

Allergy Immunotherapy

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Continuing Education Activity

Allergy immunotherapy (AIT), which is also termed allergen desensitization or hypo-sensitization was first introduced by Leonard Noon and John Freeman in 1911. They proposed that people with hay fever were sensitive to grass pollen toxins. Desensitization is "a method, to develop a temporary state of tolerance to an agent responsible for an allergic or hypersensitivity reaction." This activity reviews the indications, contraindications, and techniques for allergy immunotherapy and highlights the role of the interprofessional team in the management of patients with allergies.

Objectives:

- Describe the indications for allergy immunotherapy.
- Describe how allergy immunotherapy is done.
- Outline the importance of collaboration and coordination within the interprofessional team in optimizing the care of patients requiring allergy immunotherapy.
- Discuss future trends in allergy immunotherapy

Introduction

Allergy immunotherapy (AIT), also referred to as allergen desensitization or hypo-sensitization was first introduced by Leonard Noon and John Freeman in 1911, they proposed that people with hay fever were sensitive to grass pollen toxins. [1] Noon is credited for developing a process involved in the extraction of timothy pollen in distilled water and then boiling it to create an extract. [1] This extract was then injected in increasing doses to alleviate symptoms in patients. This concept is widely in use today with a modified approach. Currently, the term immunotherapy is used to describe all methods to overcome abnormal immune responses with induction of clonal deletion, anergy, immune tolerance, and immune deviation. [2] However, the term desensitization is "a method, to develop a temporary state of tolerance to an agent responsible for an allergic or hypersensitivity reaction." [3] Furthermore, immunotherapy is a disease-modifying treatment and the effects can last longer even after stopping the treatment, which then provides prophylactic effects. [3][4][5][6][7][8]

Anatomy and Physiology

Several cellular and molecular mechanisms explain the beneficial effects of immunotherapy including allergic specific suppression of inducible CD4(+), CD 25+, forkhead box p3+ T-regulatory cells, and IL-10 secreting T-regulatory cells, preventing their increase in peripheral blood. Other mechanisms include suppression of eosinophils, mast cells, and basophils, and the switching of antibodies from IgE to IgG4 blocking antibodies. [9][10][11] Other mechanisms, including a switch from

a TH2 to a TH1 immune deviation, and other changes in humoral/cellular immunity, are still being elucidated.[\[10\]](#)[\[12\]](#)[\[13\]](#)[\[12\]](#)

Indications

Indications for Allergen Immunotherapy [\[2\]](#) [\[3\]](#)

- Moderate-to-severe allergic rhinitis
- Allergic asthma
- Allergic conjunctivitis
- Allergic rhino-conjunctivitis
- Atopic dermatitis
- Immune-mediated and IgE-mediated food allergy
- Insect allergy that causes significant local reaction and anaphylaxis

Note: Allergen immunotherapy is only indicated when there is evidence of an IgE-mediated reaction that correlates with clinical symptoms. These IgE-mediated reactions can be identified via a blood IgE test or the more preferable skin testing.

Other Immunotherapies [\[3\]](#)

- Vaccination and biological agents in infectious disease and primary immunodeficiencies.
- Immunosuppressive agents in autoimmune disease and organ transplant
- Biological and monoclonal agents
- Food hypersensitivity

Contraindications

There is no evidence to suggest that immunotherapy will be effective if a specific IgE antibody is negative.[\[3\]](#) Furthermore, if IgE testing results are positive but suspected clinical symptoms and exposure do not correlate, then it is also not likely to work.

The use of concomitant B-blockers is contraindicated with immunotherapy in the rare chance that the patient needs epinephrine to treat anaphylaxis. However, according to the U.S. practice parameters on anaphylaxis, the benefits of Hymenoptera venom immunotherapy (VIT) outweigh the potential risks associated with b-blockers or ACEIs in patients with anaphylaxis to stinging insects who also have cardiovascular disease that requires these medications. [\[14\]](#) As per the EAACI guidelines, the risk/benefit profile also suggests that there should be no contraindication for venom immunotherapy in patients on B-blockers. [\[15\]](#)

If a patient is having an asthma exacerbation, they should not receive an immunotherapy injection [\[2\]](#)

Equipment

Required Equipment and Procedures [\[3\]](#)

- All extracts require storage in a refrigerator at 4 C
- Administration can be done via subcutaneous injection or sublingually
- Seventy percent isopropanol for sanitization
- Sterile syringes and vials
- Mixing log with information on expiration
- Policy and procedure manual
- Emergency treatment, i.e epinephrine

Personnel

Because allergy immunotherapy can cause severe reactions, including anaphylaxis, a physician should supervise trained personnel. [\[2\]](#) Required training include: [\[2\]](#)

- Preparation of allergenic products
- Successful completion of a written test on aseptic technique and extract preparation and media-fill testing
- Knowledge of antiseptic hand cleaning and disinfection of mixing surfaces
- Ability to identify, measure, and mix different allergen extracts
- Understand who are the appropriate candidates for allergy immunotherapy
- Review with the patients the risk and benefits of the procedure
- Learn to identify signs and symptoms of a possible severe reaction
- Discuss with the patient what are some expectations during the course of treatment and when it will be successfully completed

Preparation

The prescribing physician should select allergen extracts based on IgE results and clinical correlation. The physician should consider several important factors including the quality of allergen extracts, cross-reactivity, and degradation of allergens and immunotherapy doses, for example, the starting dose should be lower than the maintenance dose. [\[2\]](#) Keep in mind that some patients will not be able to achieve the maintenance dose due to possible side effects. There are also ranges of what are considered maintenance doses for standardized and non-standardized extracts.

Technique or Treatment

Allergenic proteins from pollen, dander, dust mites, insects, mold, among others are the main ingredient of allergen extract. However, the final product is a mixture of diluents or solvents and preservatives. Different extracts including aqueous, glycerinated, lyophilized, acetone precipitated, alum-precipitated are available. Diluents will keep the allergen in liquid form; commonly used agents are glycerin, phenol saline, and HSA. The staff should use measures that include good personal hygiene, hand washing, and antiseptics to clean working areas. These include a water-based disinfectant followed by the application of alcohol on working surfaces for preparing allergen extracts. Alcohol kills organisms by dehydration. Sanitization will prevent bacterial contamination.[\[2\]](#)

Complications

Giving allergy immunotherapy should be given with tremendous care since it involves administering an agent that a patient is already known to be allergic to. Complications due to immunotherapy include systemic reactions such as anaphylaxis, large cutaneous reactions, and a local reaction at the injection site. [\[2\]](#) Although rare, even fatal reactions to subcutaneous allergy immunotherapy can occur. One of the greatest risk factors for such reactions is asthma, especially uncontrolled or unstable asthma.[\[16\]\[17\]](#) Another risk factor is an accidental intramuscular injection which can cause an increased risk of systemic reaction due to rapid absorption. Sublingual administration has only shown severe reactions associated with the first dose and subsequent doses cause less severe symptoms of the oral mucosa, throat, or gastrointestinal tract. [\[18\]\[19\]](#) Due to these complications, patients must be aware of the risk vs benefits associated with immunotherapy. Thus, immunotherapy should be given under the guidance of a specialist trained in the field and informed consent should be gathered.

Management of Complications [\[2\]](#)

- Topical corticosteroids, antihistamines, or cool compresses for local reaction
- Epinephrine is the mainstay treatment for anaphylaxis.

The physician should re-visit the benefit versus risk of continuing immunotherapy after systemic reactions.[\[2\]](#)

Clinical Significance

Asthma

Allergen immunotherapy can reduce short-term symptoms in allergic asthma; however, there is a moderate increase in the risk of systemic and local reactions based on a meta-analysis.[\[6\]](#) A 3-year course of either sublingual or subcutaneous immunotherapy prevents asthma for up to 2 years in children and adolescents with grass/birch pollen that triggers moderate to severe allergic rhinitis. However, this still requires further research.[\[4\]](#)

Some studies have shown that giving immunotherapy for allergic rhinitis early can prevent the development of asthma in children. [\[20\]\[21\]\[22\]](#) A study by Grembiale in 2000 showed that allergy immunotherapy to house dust mite helped to prevent the development of asthma.[\[22\]](#) In the

preventative asthma study(PAT) children aged 5 to 12 years were given a subcutaneous injection of grass pollen and/or birch pollen for 3 years and was found to have a decrease in the development of asthma over a 10 year follow up. [20] In the Grass pollen asthma prevention trial (GAP), sublingual treatment with grass pollen also showed reduced asthma symptoms and medication scores.[21]

Allergic Rhinitis

- Allergen immunotherapy is clinically effective, cost-effective, and disease-modifying in allergic rhinitis compared to standard drugs.[23][24]
- Sublingual immunotherapy for pediatric allergic rhinitis has shown improvement in symptomatic management and a decreased medication need based on a meta-analysis of the randomized controlled trials. More trials with a larger sample size are underway to assess safety in the pediatric population.[25]

Allergic Rhino-Conjunctivitis

Allergen immunotherapy is beneficial in ameliorating rhino-conjunctivitis symptoms. [26]Some evidence suggests that there is a maintenance effect on reducing symptoms after discontinuation of immunotherapy.[27]

Enhancing Healthcare Team Outcomes

Current and Future Trends in Allergen Immunotherapy

Recent advances in understanding the mechanism and the long-term effects of immunotherapy are encouraging for future therapies. There are also new approaches being used to improve safety and overcoming the risk of severe adverse allergic reactions during immunotherapy. Newer allergen preparations available include allergoids, recombinant allergens (recA), and modified-recombinant allergens (recA). Studies on virus-like particles and CpG-motifs, adjuvants like MPL, and aluminum hydroxide have been shown to increase immunological response and can improve safety and efficacy.[8] Other newer approaches to allergen immunotherapy include the application of extract patches on the skin and/or inguinal lymph node injection. Furthermore, recombinant technology or chemicals may alter allergen molecules that make them less reactive; this may be due to suppression of Th2 responses or stimulation of toll-like receptors (approval is pending).[28] The new advances in allergy immunotherapy not only provide disease-modifying treatments but are also cost-effective and improve the quality of life.[29] Yet, with the historical efficacy and safety of immunotherapy, it remains underutilized.

Safety, Doses, Delivery, and Application of Immunotherapy

- Comparison of pediatric and adult systemic reactions to subcutaneous immunotherapy shows significant Grade 1 and Grade 2 systemic reactions that are higher in a pediatric population than adults. However, further studies are needed to evaluate the dosing strategy in children.[30]
- Subcutaneous allergen immunotherapy has shown that SCIT rarely causes any major clinical problems; there is a risk of less than 1.5% in patients who are HIV positive without AIDS,

cancer (in remission), severe asthma, transplantation, and during pregnancy, based on web-based survey.[\[31\]](#)

- Food immunotherapy has exploded due to numerous studies suggestive of its benefit. One such study was the LEAP (Learning Early About Peanut Allergy) that showed that high-risk infants with atopic dermatitis and egg allergy were able to build a tolerance to the ingestion of peanut if given early.[\[32\]](#) Studies investigating oral immunotherapy with other foods and various delivery methods are currently being done.

Future trends in allergy immunotherapy support the concept of precision medicine. It should always be individualized and specific for a particular patient. Although it has been shown to prevent the development of asthma and new sensitization, this has only been shown in children. On the other hand, adults should be evaluated differently, and it should be used for the primary objective of bringing relief to their allergic symptoms. Further research is needed to address research gaps in allergy immunotherapy. Such gaps include which sensitivities should be targeted to prevent disease, timing of immunotherapy, length of treatment, monoallergen vs polyallergen treatment, etc. However, the future is exciting, and with the increasing understanding of the immune system, the age of precision medicine has arrived.

Nursing, Allied Health, and Interprofessional Team Interventions

When using allergy immunotherapy, an interprofessional team including clinicians, mid-level practitioners nursing staff, and pharmacists is the best approach to achieving improved patient outcomes.

Nursing, Allied Health, and Interprofessional Team Monitoring

When administering allergy immunotherapy, an interprofessional team including clinicians, mid-level practitioners, and nursing staff should be vigilant in looking for signs of an allergic reaction.

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