

Volume 2, Issue 1, 2019, PP: 01-07

Allergy-The Voice of the People

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Abstract

Allergy-The voice of the people. We need to do more. The adaptive immune response provides specific protection against infection with bacteria, viruses, parasites, and fungi. The immune system is devised by nature primarily to protect the human body against pathogens. Sometimes the system becomes over enthusiastic and brings discomfort This phenomenon is similar to the over-enthusiastic servant who tried to kill the fly sitting on the King's nose with a strong sharp knife. Immune response is always directed towards the protection of the host. But in Hypersensitivity, the immune response becomes injurious to the host. Hence the immune response becomes a destructive process in hypersensitivity

In a protective immune response, the antigen or bacterium or virus is killed or neutralized.But in Hypersensitivity, the cells of the host are killed or the host itself isdamaged or killed.Hypersensitivity is the changed reactivity of the immune system.It is a beneficial protective system gone out of order.In clinical terms hypersensitivity is called Allergy.Some immune responses, however, give rise to an excessive or inappropriate reaction-this is usually referred to as hypersensitivity term "hypersensitivity", or "allergy", (1).In a given individual, such reactions typically occur after the second contact with a specific antigen(allergen). Your immune system process antibodies to halt the "invasion". The resulting chemical release can cause skin reactions, breathing problems and digestive difficulties

Keywords: *Atopic dermatitis, Drug hypersensitivity reactions (DHRs, Antihistamines,Prostaglandins and thromboxane, Omalizumab, Anaphylaxis, Serum sickness.*

INTRODUCTION

An analysis of patients with uncontrolled persistent allergic asthma who commenced Omalizumab treatment within the previous 15 weeks showed that approximately 29% of these patients were also receiving oral corticosteroids (OCSs) (2) Over the past 5 years, there have been to reports of challenge-proven FA prevalence in South Africa.(3). An earlier study among children with atopic dermatitis found high rates of FS (66%) and challenge-proven FA (40%),(4) IgE-mediated food allergy is a global health problem that affects millions of persons and every aspect of the life of a patient with food allergy. (5) In the United States, food allergy affects 15 million Americans, including 5.9 million children less than 18 years old, with epidemiologic studies demonstrating an increasing prevalence in the last two decades. (6) The prevalence of food allergy is increasing, and the development of more accurate diagnostic methods, prevention, and treatment require a better

understanding of the underlying mechanisms. Oral tolerance is the normal physiologic response to ingested antigens, and a breakdown in this process results in sensitization to food allergens. (7) Studies for a better understanding of the mechanisms leading to sensitization and disease versus desensitization and short- and long-term tolerance are being pursued intensively.(8) Drug hypersensitivity reactions (DHRs) are drug-induced immune and/or inflammatory reactions. They go beyond classical IgE-mediated reactions, such as anaphylaxis, and comprise many T cell-mediated reactions, which altogether are likely more common than IgE reactions (9) It is still unclear whether IL-22 is among the specific characteristics of drug-reacting T cells and whether IL-22 drives drug-reacting T cells to affect the skin in particular.. There are four types of histamine receptors in the body (H1 -H4), with H1 and H2 being most widely expressed.(11) H1 histamine receptors are found on a variety of cells including airway and vascular smooth muscle cells, endothelial cells, epithelial cells, eosinophils and neutrophils.(12) Allergic rhinitis (AR) is defined as a symptomatic disorder of the nose, induced after allergen exposure, by an IgE-mediated inflammation of the nasal membranes. (13) Nasal congestion is the predominant symptom in AR, described as the most troublesome symptom and occurring in up to 90% of patients.(14) Allergic rhinitis (AR) is a global health problem that causes major illness and disability. The incidence and prevalence of AR are high affecting over 10%-40% of the population worldwide, which continue to rise rapidly in recent years.(15) Classically, outdoor allergens appear to constitute a greater risk for AR than indoor allergens, as outdoor pollen allergens are a major cause of seasonal AR.(16) Omalizumab (Omab) has been demonstrated to be safe and effective in the treatment of various allergic disorders other than asthma e.g. allergic rhinitis (AR), allergic conjunctivitis, eczema and food allergy.(17) Use of Omab and other biological agents have been increasing for the last decade.(18) Atopic diseases represent a public health concern, particularly in the developed world (19) Atopic conditions rarely occur in isolation, and children frequently have multiple allergic diseases. For example, infants with eczema are at higher risk of food allergy and asthma, children with egg allergy are at increased risk of allergic respiratory diseases, and children with a single food allergy frequently have additional food allergies.(20)

History

The term hypersensitivity evolved from the observation of Richet and Portier one hundred years ago, who described the catastrophic result of exposing a pre-sensitized animal to systemic antigen. The first allergic disease to be defined was seasonal hay fever caused by pollen grains (which have a defined season of weeks or months) entering the nose (rhinitis) and eyes (conjunctivitis). In severe cases, patients may also get seasonal asthma and seasonal dermatitis. He also demonstrated that pollen extract could produce a wheal and flare skin response in patients with hay fever.The wheel and flare skin response is an extremely sensitive method of detecting specific IgE antibodies. The timing and form of the skin response in indistinguishable from the local reaction to injected histamine. Furthermore, the immediate skin response can be effectively blocked with antihistamines.

In 1903, Portier and Richet discovered that immunization of guinea pigs with a toxin from the jellyfish *Physialia* could sensitize them so that a subsequent injection of the same protein would cause rapid onset of breathing difficulty, the influx of fluid into the lungs, and death. They coined the term anaphylaxis (from the Greek *ana*, non, and *phylaxis*, protection) and speculated about the relationship to other hypersensitivity diseases Allergens can only become airborne in sufficient quantity to cause an immune response or symptoms when they are carried on particles. Pollen grains, mite fecal particles, particles of fungal hyphae or spores, and animal skin flakes (or dander) are the best-defined forms in which allergens are inhaled.(22) The concept of “allergy” was originally introduced in 1906 by the Viennese pediatrician Clemens von Pirquet, after he noticed that patients who had received injections of horse serum or smallpox vaccine usually had quicker, more severe reactions to second injections. (23) Pirquet called this phenomenon “allergy” from the Ancient Greek words *allos* meaning “other” and *ergon* meaning “work”(24)

All forms of hypersensitivity used to be classified as allergies, and all were thought to be caused by an improper activation of the immune system. (25) With this new classification, the word *allergy*, sometimes clarified as a true allergy, was restricted to type I hypersensitivities (also called immediate hypersensitivity), which are characterized as rapidly

developing reactions involving IgE antibodies. (26)A major breakthrough in understanding the mechanisms of allergy was the discovery of the antibody class labeled immunoglobulin E (IgE). IgE was simultaneously discovered in 1966–67 by two independent groups. (27)Ishizaka's team at the Children's Asthma Research Institute and Hospital in Denver, Colorado. (28) and by Gunnar Johansson and Hans Bennich in Uppsala, Sweden. (29)Their joint paper was published in April 1969 (30).

Significant Gap in Research

Histamine exists in a preformed state in platelets and in granules of mast cells and eosinophils. Antihistamine drugs can block histamine receptor sites and are relatively effective in allergic rhinitis. Histamine is one of the primary mediators of a type I reaction. Prostaglandins and thromboxane-Related to leukotrienes, prostaglandins, and thromboxane are derived from arachidonic acid via the cyclooxygenase pathway.The mediators, along with cytokines such as TNF-αand IL-4, are referred to as secondary mediators of type 1 reaction. Treatment aims to reverse the action of mediators by maintaining the airway, providing artificial ventilation if necessary, and supporting cardiac function. One or more of the following may be given: epinephrine, antihistamines, and corticosteroids. Atopic hypersensitivity disorders exhibit a strong familial predisposition and are associated with elevated IgE levels. Predisposition to atopy is clearly genetic, but symptoms are induced by exposure to specific allergens. These antigens are typically environmental (e.g. respiratory allergy to pollens, ragweed, or house dust) or foods (e.g. intestinal allergy to selfish). Common clinical manifestations include hay fever, asthma, eczema, and urticaria. Many sufferers give immediate-type reactions to skin tests (injection, patch, scratch) using the offending antigen. (31)

Bringing on Positivity

If you have a food allergy, you probably won't have a reaction to the food the first time you eat it. After the first exposure, your body classifies a particular food as foreign and will be prepared to attack quickly at the next encounter. The second time you eat the offending food your body may respond in a number of ways, including swollen lips, stomach cramps, vomiting or diarrhea, skin reaction, including hives or rashes, wheezing or breathing difficulties, migraine headache, fluid buildup behind the ear drum-this reactions is usually only seen in children. :. In worst cases, an allergic reaction may trigger anaphylactic shock. Without immediate treatment, breathing becomes extremely difficult, blood pressure drops, the mouth and throat swell, the victim has a feeling of impending disaster and may lose consciousness. Anaphylaxis can be fatal.(32). This type of reaction often occurs within 15 minutes of eating the offending food. Symptoms can last for several hours. The quicker the anaphylaxis is treated, the greater the chance of survival. Anyone with the symptoms of anaphylaxis should go to hospital emergency room, even if symptoms seem to subside on their own. Treatment of anaphylaxis requires an injection of epinephrine, a synthetic version of the natural hormone adrenaline. If you have ever experienced a severe food allergy, you should carry an emergency dose of epinephrine if you need one. Recent studies show that some adults may also have cross-reactive allergies. For example, people who tested allergic to fruits such as avocados and bananas may also be allergic to latex used clothing, in surgical gloves and in some medical equipment(33)

Where the Research Go Next?

The management of patients with AR includes patient education, allergen avoidance, pharmacotherapy, and immunotherapy in selected cases. (34) Omalizumab is an anti-human IgE humanized monoclonal antibody produced against CƐ3 domain of the Fc fragment of IgE molecule. Omalizumab is helpful mainly in ragweed/birch pollen-induced seasonal and perennial allergic rhinitis rather than uncontrolled and concomitant allergic rhinitis and asthma/chronic rhino-sinusitis/nasal polyposis. (35) Food allergies are defined as adverse immune responses to food proteins that result in typical clinical symptoms involving the dermatologic, respiratory, gastrointestinal, cardiovascular, and/or neurologic systems.(36) Food allergies are defined as adverse immune responses to food proteins that result in typical clinical symptoms involving the dermatologic, respiratory, gastrointestinal, cardiovascular, and/or neurologic systems. IgE-mediated food-allergic disease differs from non-IgE-mediated disease because the pathophysiology results from activation of the immune system, causing a T helper 2 response which results in IgE binding to Fcε receptors on effector cells like mast cells and basophils (37)

Major Advances and Discoveries

Rhinitis is an inflammation of the mucous membrane of the nose and is characterized by sneezing, itchy nose/eyes, watery rhinorrhea, nasal congestion, and some times, a nonproductive cough. An attack may be precipitated by inhalation of an allergen (such as dust, pollen, or animal dander). The foreign material interact with mast cells coated with IgE generated in response to a previous allergic exposure. The mast cells release mediators, such as histamine, leukotrienes, and chemotactic factors that promote bronchiolar spasm and mucosal thickening from edema and cellular infiltration. Antihistamines and/or intranasal corticosteroids are preferred therapies for allergic rhinitis. Antihistamines (H1-receptor blockers) are useful for the management of symptoms of allergic rhinitis caused by histamine releases (sneezing, watery rhinorrhea, itchy eyes/nose). However, they are more effective for prevention of symptoms, rather than treatment once symptoms have begun. Ophthalmic and nasal antihistamine delivery devices are available for more targeted tissue delivery. First generation antihistamines, such as diphenhydramine and chlorpheniramine, are usually not preferred due to adverse effects, such as sedation, performance impairment and other anticholinergic effects. The second generation antihistamines example fexofenadine, loratadine, desloratadine, cetirizine, and intranasal azelastine) are generally better tolerated. Combinations of antihistamines with decongestants are effective when congestion is a feature of rhinitis.

Intranasal corticosteroids, such as beclomethasone, budesonide, fluticasone, ciclesonide, mometasone, and triamcinolone, are the most effective medications for treatment of allergic rhinitis. They improve sneezing, itching, rhinorrhea, and nasal congestion. Systemic absorption is minimal, as side effects of intranasal corticosteroid treatment are localized. These include nasal irritation, nosebleed, sore throat, and, rarely, candidiasis. For patients with chronic rhinitis, improvement may not be seen until 1 to 2 weeks after starting therapy.

Short-acting α-adrenergic agonists ("nasal decongestants"), such as phenylephrine, constrict dilated arterioles in the nasal mucosa and reduce airway resistance. Longer-acting oxymetazoline is also available. When administered as an aerosol, these drugs have a rapid onset of action and show few systemic effects. Unfortunately, the α-adrenergic agonist intranasal formulations should be used no longer than 3 days due to the risk of rebound nasal congestion (rhinitis medicamentosa). For this reason, the α-adrenergic agents have no place in the oral α-adrenergic agonist formulations results in a longer duration of action but also increased systemic effects. (38)

Clinical Assessments

When assessing possible allergic disease, it is important to identify what the patient means by allergy, as up to 20% of the UK population describe themselves as having a food allergy, although < 1% have an IgE-Mediated hypersensitivity reaction confirmed on the double-blind challenge. The nature of symptoms should be established and specific triggers identified, along with predictability of a reaction and the time lag between exposure to a potential allergen and onset of symptoms. An allergic reaction usually occurs within minutes of exposure and provokes predictable symptoms (Angioedema, urticaria, wheezing and so on) Specific inquiry should be made about the family history of allergic disease. Potential allergens in the home and workplace should be identified and a detailed drug history should always be taken including compliance, side effects and the use of complementary therapies. (39)

Allergy Disorders and Therapeutics

Allergic disorders may be local or systemic Because the allergen is a foreign, the skin and respiratory tract are the organs most frequently involved in allergic disease. Allergic reactions may also localize to the vasculature, gastrointestinal tract, or other visceral organs. Anaphylaxis is the most extreme form of systemic allergy. Serum sickness occurs when an antibody response to exogenously administered antigens results in the formation of immune complexes. The skin joins, the kidney is frequently affected It is self-limited and resolves after the antigen is cleared.(40) The management of patients with AR includes patient education, allergen avoidance, pharmacotherapy, and immunotherapy in selected cases. Although a variety of drugs can be considered for the pharmacological treatment of allergic rhinitis, INCSs is the single most effective class of medication in the treatment of allergic rhinitis.(41)

Current Debate

The immune system is no different from any other human system. In balance, we do not even know it is there, but in an exaggerated state we call hypersensitivity, it can cause injury and even chronic disease. The hypersensitivity diseases include allergy, anaphylaxis, asthma, transfusion reactions, rheumatoid arthritis, and type 1 diabetes. (42)In addition to exocytosis, aggregation of FcεRI initiates two other pathways for the generation of bioactive products, namely, lipid mediators and cytokines. The chemical steps involved in the expression of such cytokines like tumor necrosis factor-α (TNF-α), interleukin (IL) I, IL-6, IL-4, IL-5, IL-13, granulocyte-macrophage-colony-stimulating factor (GM-CSF), and others, including an array of chemokines, have not been specifically defined for mast cells. Inhibition studies of cytokine production (IL-1β, TNF-α, and IL-6) in mouse mast cells with cyclosporine or FK506 reveal binding to the ligand-specific immunophilin and attenuation of the calcium ion-and calmodulin-dependent serine/threonine phosphatase, calcineurin. Lipid mediator generation involves translocation of calcium ion-dependent cytosolic phospholipase A2 to the outer nuclear membrane, with subsequent release of arachidonic acid for metabolic processing by the distinct prostanoid and leukotriene pathways. The constitutive prostaglandin- end peroxide synthase-1 (PGHS-1/cyclooxygenase-1) and the de novo inducible PGHS-2 (cyclooxygenase-2) convert released arachidonic acid to the sequential intermediates, prostaglandin G2 and H2. The glutathione-dependent hematopoietic prostaglandin D2 (PGD2) synthase then converts PGH2 to PGD2, the predominant mast cell prostanoid. The PGH2 receptors, DP1 and DP2 are distributed to smooth muscle as well as to TH2 lymphocytes, eosinophils, and basophils implicated in allergic inflammation. (43)

Summary

Bronchiectasis usually affects the lower lobes bilaterally, particularly air passages that are vertical, and is most severe in the more distal bronchi and bronchioles. When tumors or aspiration of foreign bodies leads to bronchiectasis, the involvement may be localized to a single lung segment. The airways are dilated, sometimes up to four times normal size. Characteristically, the bronchi and bronchioles are so dilated that they can be followed almost to the pleural surfaces. By contrast, in the normal lung, the bronchioles cannot be followed by eye beyond a point 2 to 3 cm from the pleural surfaces. (44)A large variety of bacteria can be found in the usual case of bronchiectasis. These include staphylococci, streptococci, pneumococcal, enteric organisms, anaerobic and microaerophilic bacteria, and (particularly in children) Homophilesinfluenza and Pseudomonas aeruginosa. In allergic Broncho pulmonary aspergillosis, a few fungal hyphae can be seen on special stains within the much inflammatory contents of the dilated segmental bronchi. In late stages, the fungus may infiltrate the bronchial wall. Allergic rhinitis (hay fever) is initiated by hypersensitivity reactions to one of a large group of allergens, most commonly the plant pollens, fungi, animal allergens, and dust mites. It affects 20% of the U.S. population. As is the case with asthma, allergic rhinitis is an IgE-mediated immune reaction with an early- and late-phase response. The allergic reaction is characterized by marked mucosal edema, redness, and mucus secretion, accompanied by a leukocytic infiltration in which eosinophils are prominent.(44)

All about Allergy-Conclusion

The immune system is devised by nature primarily to protect the human body against pathogens. Sometimes the system becomes over enthusiastic and brings discomfort This phenomenon is similar to the over-enthusiastic servant who tried to kill the fly sitting on the King's nose with a strong sharp knife. The immune response is always directed towards the protection of the host. But in Hypersensitivity, the immune response becomes injurious to the host. Hence the immune response becomes a destructive process in hypersensitivity. In a protective immune response, he antigen or bacterium or virus is killed or neutralized. But in Hypersensitivity, the cells of the host are killed or the host itself is damaged or killed. Hypersensitivity is the changed reactivity of the immune system. It is a beneficial protective system gone out of order. In clinical terms, hypersensitivity is called allergy is increasing in prevalence and severity. Suddenly, your airways narrow as lung muscles contract, the airway walls swell, and thick mucus is produced.. It inflames the airways. It produces air hunger and makes it difficult to breathe. The lining of airways swells and mucus blocks and clogs the airways. Mucus tightens the airways and produces bronchospasm

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Citation: **Raghavendra Rao M. V et. al,** *Allergy-The Voice of the People. Archives of Immunology and Allergy. 2019; 2(1): 01-07.*