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## ALLERGIC RHINITIS: DIAGNOSIS AND TREATMENT



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### **Abstract**

The study focused on the classroom management skills of Junior High School Teachers during the resumption of Face to Face Classes. The study will make use of the descriptive correlational design. Moreover, the target population will be Junior High School teachers of Babag National High School. A randomized sampling technique will be used to select the sample. The sample size will be determined based on the required confidence level and margin of error. A survey questionnaire will be used to gather data on various aspects of classroom management. These aspects will include organizational, instructional, and behavior management techniques used by teachers. In addition, the outcome suggested that the teacher has strong classroom management skills. The study found that when it comes to classroom management, teachers are skilled and prepared. To efficiently handle the students in their class and conduct the lessons, they have put multiple strategies into practice. Despite the challenges encountered along the way, they are eager to put these plans into action.

**Keywords**: Classroom Management Skills, Resumption of classes, Junior High School Teachers.

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#### Introduction

Allergic rhinitis (AR) is considered as a great health problem. AR affects about 400 million people around the world. The disease prevalence increased to reach about 25-40% (*Pawanka*, 2014). Urbanization and environmental pollutants could be the causes of increased prevalence of the disease (*Husna etal.*, 2022).

It is very essential to know all about the AR. In the following short review, we will try to give a well-established and vital aspects of the disease concerning pathophysiology of AR, clinical and laboratory diagnostic criteria, as well as pharmacological and immunomodulating therapies for AR patients.

Hypersensitivity reactions defined as normal protective immune system responds abnormally producing harmful effect to the Symptoms only develop with sensitized individuals i.e., they must had a previous exposure with the specific antigen. According to Coombs and Gell (1975) classification, hypersensitivity can be divided into the following types (Rajan, 2003): *Immediate Hypersensitivity* (Anaphylactic Reaction) or type I: which can be localized or systemic, Cytotoxic Reaction (Antibody-dependent) or type II, Immune Complex Reaction or type III, Cell-Mediated (Delayed Hypersensitivity) or type IV and Stimulatory Hypersensitivity or type V

Allergic rhinitis is type I hypersensitivity reaction and considered as nose inflammatory disease happened when the immune system gives exaggerated reaction to allergens in the air. The patient suffers from runny or obstructed nose, red, watery and itchy eyes, sneezing and edema around the eyes (NIAID, 2015). There is clear nasal fluid and symptoms usually happens minutes after exposure and patients can be incapable to work, sleep and decrease concentrate at school (Wheatley and Togias, 2015). Patients give symptoms due to pollens exposure arise symptoms at certain times of the year (NIAID, 2015).

Allergic rhinitis may be associated with asthma, atopic dermatitis and allergic conjunctivitis (*Wheatley and Togias*, 2015). Allergic rhinitis is usually exaggerated by environmental allergens such as pollen, dust, mold or pet hair. Environmental exposure and Inherited genetics and contribute to the development of allergies (*NIAID*, 2015).

### Pathophysiology of allergic rhinitis(AR):

It has two types IgE mediated allergic rhinitis and non-IgE mediated.

The IgE mediated allergic rhinitis has both forms systemic and local allergic rhinitis.

Concerning the systemic form of allergic *rhinitis* (SAR): Allergens are phagocytosed by dendritic cells that travel to lymphoid organs at the site where the antigen is introduced to naïve helper T (Th0) cells on MHC class II molecules (Chaplin, 2010). Structural cells like mast cell, epithelial cells and the infiltrated inflammatory cells as basophils, eosinophils and T cells have a role in producing and maintaining allergic inflammation process. While cytokines such as IL-4, and IL-13 produced from mast cells and T cells direct B cells toward IgE synthesis and could participate in the synthesis of local IgE in the nasal mucosa of patients with allergic rhinitis (Pawankar, *2001*).

The local form of allergic rhinitis (LAR): is a regional inflammatory status caused by local symptoms and sIgE-mediated inflammation with no prove of systemic hypersensitivity (Rondon et al., 2017).

Non IgE mediated allergic rhinitis: The nasal epithelium is harboring the inhaled aeroallergens. Intrinsic proteolytic activity of allergens causes disrupting of the nasal epithelial barriers allowing allergen to penetrate and produce chronic inflammation (Bashir et al., 2013).

### Risk elements for allergic rhinitis:

Genetics: the strongest risk element is the presence of disease in first-degree family members (*Thomsen et al.*, 2006).

Inhalant allergens (in utero and early childhood exposure): include pollens, mites, fungal allergens and animal dander (*Erbas et al.*, 2013).

**Pollution:** pollution may disrupt the nasal mucosa and disturb mucociliary clearance (MCC) so facilitating the entrance of inhaled allergens to cells of the immune system (*D'Amato et al.*, 2001).

**Tobacco smoke:** exposure to tobacco smoke can enhance the development of atopic diseases through many mechanisms include direct surface damage to nasal mucosa (*Yang*, 2016).

*Diagnosis*: usually done by history taking and physical examination, skin prick test and Lab investigations.

**History Taking** includes the type, time, frequency and duration of symptoms, any environmental exposures producing symptoms at work/school/home and medications other measures or that decrease or increase symptoms (Seidman et al., 2015). History taking is the most effective key in proper diagnosis and it help the proper selection of different antigen for SPT.

**Physical examination** and assessment of the multiple organ systems of the head and neck (*Seidman et al.*, 2015).

### Skin prick testing (SPT):

*Indications*: SPT is based on a detailed history (*Heinzerling et al.*, 2013). SPT can be used in a combination with the history and physical examination to confirm the diagnosis of AR (*Ryan et al.*, 2008).

Performance parameters for SPT: The following are important performance parameters for SPT (Bousquet et al., 2012): Always use both negative and positive controls (Histamine hydrochloride at a concentration of 10 mg/mL is used as a positive control and glycerinated buffer

saline is used as a negative control). Test on a normal skin. Read the reactions and wheal sizes after 15-20 minutes, size will be affected after the required time. Rule out dermographism before performing SPT. Ask for medications taken and which of those can affect the SPT and its last dose. Medications interfering with SPT, for examples oral antihistamine needs from 2 to 7 days, while topical steroids at the site of SPT needs up to 7days. Oral steroids need 3 weeks (Bousquet et al., 2012). The extracts should be stored between +2 to +8 degree centigrade to maintain their potency. During pregnancy it is better to test with high dilutions rather than the standard concentration (Bernstein and Storms, *1995*).

Interpretation of Skin Prick Test results is according to the wheal size (*Liang 2002*). There are many methods to interperate SPT results in type-I allergy testing. The common method is to recognize the wheal size by its 'average diameter'. The more accurate method is to calculate the actual size of the wheal. In both methods, skin prick test (SPT) results can be measured for histamine-sensitivity of the skin by dividing the results of the allergic reaction by the histamine control (*J P M van der Valk et al 2016*).

### Concerning lab. Investigation:

Measuring serum antigen specific IgE (sIgE): By using radioactive technique called RAST. That test can be replaced with other tests using enzymatically-driven reactions to produce a chemiluminescent, or colorimetric fluorimetric quantified or "read" by an autoanalyzer (Hamilton, 2010). Benefits of measuring serum specific IgE (Brown et al., 2016): There is no risk for anaphylaxis that may occur in some cases with skin testing. It provides a safe and beneficial element to determine the presence of sensitization as a biomarker of IgE-mediated hypersensitivities and confirming specific allergen and to confirm the SPT and clinical history.

Nasal specific IgE: AR patients have sIgE in the nasal mucosa which demonstrate the class switching, and antibody production that happened locally (Powe et al., 2010). The result can be positive in some patients that have negative SPT or serum sIgE despite a clinical history suggestive of AR (Rondon et al., 2008).

Basophil activation test (BAT) is an in vivo peripheral blood test that can be used in the diagnosis of allergy to food, drugs and hypersensitivity syndromes after using primary line tests (Hoffmann et al., 2016).

CRD): component resolved diagnosis (CRD): component resolved diagnosis (CRD) or Molecular diagnosis (MD) is used to identify the allergen sensitization of a patient by measuring sIgE to purified natural or recombinant allergens; so able the identification of the potential disease-eliciting molecules (Matricardi et al., 2016).

Allergen challenge chambers (ACCs) or can be called by Environmental exposure chambers (EECs) are used for under controlled exposure of subjects to a well-known atmosphere of several substances such as particulate, allergens and gaseous air pollutants or climate conditions or chemicals. There are a few number of EECs worldwide (Rosner-Friese et al., 2015)

Local allergen challenge tests by facing the target organs of respiratory allergy (i.e. nose, eye, bronchi) with a suspected allergen to determine the actual clinical reactivity when the results of the initial allergy tests (skin tests or measurement of sIgE) are inconclusive (Agache et al., 2015).

Nasal challenge tests aims to stimulate the response of the upper airway after nasal exposure to allergens (Dordal et al., 2011 and Edyta Krzych-Falta et al 2019)

Conjunctival challenge is performed by dropping 20 to 30  $\mu$ L of an allergen solution into the ocular conjunctiva in one eye and using diluent in the contralateral eye as a control (Agache et al., 2015). Positive response to conjunctival

provocation test CPT is simple to evaluate as it provide an immediate reaction (from 5 to 20 minutes from the allergen eye drop) with ocular tearing, itching, redness, and may cause conjunctival edema (*Moller et al.*, 1984).

Nasal cytology and histology is a simplified diagnostic procedure that is used to evaluate the health of the nasal mucosa by determine and numbering cell types (e.g esionophil and basophil) and identify their morphology (Gelardi et al., 2016).

### Management of allergic rhinitis

Management of allergic rhinitis divided into 3 major categories of treatment (Javed and Michael, 2018): Environmental control measures and allergen avoidance, pharmacological therapy, non-pharmacological therapy.

### Concerning Environmental control measures:

They include avoidance of specific known allergens (substances to which the patient has IgE-mediated hypersensitivity) and avoidance of nonspecific or irritant triggers (*Platts-Mills*, 2004).

### As regard pharmacological therapy:

Pharmacologic methods for the treatment of allergic rhinitis include intranasal corticosteroids, topical and oral antihistamines, decongestants, (Nasalcrom )intranasal cromolyn, intranasal anticholinergies, and leukotriene receptor antagonists (*Scadding et al.*, 2008).

### For nonpharmacologic therapy:

Acupuncture is of one nonpharmacological therapeutic techniques. It's mechanism of action suggested by secreate neurochemicals such as beta endorphins and serotonin which in can mediate the anti-inflammatory pathway (Brinkhaus et al., 2008). Using probiotics can have an impact on the intestinal microbiota or enhance the immune function (Schlundt, 2012). Administration herbal preparation sativa as *N*.

(Nikakhlagh et al., 2011) and Nasal irrigation by saline (Pynnonen et al., 2007) may help in reducing the symptoms.

### Allergen immunotherapy

Defined as hyposensitization or desensitization. It is a medical treatment for environmental allergies for examples: insect bites, and asthma. Immunotherapy done by exposing people to a small increasing amounts of allergen as a trial to change the immune system's response (NIAID, 2105). Aim is to produce tolerance to the allergen by decreasing its ability to induce IgE production (Burks, 2014).

Types of allergen immunotherapy (Cox, 2014): Subcutaneous Immunotherapy (SCIT) and Sublingual Immunotherapy (SLIT).

### Subcutaneous immunotherapy (SCIT):

It is defined as allergy shots and defined as long-term treatment aim to decrease symptoms of patients suffering from allergic asthma, allergic rhinitis, conjunctivitis (eye allergy) or insect sting allergy by minimize the sensitivity to allergens leading to prolonged relief of allergic symptoms even after quitting treatment (*Cox*, 2014).

### Sublingual immunotherapy (SLIT):

Sublingual immunotherapy could be in the form of tablet or drop. The patient is instructed to place it underneath the tongue for one to two minutes and then swallow it. The administration is repeated from three days to seven days a week according to recommendations. It's advisable to continue the therapy form three to five years to develop a prolonged immunity (*Catherine*, 2019)

Adverse effects among both adults and children are usually local and mild. Extremely rare, severe allergic reactions (anaphylaxis) have been demonstrated

using SLIT. Therefore SLIT is best prescribed by physician (*Cox*, *2014*).

#### Administration

Administration of SLIT is performed with a full dose or a short rapid increasing dose and the first dose is given under medical supervision and then administration continues once daily and is administered by the patient or care giver at home (*Creticos et al.*, 2019).

# General precaution for the administration of allergen immunotherapy (Cox et al., 2011):

Allergen immunotherapy must be administrated in specialist allergy centers with adequate facilities including presence of drugs used for the treatment of anaphylaxis which can be used by health professionals with adequate experience, knowledge and the ability to diagnose and treat early symptoms and signs of anaphylaxis.

Patients must informed about their planned immunotherapy schedule with written informed consent must be done by all patients (or parent/guardian in pediatrics practice) and placed in the patient's hospital record.

Before each injection, patients should be known by name, date of birth and the vaccine type to be administered and should be asked about any local or general side effects after receiving the previous injection. Any side effects should be recorded and if necessary dosage adjustment made.

The timing after the previous injection should be checked, any change from the planned schedule should be noted and if necessary dosage adjustment performed and any change in the patient's clinical status should be noted including any new medications, pregnancy, any infection, other recent illness or feelings of malaise or tiredness should be filled.

In patients with associated asthma, it is important to ensure that their asthma has

been stable and under control before administration of immunotherapy. In patients suffering from seasonal allergic rhinitis, the maintenance subcutaneous dose may be decreased or postponed if the patient is symptomatic. Patients should remain under observation within the clinic for at least an hour after their last injection.

# The following equipment and drugs are required for immunotherapy (Self et al., 2009):

Adrenaline (1: 1000) should be immediately available. Antihistamines and corticosteroids (intravenous and oral preparations). β-agonist (with accessible methods for inhalation with or without a spacer and nebulization). Saline/colloids for intravenous infusion. Oxygen and suction. monitoring blood pressure equipment, nebulizer, and mask. Needles, syringes and intravenous cannulae.

### Dose schedules for administrating of subcutaneous immunotherapy:

A number of up dosing schedules are used for children and adults including the conventional one injection per week (*Durham et al.*, 2006 and Frew et al., 2006).

Schedule selection will be determined by the product, time to reach maintenance, patient choice, particularly with consideration of side-effect profiles and convenience. Generally, more rapid administration is likely to cause more adverse effects. (*Bousquet et al.*, 1998).

### Dose schedules for administration of sublingual immunotherapy:

SLIT involves administration of the vaccine either in solution under the tongue or tablet for 1–2 min without swallowing. Allergen extracts must not be placed in raw areas or bleeding in the oral cavity or after dental procedures until the wound is completely healed. (*Cox et al.*, 2006).

### Common methods for administrating the allergen extracts (Bousquet et al., 2009):

Should be taken on an empty stomach in the morning, maintain the drops or tablet under the tongue for at least 2 minutes, then swallow. Do NOT eat/drink anything for 15 minutes, caution on having crunchy cereals as these may cut the tongue and increase the ability of mouth irritation from the extracts. If you missed morning dose, continue treatment the next morning at the usual dosage. Currently, sublingual immunotherapy is not prepared for insect venom immunotherapy.

### Contraindications and interactions of immunotherapy:

General contraindications to allergenspecific immunotherapy include permanent target organ changes, inflammatory/febrile disorders, severe acute or chronic diseases (especially cardiovascular disease) and severe psychiatric disorders, controlled and/or irreversible asthma airway obstruction, severe autoimmune diseases, immunodeficiency syndromes and malignant neoplastic diseases (Kleine-Tebbe et al., 2009).

### Contraindications of SLIT-tablets:

In patients with severe, unstable, or uncontrolled asthma, history of eosinophilic esophagitis, hypersensitivity to any of the inactive ingredients, oral wounds (*Egan and Atkins*, 2018).

### Side effect of SLIT:

SLIT may produce oral inflammation (e.g. thrush, mouth ulcers and oral lichen planus), it should be discontinued to allow complete healing of the oral mucosa before re-administration (*Creticos et. al 2019*).

### Safety of SLIT:

Clinical trials proved that SLIT is safer than subcutaneous immunotherapy (SCIT) although the presence of local oral mucosal-type adverse effects (*Creticos et al.*, 2014). Anaphylaxis is uncommon (*Wahn et al.*, 2012).

**Eosinophilic esophagitis:** A rare association has been reported between eosinophilic esophagitis and aeroallergen SLIT and with oral immunotherapy of food allergens as well (*Miehlke et al.*, 2013).

Use in pregnancy: Treatment should not be started in a pregnant patient, but if a woman becomes pregnant during treatment so it could be continued (*Paul et al.*, 2015).

Compliance: Sublingual immunotherapy (SLIT) need a commitment by the patient to a long-term daily maintenance therapy that is self-administered (*Röder et al.*, 2008).

### Comparison between SLIT and SCIT:

SLIT is safer, with fewer local and systemic allergic reactions than SCIT, more comfortable for patients because of route allergens administrations are by ingestion not by injection and more easy for patients and clinicians as the therapy is self-administered by the patient (or caregiver) at home (Yukselen et al., 2012).

Patient will be instructed to deal with missing dose to ensure that it is carried out safely and effectively (Yukselen et al., 2012).

### Nasal immunotherapy:

LNIT is taken (by spray) of gradually increasing dose of allergen (build-up or updosing phase) into the nasal cavity to reach a maintenance dose (*Passali et al.*, 2002)

### Omega-3 fatty acids with SLIT

Combination of omega-3 fatty acids and sublingual immunotherapy showed promising effect in treatment of asthma by using asthma control test ACT that showed decrease in peak expiratory flow rate PEFR, forced expiratory volume in the first second (FEV1) and serum interleukin 17A (Mustafa K Abdo Sultan et. al 2019).

### Causes of immunotherapy failure (Abramson et al., 2003):

Missed the connection between allergy testing results and clinical history,

insufficient dosing, use of low dose treatment and mixing several antigens in the same vial causing dilution of dose, mixing unsuitable antigens in the same vial (i.e. dust and pollen or mold and pollen. missing clinically relevant allergens in allergy serum, inadequate compliance with scheduled dosing.

### COVID 19 and allergic rhinitis

The onset of seasonal allergic rhinitis (SAR) and acute COVID-19 share a limited similarities in their phenotype, as COVID-19 has symptoms as a flu-like illness with persistent cough and fever as its main symptoms but it may be represented with milder symptoms especially in younger people. According to the World Health Organization (WHO) some patients may also have a nasal congestion, runny nose, sore throat, body aches and pains or diarrhea. Some presented with abrupt and complete loss of smell and taste (*Carol et al.*, 2020).

About 80% of COVID-19 patients presented with mild symptoms similar in the severity to a common cold and cured without requiring any treatment. Fever and cough are the most important symptoms of COVID-19 while itching and conjunctivitis referred to allergic rhinitis (AR) as the diagnosis by *CDC* (2020).

Allergic patients with clinical picture of rhinitis, asthma and conjunctivitis had acute relapses during the COVID-19 emergency both due to intense spring exposure to allergens and other precipitating factors such as external and internal pollutants. Currently intranasal corticosteroid therapy for allergic rhinitis can be continued in COVID-19 patients (*Pfaar et al.*, 2020).

#### Conclusion

Skin prick test and patients clinical symptoms are more efficient in diagnosis of allergy. It helps to determine the causative allergens. Sublingual and subcutaneous immunotherapy show significant

improvements in allergic symptoms. It is much better to use sublingual immunotherapy because it is much safer and easy to use by the patients.

#### References

- **Abramson MJ, Ledford DK and Lockey RF** (2003): "Allergen immunotherapy for asthma". Cochrane Database Syst. Rev.(4).
- **Agache I, Bilo M and Braunstahl GJ** (2015): In vivo diagnosis of allergic diseases allergen provocation tests Allergy; 70:355–365.
- Bashir ME, Ward JM, Cummings M, Karrar EE, Root M, Mohamed AB, Naclerio RM and Preuss D (2013): Dual function of novel pollen coat (surface) proteins: IgE-binding capacity and proteolytic activity disrupting the airway epithelial barrier. PLoS One; 8:e53337.
- Bernstein IL and Storms WW (1995):

  Practice parameters for allergy diagnostic testing. Joint Task Force on Practice Parameters for the Diagnosis and Treatment of Asthma. The American Academy of Allergy, Asthma and Immunology and the American College of Allergy, Asthma and Immunology. Ann Allergy Asthma Immunol; 75(6 Pt 2): 543-625
- Bousquet J, Heinzerling L, Bachert C, Papadopoulos N G, Bousquet P J, Burney P G (2012): Practical guide to skin prick test in allergy to aeroallergens. Allergy; 67(1):18-24. doi: 10.1111/j.1398-9995.2011.02728.x
- **Bousquet J, Lockey R and Malling H J** (1998): Allergen immunotherapy: therapeutic vaccines for allergic diseases. J Allergy Clin Immunol; 102(4 Pt 1):558-62
- **Bousquet PJ (2009):** Sublingual Immunotherapy World Allergy

- Organisation Position Paper WOA Journal; 233-281.
- Brinkhaus B, Witt CM, Jena S, Liecker B, Wegscheider K and Willich SN (2008): Acupuncture in patients with allergic rhinitis: a pragmatic randomized trial. Ann Allergy Asthma Immunol; 101(5):535–543. doi: 10.1016/S1081-1206(10)60294-3.
- Brown CE, Jones CJ, Stuttaford L, Robertson A, Rashid RS and Smith HE (2016): A qualitative study of the allergy testing experiences, views and preferences of adult patients. Clin Transl Allergy; 6: 34.
- **Burks AW** (2014): "Oral and sublingual immunotherapy for food allergy". The World Allergy Organization Journal; 7 (1): 35. doi:10.1186/1939-4551-7-35. PMC 4325942. PMID 25709745.
- Carol H, YanFaraji F, Prajapti D P, Boone C E, DeConde A S (2020): International Forum of Allergy & Rhinology; Association of Chemosensory Dysfunction and Covid-19 in Patients Presenting with Influenza-like Symptoms.
- Catherine C Peng and Pharm D (2019):
  About Allergy Drops sublingual immunotherapy, healthline. https://www.healthline.com/health/allergy-drops#1
- Centers for disease control and prevention (CDC) (2020): COVID-19 Response Team Coronavirus disease 2019 in children United States. MMWR Morb Mortal Wkly Rep. 2020 Apr 10;69(14):422–426.
- **Chaplin DD** (2010): Overview of the immune response. J Allergy Clin Immunol; 125: S3–S23.
- Coombs RRA and Gell PGH (1975):

  Classification of allergic reactions responsible for clinical hypersensitivity and disease. In:
  Clinical Aspects of Immunology, 3<sup>rd</sup> edn. (ed. By P.G.H. Gell, R.R.A.

- Coombs, P.J. Lachmann), pp. 761–781. Blackwell Scientific Publications, London.
- Cox L (2014). Allergy Immunotherapy, American College of Allergy, Asthma & Immunology (ACAAI). <a href="https://acaai.org/allergies/">https://acaai.org/allergies/</a> allergytreatment/allergy-immunotherapy
- Cox L, Nelson H, Lockey R, Calabria C, Chacko T, Finegold I, Nelson M, Weber R, Bernstein DI, Blessing-Moore J, Khan DA, Lang DM, Nicklas RA, Oppenheimer J, Portnoy JM, Randolph C, Schuller DE, Spector SL, Tilles S and Wallace D (2011): Allergen immunotherapy: a practice parameter third update. J Allergy Clin Immunol; 127 (1 Suppl): S1-55.
- Cox LS, Larenas LD, Nolte H, Weldon D, Finegold I and Nelson HS (2006): J Allergy Clin Immunol, 117:1021–35.
- Creticos PS, Corren J and Feldweg AM (2019): Sublingual immunotherapy for allergic rhinoconjunctivitis and asthma. Literature review current through: Sep 2020. This topic last updated: May 21, 2019. https://www.uptodate.com/contents/sublingual-immunotherapy-for-allergic-rhinoconjunctivitis-and-asthma
- Creticos PS, Esch RE, Couroux P, Gentile D, D'Angelo P, Whitlow B, Alexander M and Coyne TC (2014): Randomized, double-blind, placebocontrolled trial of standardized ragweed sublingual-liquid immunotherapy for allergic rhinoconjunctivitis, J Allergy Clin Immunol; 133(3):751-8.
- D'Amato G, Liccardi G, D'Amato M and Cazzola M (2001): The role of outdoor air pollution and climatic changes on the rising trends in respiratory allergy. Respir Med; 95: 606–611.
- Dordal MT, Lluch-Bernal M, Sánchez MC, Rondón C, Navarro A,

- Montoro J, Matheu V, Ibáñez MD, Fernández-Parra B, Dávila I, Conde J, Antón E and Colás C and Valero A (2011): SEAIC Rhinoconjunctivitis Committee. Allergen-specific nasal provocation testing: review by the rhinoconjunctivitis committee of the Spanish Society of Allergy and Clinical Immunology. J Investig Allergol Clin Immunol; 21: 1–12.
- Durham S R, Yang W H, Pedersen M R, Johansen N and Rak S (2006): Sublingual immunotherapy with oncedaily grass allergen tablets: a randomized controlled trial in seasonal allergic rhinoconjunctivitis. J Allergy Clin Immunol; 117(4): 802.
- Edyta Krzych-Fałta, Konrad Furmańczyk, Diana Dziewa-Dawidczyk, Oksana Wojas, Katarzyna Retlewska, and Bolesław K. Samoliński 2019: The role of the nasal allergen provocation test in local allergic rhinitis cases: a preliminary report doi: 10.5114/ada.2019.84719
- Egan M and Atkins D (2018): What Is the Relationship Between Eosinophilic Esophagitis (EoE) and Aeroallergens? Implications for Allergen Immunotherapy. Curr Allergy Asthma Rep; 18(8): 43. doi: 10.1007/s11882-018-0798-2.
- Erbas B, Lowe AJ, Lodge CJ, Matheson MC, Hosking CS, Hill DJ, Vicendese D, Allen KJ, Abramson MJ and Dharmage SC (2013): Persistent pollen exposure during infancy is associated with increased risk of subsequent childhood asthma and hayfever. Clin Exp Allergy; 43:337–343.
- Frew AJ, Powell RJ, Corrigan CJ and Durham SR (2006): J Allergy Clin Immunol; 117: 319–25.
- Gelardi M, Iannuzzi L, Quaranta N, Landi M and Passalacqua G (2016): NASAL cytology: practical aspects

- and clinical relevance. Clin Exp Allergy; 46: 785–792.
- Hamilton RG (2010): Clinical laboratory assessment of immediate-type hypersensitivity. J Allergy Clin Immunol; 125: S284–S296.
- Heinzerling L, Mari A, Bergmann KC, Bresciani M, Burbach G, Darsow U and Lockey R (2013): The skin prick test, European standards. Clin Transl Allergy; 3(1): 3.doi 10.1186/2045-7022-3-3.
- Hoffmann HJ, Knol EF, Ferrer M, Mayorga L, Sabato V, Santos A F, Eberlein B, Nopp A and MacGlashan D (2016): Pros and cons of clinical basophil testing (BAT). Curr Allergy Asthma Rep; 16: 56.
- Husna S.M.N., Tan HT, Shukry NMd, Ashari MSM and WongKK (2022): A Clinical and Pathophysiological Overview. Front. Med., Pulmonary Medicine Volume 9 https://doi.org/10.3389/fimed.2022.87 4114
- J P M van der Valk, R Gerth van Wijk, E Hoorn, L Groenendijk, I M Groenendijk and N W de Jong (2016): Measurement and interpretation of skin prick test results, PMID: 26909142, PMCID: PMC4763448 , DOI: 10.1186/s13601-016-0092-0
- Javed Sheikh and Michael A Kaliner (2018): Allergic Rhinitis Treatment and Management, Medspace.
- Kleine-Tebbe J, Bufe A, Ebner C, Eigenmann P, Friedrichs F and Fuchs T. Die (2009): Spezifische Immuntherapie (Hyposensibilisierung) bei IgE-vermittelten allergischen Erkrankungen. Schweizerischen Gesellschaft für Allergologie und Immunologie (SGAI). Allergo J; 18: 508-37.

- **Liang A.** (2002): Skin testing in asthma and hay fever. DermNet NZNZFP, 29(6): 419 -421.
- Matricardi PM, Kleine-Tebbe J, Hoffmann HJ, Valenta R, Hilger C, Hofmaier S, Aalberse RC, Agache I, Asero R, Ballmer-Weber B, Barber D, Bever K, Biedermann T, Bilò MB, Blank S, Bohle B, Bosshard PP, H, **Brough Breiteneder** HA. Caraballo L, Caubet JC, Crameri R, Davies JM, Douladiris N, Ebisawa M, Eigenmann PA, Fernandez-Rivas M, Ferreira F, Gadermaier G, Glatz M, Hamilton RG, Hawranek T, Hellings P, Hoffmann-Sommergruber K, Jakob T, Jappe U, Jutel M, Kamath SD, Knol EF, Korosec P, Kuehn A, Lack G, Lopata AL, Mäkelä M, Morisset M, Niederberger V, Nowak-Wegrzyn AH, Papadopoulos NG, Pastorello EA, Pauli G, Platts-Mills T, Posa D, Poulsen LK, Raulf M, Sastre J, Scala Ε, Schmid JM. Schmid-Grendelmeier P, van Hage M, van Ree R, Vieths S, Weber R, Wickman M, Muraro A and Ollert M (2016): EAACI Molecular Allergology User's Guide, Pediatr Allergy Immunol; 27 Suppl 23:1-250. doi: 10.1111/pai.12563.
- Miehlke S, Alpan O, Schröder S and Straumann A (2013): Induction of eosinophilic esophagitis by sublingual pollen immunotherapy. Case Rep Gastroenterol; 7(3): 363-8. Epub 2013 Sep 3.
- Moller C, Bjorksten B, Nilsson G and Dreborg S (1984): The precision of the conjunctival provocation test. Allergy; 39: 37–41.
- Mustafa K Abdo Sultan, Randa S Abd EL-Lateef, Fatma Z Kamel (2019): Efficacy of Omega-3 Fatty Acids Supplementation versus Sublingual Immunotherapy in Patients with Bronchial Asthma, The Egyptian journal of immunology / Egyptian

Association Immunologists 26(1):79-89

of

- National Institute of Allergy and Infectious Diseases (NIAID) Immunotherapy for Environmental Allergies (2015): Archived from the original on 17 June 2015. Retrieved 19 June 2015. <a href="https://en.wikipedia.org/wiki/Allergic\_rhinitis#cite\_note-NIH2015Cause-3">https://en.wikipedia.org/wiki/Allergic\_rhinitis#cite\_note-NIH2015Cause-3</a>
- National Institute of Allergy and Infectious Diseases (NIAID) Immunotherapy for Environmental Allergies (2015): Archived from the original on 17 June 2015. Retrieved 19 June 2015. <a href="https://en.wikipedia.org/wiki/Allergic\_rhinitis#cite\_note-NIH2015Cause-3">https://en.wikipedia.org/wiki/Allergic\_rhinitis#cite\_note-NIH2015Cause-3</a>
- Nikakhlagh S, Rahim F, Aryani F H, Syahpoush A, Brougerdnya M G and Saki N (2011): Herbal treatment of allergic rhinitis: the use of Nigella sativa. Am J Otolaryngol; 32(5): 402-7.
- Passali D, Bellussi L, Passali GC and Passali FM (2002): Nasal immunotherapy is effective in the treatment of rhinitis due to mite allergy. A double-blind, placebocontrolled study with rhinological evaluation. Int J Immunopathol Pharmacol; 15: 141-7. 119:881-91.
- Paul Oykhman, Harold L Kim, and Anne K Ellis (2015): Allergen immunotherapy in pregnancy, Allergy Asthma Clin Immunol; 11: 31 Published online 2015 Nov 10. doi: 10.1186/s13223-015-0096-7.
- **Pawankar R** (2001): Mast cells as orchestrators of the allergic reaction: the IgE-IgE receptor mast cell network. Curr Opin Allergy Clin Immunol; 1:3–6.
- Pawankar R. (2014): Allergic diseases and asthma: global public health concern and a call to action. World Allergy Organ J. 7:12. DOI:10.1186/1939-4551-7-12

- Pfaar O, Klimek L, Jutel M, Akdis C A, Bousquet J, **Breiteneder** Chinthrajah S, Diamant Z, Eiwegger Fokkens WJ, Fritsch HW, Nadeau KC. O'Hehir RE, O'Mahony L, Rief W, Sampath V, Schedlowski M, Torres M, Traidl-Hoffmann C, Wang DY, Zhang L, Bonini M, Brehler R, Brough HA, Chivato T, Del Giacco S, Dramburg S, Gawlik R, Gelincik A, Hoffmann-Sommergruber K, Hox V, Knol E, Lauerma A, Matricardi PM, Mortz Ollert M. **Palomares** Riggioni C, Schwarze J, Skypala I, Untersmayr S, Walusiak-Skorupa J, Ansotegui I, Bachert C, Bedbrook A, Bosnic-Anticevich S, Brussino L, Canonica GW, Cardona Carreiro-Martins P, Cruz Czarlewski W, Fonseca JA, Gotua M, Haatela T, Ivancevich JC, Kuna Kvedariene V, Larenas-Ρ, Linnemann D, Latiff A, Morais-Almeida M, Mullol J, Naclerio R, Ohta K, Okamoto Y, Onorato GL, **Papadopoulos** NG, Patella Regateiro FS, Samolinski B, Suppli Ulrik C, Toppila-Salmi S, Valiulis A, Ventura MT, Yorgancioglu **Zuberbier T and Agache I (2020):** pandemic: practical COVID-19 considerations on the organization of an allergy clinic an EAACI/ARIA Position Paper. Allergy 2020. https://doi.org/10.1111/all.14453.
- Platts-Mills TA (2004): Allergen avoidance. J Allergy Clin Immunol; 113(3): 388-91.
- Powe DG, Groot Kormelink T, Sisson M, Blokhuis BJ, Kramer MF, Nicholas S, Jones NS and Redegeld FA (2010) Evidence for the involvement of free light chain immunoglobulins in allergic and nonallergic rhinitis. J Allergy Clin Immunol; 125:139–145.e3. doi: 10.1016/j. jaci. 2009.07.025. Epub 2009 Oct 8.

- Pynnonen MA, Mukerji SS, Kim HM, Adams ME and Terrell JE (2007): Nasal saline for chronic sinonasal symptoms: a randomized controlled trial. Arch Otolaryngol Head Neck Surg; 133(11): 1115–1120
- **Rajan TV** (2003): "The Gell-Coombs classification of hypersensitivity reactions: a re-interpretation". Trends Immunol; 24 (7): 376–9.
- Röder E, Berger MY, de Groot H and Gerth van Wijk R (2008): Sublingual immunotherapy in youngsters: adherence in a randomized clinical trial, Clin Exp Allergy; 38(10):1659-67. Epub 2008 Jul 02.
- Rondon C, Bogas G, Barrionuevo E, Blanca M, Torres MJ and Campo P. (2017): Nonallergic rhinitis and lower airway disease. Allergy; 72:24–34.
- Rondon C, Dona I, Lopez S, Campo P, Romero JJ, Torres MJ, Mayorga C and Blanca M (2008): Seasonal idiopathic rhinitis with local inflammatory response and specific IgE in absence of systemic response; 63:1352–1358. doi: 10.1111/j.1398-9995.2008.01695.x
- Rosner-Friese K, Kaul S, Vieths S and Pfaar O (2015): Environmental exposure chambers in allergen immunotherapy trials: current status and clinical validation needs. J Allergy Clin Immunol; 135: 636–643.
- Ryan D, Van Weel C, Bousquet J, Toskala E, Ahlstedt S, Palkonen S, Van Den Nieuwenhof L, Zuberbier T, Wickman M and Fokkens W (2008): Primary care: the cornerstone of diagnosis of allergic rhinitis. Allergy Volume 63, Issue 8. <a href="https://doi.org/10.1111/j.1398-9995.2008.01653.x">https://doi.org/10.1111/j.1398-9995.2008.01653.x</a>
- Scadding G K, Durham S R and Mirakian R (2008): British Society for Allergy and Clinical Immunology. BSACI guidelines for the management of allergic and non-allergic

- rhinitis. Clin Exp Allergy; 38(1):19–42.
- Schlundt Jorgen (2012): Health and Nutritional Properties of Probiotics in Food including Powder Milk with live lactic acid bacteria ". report of a Joint FAO/WHO Experts.
- MD, Gurgel RK. Lin Seidman SY, Schwartz SR, Baroody FM, Bonner JR, Dawson DE, Dykewicz MS, Hackell JM, Han JK, Ishman SL, Krouse HJ, Malekzadeh S, Mims JW, Omole FS, Reddy WD, Wallace DV, Walsh SA, Warren BE, Wilson MN and Nnacheta LC (2015): Clinical practice guideline: allergic rhinitis. Otolaryngol Head Neck Surg; 152: S1-S43. doi: 10.1177/0194599814561600.
- Self, Timothy, Chrisman Cary and Finch Christopher (2009): 22 Asthma. In Mary Anne Koda –Kimble, Brian K Alldredg. Applied therapeutics: the clinical use of drugs (9<sup>th</sup> ed.). Philadelphia: Lippincott Williams & Wilkins.
- Thomsen SF, Ulrik CS, Kyvik KO, Hjelmborg JVB, Skadhauge LR, Steffensen I and Backer V (2006): Genetic and environmental contributions to hay fever among young adult twins. Respir Med; 100:2177–2182.\_doi: 10.1016/j.rmed .2006. 03. 013. Epub 2006 May 2.
- Wahn U, Klimek L, Ploszczuk A, Adelt T, Sandner B, Trebas-Pietras E and Eberle P and Bufe A (2012): High-dose sublingual immunotherapy with single-dose aqueous grass pollen extract in children is effective and safe: a double-blind, placebo-controlled study. J Allergy Clin Immunol; 130(4):886-93.e5.
- Wheatley LM and Togias A (2015): Clinical practice. Allergic rhinitis". The New England Journal of Medicine; 372 (5): 456–63.doi: 10.105

- 6 /NEJMcp 1412282.PMC 4324099. PMID 256 29743.
- Yang HJ (2016): Impact of perinatal environmental tobacco smoke on the development of childhood allergic diseases. Korean J Pediatr; 59: 319–327.
- Yukselen A, Kendirli S G, Yilmaz M, Altintas D U and Karakoc G B

(2012): Effect of one-year sublingual subcutaneous and clinical and immunotherapy on laboratory parameters in children with rhinitis and asthma: a randomized, placebo-controlled, double-blind, double-dummy study Int Arch Allergy Immunol; 157(3): 288-98.