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Assessment of Allergic Rhinitis from Medical Microbiology Background: Review Article

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ABSTRACT

Background: Sneezing, postnasal drip, nasal pruritis, and nasal congestion are all signs of allergic rhinitis (AR), an atopic condition. It affects one in six people and is linked to high morbidity, severe productivity loss, and high healthcare expenses. In the past, AR was believed to be a nasal airway-specific disease. However, the emergence of the unified airway hypothesis has identified the atopic dermatitis (AD) and other related disorders, such as asthma, as components of systemic allergic reaction.

Objective: Review of literature about assessment of Allergic Rhinitis from Medical Microbiology Background

Methods: We searched PubMed, Google Scholar, and Science Direct for relevant articles on allergic rhinitis and medical microbiology background. However, only the most recent or thorough studies were taken into account between February 2001 and May 2023. The authors also evaluated the value of resources culled from other works in the same genre. Therefore, documents written in languages other than English have been ignored due to a lack of translation funds. Unpublished works, oral presentations, conference abstracts, and dissertations were generally agreed upon not to qualify as scientific research.

Conclusion: Due to changes in the immune system, AR is an IgE-mediated illness that develops in genetically vulnerable people after exposure to environmental allergens. The majority of the common allergens linked to AR are proteins and glycoproteins present in airborne particles. As a result of the inhalation of allergen particles, the nasal epithelium becomes coated, allowing soluble allergenic proteins to elute and diffuse into the nasal mucosa. Numerous aeroallergens enhance allergen entry to antigen presentating cells (APCs) during the early sensitization process. In AR tight junctions in the airway epithelium are cleaved and epithelial cells are activated thanks to the protease activities of these proteins. Skin prick testing is used to confirm an AR diagnosis alongside a patient's history and a physical exam.

Keywords: Allergic rhinitis, Medical microbiology.

INTRODUCTION

Sneezing, postnasal drip, nasal pruritis, and nasal congestion are all signs of allergic rhinitis (AR), an atopic condition. It affects one in six people and is linked to high morbidity, severe productivity loss, and high healthcare expenses. In the past, AR was believed to be a nasal airway-specific disease. However, the emergence of the unified airway hypothesis has identified the atopic dermatitis (AD) and other related disorders, such as asthma, as components of systemic allergic reaction **(1).**

Approximately 20% of cases of AR are characterized as seasonal (intermittent), 40% as perennial (chronic), and 40% as having characteristics of both. Patients with AR may also experience concomitant allergic conjunctivitis, a dry cough, eustachian tube dysfunction, and chronic sinusitis in addition to nasal symptoms. Once diagnosed, AR can be treated using a number of techniques, with intra-nasal glucocorticoids serving as the primary treatment **(2).**

Epidemiology:

According to doctor diagnoses, the prevalence of allergic rhinitis is around 15%, however the prevalence is thought to be as high as 30% based on individuals who have nasal symptoms. The known peak for AR occurs between the second and fourth decade of life, after which it gradually declines. One of the most prevalent chronic pediatric illnesses is AR, which has a significant incidence in the population of children **(3).**

According to the International Study of Asthma and Allergies in Childhood, allergic rhinitis causes symptoms of rhinoconjunctivitis in 8.5% of children aged 6-7 years and 14.6% of children aged 13-14 years. Children may be more susceptible to seasonal allergic rhinitis, but adults are more likely to suffer from chronic rhinitis **(2).**

Immunopathogenesis:

1- Sensitization to allergens:

Due to changes in the immune system, AR is an IgE-mediated illness that is triggered by exposure to environmental allergens in persons who are genetically predisposed to acquire the condition. The majority of the common allergens linked to AR are proteins and glycoproteins present in airborne particles. As a result of the inhalation of allergen particles, the nasal epithelium becomes coated, allowing soluble allergenic proteins to elute and diffuse into the nasal mucosa **(4).**

Epithelial cytokines (TSLP, IL-33, and IL-25) have been shown to be crucial for activating T-cell-receptor- and T-cell-lineage marker-negative ILC2s **(5).** Allergens are taken up by antigen-presenting cells (APCs) like dendritic cells (DCs) (expressing CD1a, CD11c) and macrophages, which then develop and travel to the draining lymph nodes, where they offer the allergen to

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immature T cells, skewing their development toward Th2 differentiation [4].

It has been demonstrated that ILC2s can also regulate and prepare Th2 cells from naïve T cells by generating IL-13, which is necessary for the operation of dendritic cells into lymph nodes [6]. Th2 cells are sustained by IL-4, which is produced by allergen-stimulated Th2 cells. Along with IL-4, IL-13 and CD40 ligand (CD40L) are also produced by Th2 cells, which together with IL4 promote IgE production and heavy-chain class switching in B lymphocytes. The high-affinity receptor (FcRI) on mast cells, basophils, and APCs is where IgE binds to sensitise these cells to allergens [4].

2-Immediate (Early) phase reactions (Mast cells activation):

Sneezing and itching are the first symptoms triggered by an allergen challenge in IgE-sensitized individuals, followed by rhinorrhea and nasal blockage. Sensitized IgE cross-links FcRI complexes on the surface of mast cells and basophils, triggering this reaction. This results in membrane lipid de novo synthesis of mediators including cysteinyl leukotrienes (leukotrienes C4, D4, and E4) and prostaglandins D2 in addition to degranulation and release of pre-existing mediators like histamine and tryptase [7].

Histamine causes a systemic reaction, such as an outbreak of sneezing, when it works on sensory nerve endings to cause itching, a common symptom of AR [8]. Tryptase and histamine levels in nasal fluid have been shown to peak after 5 minutes, showing that following allergen contact, surface activation markers such as CD63 are first expressed on circulating basophils, and then local mast cells become activated [4].

Late phase of allergen-induced airway inflammation:

Nasal blockage and watery discharge rank among the most prominent late-phase symptoms. Individuals who are allergic will display a late-phase nasal allergy response, depending on the patient's susceptibility and the allergen dose. Continuous symptoms and a decrease in peak nose inspiratory flow commonly characterise the 4–12-hour latency period of nasal late reactions that diverge to the lung. Various inflammatory cells are activated by mediators produced during the early phase response, causing the symptoms of the late phase reaction [9].

Adhesion molecules including VCAM-1, E-selectin, and ICAM-1 enable circulating eosinophils to attach to endothelial cells and migrate to the nasal mucosa, where they can cause inflammation [10]. It has been demonstrated that in AR patients, circulating ILC2s rise after nasal allergen elicitation and after allergen exposure. Along with mast cells, basophils, and T cells, ILC2s are another kind of cell that can produce Th2 cytokines and may play a role in the maintenance of the nasal allergy inflammatory response [11].

Immunohistochemistry analysis of nasal turbinate biopsies taken from an AR patient six hours after an allergen challenge showed an increase in eosinophil infiltration, cell counts that expressed mRNA for IL-4 and IL-5, and expression of the lymphocyte chemokine receptors CCR3 and CCR4 [12].

The release of eosinophil peroxidase, major basic protein, and eosinophil cationic protein occurs upon eosinophil activation. Important factors in this process are IL-4 and IL-5. The respiratory epithelium is vulnerable to them because they promote oxidative stress, a recognized epithelial-damaging agent. To counteract the prolonged late-phase reactions and consequent allergic inflammation, epithelial cells release chemokines, cytokines, and growth factors [9].

Both IL-13 and IL-4 utilize the same receptor subunit, the IL-4R chain, for a variety of purposes. Mast cells, basophils, and ILC2s produce IL-13, which stimulates B cells to switch to IgE synthesis [3].

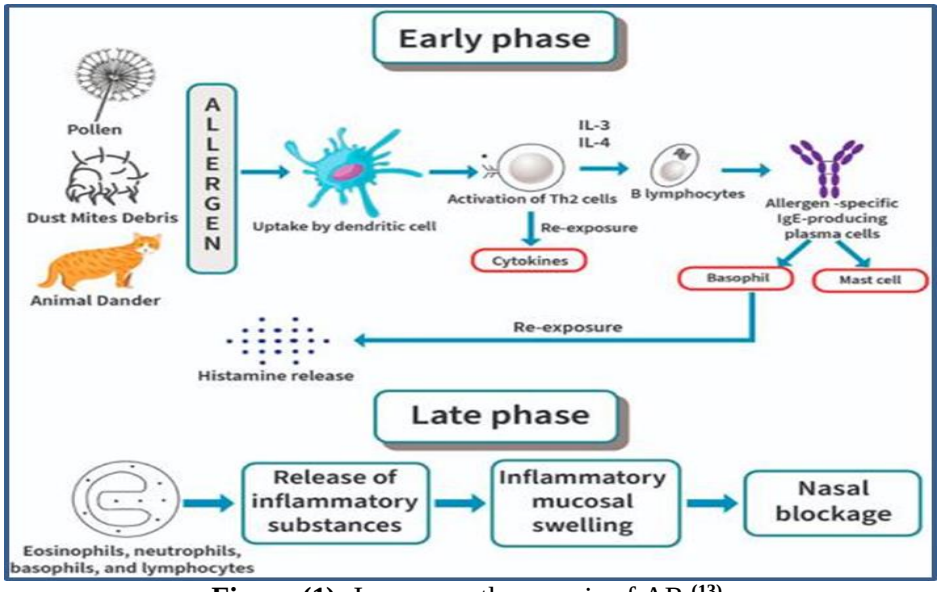


Figure (1): Immunopathogenesis of AR [13].

Diagnosis of Allergic Rhinitis

History and clinical characterization:

An important step in evaluating AR is taking a thorough, detailed history. During this process, questions should be directed toward identifying the symptoms, types, timing, duration, and frequency as well as any suspected exposures and contributing factors. Sneezing, rhinorrhea, and watery eyes are common symptoms in individuals with intermittent or seasonal AR, whereas postnasal drip, persistent nasal congestion, and obstruction are common symptoms in patients with chronic AR [(14)].

Symptoms:

Rhinorrhea: Clear secretions, bilateral is common and the infection indicated by green or yellow color [(15)].

Nasal obstruction: Partial or complete and bilateral blockage, which is either allergic rhinitis or nasal polyps to be differentiated [(16)].

Nasal crusting: Mild to moderate crusting. Sever crusting is an uncommon AR sign [(17)].

Ozena: The wasting away of the mucous membranes and bone ridges inside the nose, is another symptom of AR [(18)].

Eye symptoms: Include severe itching, conjunctival redness and swelling, and in severe cases, periorbital oedema [(18)].

Lower respiratory tract symptoms: Since bronchial hyperresponsiveness can be caused by upper airway allergies and inflammation, coughing and shortness of breath may occur with AR [(19)].

Other symptoms: Pollen-food syndrome, which is exacerbated by eating certain fruits, vegetables, and nuts that contain cross-reacting antigens, snoring, sneezing, nasal voice tone, and sleep problems [(20)].

Complications:

Although different from allergic rhinitis, chronic rhino-sinusitis can be a side effect of AR. It is characterized by nasal irritation and nasal discharge or congestion that lasts for more than three months. Nasal polyps (nasal polyposis), which develop as a result of persistent inflammation of the paranasal sinus mucosa, can also be found in chronic rhino-sinusitis [(21)].

It is also known that sensitivity to allergens in AR might change the immunological characteristics of the adenoids, leading to adenoid hypertrophy. Eustachian tube dysfunction frequently shows up in AR patients as ear fullness, otalgia, and ear-popping. Asthma is present in 10 to 40% of AR patients, and some studies indicate that moderate to severe persistent rhinitis patients are more likely to have asthma than other persistent rhinitis patients [(1)].

Symptom score of allergic rhinitis:

The Total Nasal Symptom Score (TNSS) is a quick questionnaire used to measure the severity of the most prominent symptoms of allergic rhinitis. Congestion, sneezing, itchy nose, and a runny nose are all measured on a four-point scale from 0 to 3, and the total score at each time point is the rhinorrhea score [(22)].

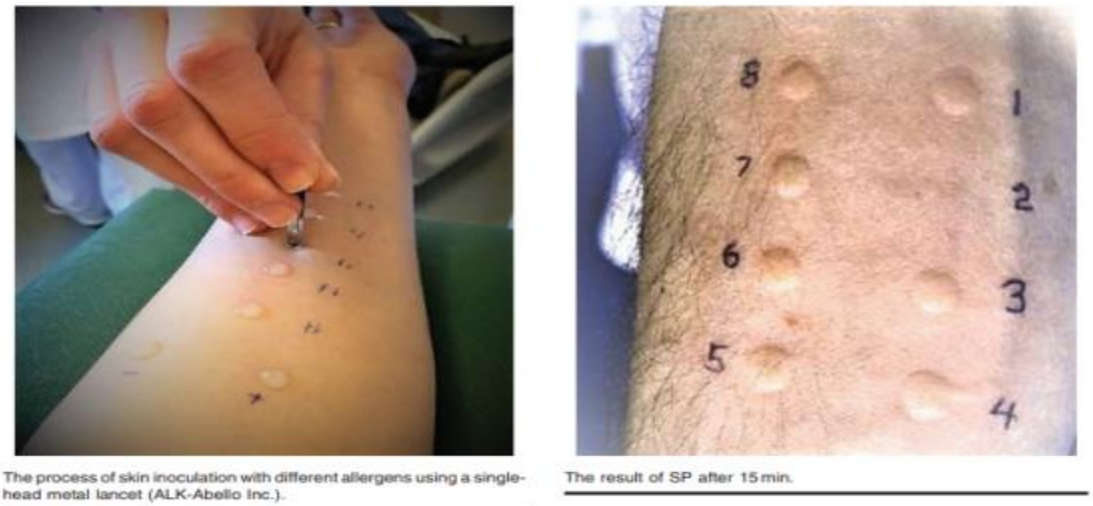
The total number of symptoms that make up the TNSS ranges from 0 (no symptoms) to 12 (very severe symptoms) (maximum symptom intensity) [(23)].

Laboratory investigations:

1- Skin testing:

Skin-prick testing (SPT):

In addition to a history and physical examination, skin prick testing is utilized to confirm an AR diagnosis. Confirmation of atopy directs preventative actions, appropriate pharmaceutical treatment, and allergen immunotherapy (AIT). When an antigen is introduced to an atopic patient's skin, the antigen causes the cutaneous mast cells and IgE antibodies to cross-link, causing the mast cells to degranulate and release histamine, which causes wheals to form within 15 to 20 minutes [(24)].



The process of skin inoculation with different allergens using a single-head metal lancet (ALK-Abello Inc.).

The result of SP after 15 min.

Figure (2): Skin prick test [(25)].

In allergic patients, skin testing is not always appropriate. Contraindications to SPT include uncontrolled asthma, unstable cardiovascular illness, the use of contemporary beta blocker treatment, and pregnancy [25].

Indications for the prick test [26]:

- Lack of response to food elimination or challenge for a suspected food allergy (such as egg, peanut, wheat, seafood, soy, or cow's milk).
- Those who suffer from poorly controlled or recurring allergic rhinitis, rhinosinusitis, eczema, or bronchial asthma may find relief from their symptoms by learning to recognize and avoid their triggers. These allergens include animal dander, pollen, cockroaches, and house dust mites.
- Suspected or known allergy to a medication, such as penicillin.

Precautions and contraindications for the prick test [26]:

- In order to prevent wheal dampening, patients who are using oral antihistamines or antidepressants must postpone their medications for 3 days for first-generation and 10 days for second-generation antihistamines before to the test.
- Stop using topical steroids at the test site two to three weeks before the test since they could taint the results. Oral or inhaled steroids, however, may still be used because doing so has no impact on the outcomes.
- In individuals who had anaphylaxis four to six weeks before to the test, the skin prick test is not recommended.
- Because skin responsiveness decreases with age, the prick test may not be accurate in elderly patients. An alternative would be serum IgE testing.
- For kids younger than 2 years, it is advisable to postpone the finger-prick test.
- Anaphylaxis during the test is a remote possibility. Therefore, testing should be carried out in areas with access to medical personnel and emergency resuscitation facilities [26].

Intradermal skin test (IDST):

Method: Using a 27-gauge hypodermic needle, IDST was carried out by injecting 0.02 mL of antigens into the outside of the right upper arm. The diluent solution (phenol-saline solution) and the histamine (0.17 mg/mL histamine dihydrochloride) from allergopharma served as the negative and positive controls, respectively. The reactions were assessed 15 minutes after injection, and measurements of the wheal and erythema diameters were taken. A positive test result was defined as 3 mm or more above the negative control. Although this test is highly reproducible, it is challenging to be administered to young children and involves a higher risk of negative outcomes than the SPT [25].

Contraindications for IDST include [24]:

- Eczema, hives, and dermographism are examples of widespread skin disorders.
- Very little help from the subject.
- Inability to discontinue antihistamines or other interfering medications.
- Insufficiently defining "food allergy".
- Asthma that persists or fluctuates.
- Younger children or infants.

In vitro testing [27]:

a) Serum total IgE (tIgE)

There is some disagreement over the role of serum tIgE in the diagnosis of atopic disorders. The capacity of the tIgE serum level to identify patients with atopy in general may be what makes it so significant**.** In AR patients, a serum tIgE level more than 140 IU/mL may be indicative of atopy. In the absence of a positive inhalant-specific IgE test, a high tIgE may indicate inhalant sensitivity to unknown allergens or another kind of chronic respiratory inflammatory illness other than AR [27].

b) Serum antigen-specific IgE (sIgE)

In 1967, a test for serum antigen-specific IgE that used a radioactive anti-IgE assay to identify the serum-bound IgE became commercially accessible [28]. It is useful in choosing candidates for AIT and is effective at identifying allergic patients. It may also correlate with the severity of AR symptoms. Due to the high probability of false positive findings when a proper clinical history is not taken, this test alone cannot offer a conclusive diagnosis of allergy [25].

Indications for serum IgE testing: There is either no skin prick test series that includes the allergen of concern, or no skin prick test itself. Due to the patient's severe dermographism or dermatitis, a positive skin prick test may be misinterpreted. The patient cannot stop using oral antihistamines. Despite a history that may point to an allergy, skin prick testing is negative, and anaphylaxis to any allergen has occurred in the past [26].

c) Nasal specific IgE

Some patients have a negative SPT or serum sIgE result despite a clinical history suggestive of AR. These patients frequently are diagnosed with idiopathic or vasomotor rhinitis. These patients have also demonstrated signs of local allergic rhinitis (LAR), a form of rhinitis characterized by the presence of a localized allergic response in the nasal mucosa, including local production of sIgE and a positive nasal provocation test (NPT) in the absence of a positive skin prick test (SPT) or an elevation of serum sIgE. Over 45% of those with AR may also have LAR. The detection of nasal sIgE can be accomplished by a variety of techniques, including nasal lavage, cellulose discs, mucosal biopsy, brushing, and others [29].

d) Nasal challenge

The nasal provocation test is designed to stimulate an allergic reaction in the upper airway. The allergen can be administered using a variety of methods, including syringes, nose droppers, micropipettes, nasal sprays, impregnated discs, and nasal sprays. However, these all have substantial limitations [30]. Total nasal symptom score (TNSS), rhinomanometry, acoustic rhinometry, optical rhinometry, peak nasal inspiratory flow, and nasal inflammatory markers are all useful ways to measure the success of a nasal challenge [31, 32].

Others

- ***Radiology:***

Although it could be used to rule out other possibilities, it is not advised for use in establishing a diagnosis of AR (i.e., rhinosinusitis) [18].

- ***Nasal cytology (NC) and histology:***

It is a simple diagnostic method to assess nasal mucosa health by detecting and counting the cells. [33]. The May Grunwald Giemsa process is used to stain a sample of nasal mucosal surface, allowing for the detection of inflammatory cells such as neutrophils, eosinophils, lymphocytes, and mast cells in addition to normal cells, bacteria, and fungus. The following step is an in-depth investigation under the microscope [33].

Different types of rhinitis, such as allergic rhinitis (AR), non-allergic rhinitis (NAR), idiopathic rhinitis, and overlapping forms, can be distinguished by the precise cytological arrangements on NC [25].

CONCLUSION

Due to changes in the immune system, AR is an IgE-mediated illness that develops in genetically vulnerable people after exposure to environmental allergens. The majority of the common allergens linked to AR are proteins and glycoproteins present in airborne particles. As a result of the inhalation of allergen particles, the nasal epithelium becomes coated, allowing soluble allergenic proteins to elute and diffuse into the nasal mucosa. Numerous aeroallergens enhance allergen entry to antigen presentating cells (APCs) during the early sensitization process. In AR, tight junctions in the airway epithelium are cleaved and epithelial cells are activated thanks to the protease activities of these proteins. Skin prick testing is used to confirm an AR diagnosis alongside a patient's history and a physical exam.

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