

ASSOCIATION NOTE SUPPLEMENT**Role of Antihistamine in Allergic Disorders : A Review and Consensus Statements by Indian Medical Association****Agam Vora¹, Amit Madan², Gautam Modi³, Jayesh Lele⁴, Ketan Mehta⁵, Meena Wankhedkar⁶, Parul Vadgama⁷, Pradyut Waghray⁸, R V Asokan⁹, Sitesh Roy¹⁰, Sushil Makharia¹¹**

Background : 20-30% of the Indian population suffers from at least one allergic disease that can have an adverse impact on the quality of life of the patients.

Aim : To develop expert opinion-related guidance for the diagnosis and management of allergic disorders.

Methodology : An advisory board meeting (hybrid mode) was conducted with 11 panel members of the Indian Medical Association (IMA). The panel members discussed issues related to the management of allergic disorders based on the Delphi method.

Result : Spirometry is helpful in selected patients of allergic rhinitis where the coexistence of asthma is suspected. In patients with urticaria second-generation antihistamines are preferred for both adults and children due to their low side effects, less drug-drug interaction, anticholinergic effects, longer duration of action, and higher safety. Diagnosis of allergic contact dermatitis can be made based on occupational and exposure history. In atopic dermatitis, patient education about lifestyle changes can prevent flare-ups. In patients with asthma, patients must be educated about the use of the peak flow meter. The diagnosis of food allergy can be made by correlating the food intake timing with the patient history and the results of allergy testing. Allergic drug reactions can be treated with oral antihistaminic drugs, emollients, and if needed topical corticosteroids.

Conclusion : The diagnosis of allergic disorders requires the clinician to consider the clinical presentation, patient history, presence of triggers, and comorbid conditions. Patient education and the new generation of antihistaminic drugs can improve the quality of life of patients with allergic disorders.

[J Indian Med Assoc 2023; 121(3): 74-8]

Key words : Cough, Diagnosis, Fixed-dose combinations, Management, Pediatric.

Allergies are chronic, inflammatory disorders with aberrant immune reactions to certain environmental allergens. Atopy is a genetic predisposition to diseases in which immunoglobulin (IgE) antibodies are produced in response to even minor exposure to environmental triggers that do not bother most people. Therefore, every atopic reaction is an allergy. According to the site of contact with the allergen, different clinical manifestations may develop in the airways, skin, or gastrointestinal tract.¹ 20-30% of the Indian population suffers from at least one allergic disease².

Methodology :

An advisory board meeting (hybrid mode) was

conducted on 13th Oct 2022 amongst 11 panel members. The Indian Medical Association (IMA) recommended panel members included Chest Physicians, Consulting Physicians, General Practitioners, ENT, Dermatologists, and Allergologists, who discussed issues related to the stepwise management of allergy. A draft document consisting of the topics of discussion and questions was shared with the panel members. The Delphi method was opted for consensus development. Post-meeting, the manuscript was shared with the panel members for final review and approval.

Pathogenesis of Allergic Disorders :

During an allergic reaction, the immune system is

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activated when it detects allergic stimuli. The T cells and B cells are sensitized to the allergens in response to the first exposure to the allergen and can then identify specific sections of antigens, which are termed epitopes. On subsequent exposure to the allergens, a robust immune response is generated. Large amounts of IgE are released by B cells. Effector cells release cytokines and inflammatory mediators involving histamine, tryptase, leukotrienes, serotonin, etc, prolonging the pro-inflammatory response¹ (Fig 1).

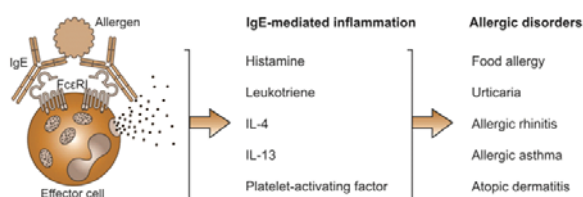


Fig 1 — Pathogenesis of allergic disorders⁴

Adapted from: Zellweger F, Eggel A — IgE-associated allergic disorders: recent advances in etiology, diagnosis, and treatment. *Allergy* 2016; **71**(12): 1652-61.

Histamine is an important effector chemical released during an allergic reaction. Histamine release results in vasodilatation, increased vascular permeability, itching, smooth muscle contraction, and coronary spasm³.

Role of Antihistamines in Allergic Disorders :

By blocking histamine, antihistamines reduce symptoms such as itching, redness, and swelling that occur in response to allergens. The first-generation antihistamines have poor H1 receptor selectivity, anti-muscarinic, anti- α adrenergic, and anti-serotonergic effects. This non-selective action at other receptors results in drowsiness, sedation, and somnolence as a consequence of crossing the blood-brain barrier. The second-generation H1-antihistamines cross the blood-brain barrier significantly less than the first-generation antihistaminic drugs which enhances their safety profile³.

IMA Consensus on Role of Antihistaminic Drugs

In —

Allergic Rhinitis (AR) :

AR is characterized by nasal congestion, clear rhinorrhea, sneezing, postnasal drip and nasal pruritus⁵. Treatment includes avoidance of allergens, drugs such as antihistamines, intranasal steroids, and Leukotriene Receptor Antagonists (LTRAs). Allergen-specific immunotherapy is prescribed in non-responders⁶.

Second-generation antihistamines (like bilastine, levocetirizine, and cetirizine) are less sedating than older agents and are the preferred first-line treatment

option due to their relatively rapid onset of action. Antihistamines can be used on an as-needed basis⁷.

Urticaria :

Urticaria is characterized by erythematous, edematous, itchy, and transient urticarial plaques (hives), covering the skin and mucous membranes. Treatment consists of avoidance of the drug, or food implicated. Patients are advised to avoid stress, alcohol and improve sleep. For relief of symptoms, second-generation agents such as levocetirizine, bilastine, and loratadine are preferred for both adults and children due to their low side effects, less drug-drug interaction, anticholinergic effects, longer duration of action, and higher safety⁸.

Allergic Contact Dermatitis (ACD) :

Contact dermatitis is a common inflammatory skin condition characterized by erythematous and pruritic skin lesions after contact with a foreign substance⁹. The definitive treatment of ACD is the identification and removal of the offending agent¹⁰. Cool compresses can soothe the symptoms of acute contact dermatitis⁹.

Calamine lotion and colloidal oatmeal baths may help dry and soothe acute, oozing lesions. (Usatine RP) Symptomatic management includes oral antihistamines and topical hydrocortisone. If ACD involves a delicate area such as skin folds or eyelids, topical calcineurin inhibitors or PDE4 inhibitors may also be effective¹⁰.

In severe cases, topical immunomodulators and immunosuppressive agents may be required. Some patients respond to phototherapy using UV-A plus psoralen¹⁰.

Antihistamines such as hydroxyzine and cetirizine are recommended to control pruritus associated with allergic contact dermatitis^{9,11}.

Atopic Dermatitis (AD) :

AD (atopic eczema) is a chronic, pruritic inflammatory skin disease, with a relapsing course, often seen in children but can also occur in adults¹².

Treatments for atopic dermatitis include topical treatments (moisturizers, corticosteroids, calcineurin inhibitors, antimicrobial ointments), phototherapy, systemic medications (antihistamines, antibiotics, immunosuppressants), and lifestyle changes (moist skin, avoiding triggers, reducing stress)¹³.

Second-generation antihistamines, may be an appropriate treatment modality for managing itch and sleep disturbance in patients with AD¹⁴.

Asthma :

Asthma is an episodic reversible chronic airway

inflammation that is triggered by the common cold, allergens, cold weather, irritants, smoke, etc^{15,16}.

To achieve and maintain symptom control, a stepwise approach is recommended. Antihistamines are not considered a first line of treatment for asthma, but they can help reduce allergy symptoms and improve asthma control by blocking histamine and exhibiting anti-inflammatory effects. Antihistamines have bronchodilatory effects, reduce allergen-induced airway hyper-responsiveness, and delay or prevent the development of asthma in some children.

Leukotriene Receptor Antagonists (LTRAs), such as montelukast, have benefits for patients with exercise-induced asthma and can improve lower airway disease and congestion. LTRAs can be used as monotherapy or in combination with antihistamines or intranasal corticosteroids. The combination of montelukast and an oral antihistamine has been shown to have synergistic effects and is more effective than either drug alone.¹⁷

Oral H1 antihistamines can be recommended for asthma patients with concurrent Allergic Rhinitis (AR) or significant allergic triggers¹⁸.

Food allergy :

Food allergy is an adverse immunologic response to a specific food/food component that can be reproduced on exposure to a given food. It must be distinguished from food intolerance, which is a non-immune reaction. According to the EAACI treatment guidelines, first-line medication for the treatment of anaphylaxis is an intramuscular epinephrine injection which could be repeated within 10 minutes if indicated, second-line are inhaled β_2 agonists for wheezing and inhaled adrenaline for stridor, and third-line are H1 antihistamines, H2 antihistamines, and glucocorticoids¹⁹.

Drug Allergy :

Drug allergy comprises a spectrum of immunologically-mediated hypersensitivity reactions with diverse mechanisms and clinical presentations ranging from mild to severe and even death²⁰.

Treatment for drug allergy varies based on severity and may include discontinuing the drug, antihistamines, corticosteroids, epinephrine for severe reactions, and hospitalization in extreme cases. Allergic drug reactions such as rash, eczematous reactions eruptions, hives, and itching can be treated with oral antihistaminic drugs and emollients, and if needed topical corticosteroids²¹.

Anaphylaxis :

Anaphylaxis is a sudden-onset life-threatening

systemic hypersensitivity reaction, which is considered to be the most severe manifestation of allergy.

For treatment, the key advice is to strictly avoid any known triggering allergens as far as possible. An antihistamine tablet or syrup can be very effective for a mild allergic reaction involving only the skin or upper respiratory system. If the reaction becomes systemic (2 or more systems involvement) and/or life-threatening, then the use of adrenaline/epinephrine injection immediately can be life-saving. Antihistamines, steroids, and bronchodilators can be used subsequently after the adrenaline has been administered²².

Other IMA recommendations for managing allergic disorders —

Allergic Rhinitis :

1. Ask whether symptoms were present in childhood and the type of discharge.
2. Look for key symptoms and signs of rhinitis such as:
 - a) Nasal blockage, nasal crusting
 - b) Sneezing and itching
 - c) Dennie-Morgan folds
 - d) Allergic shiners
 - e) Coexistence of allergic conjunctivitis with AR
3. Perform a peak flow meter test for early diagnosis of asthma and spirometry in selected patients where the coexistence of asthma is suspected.
4. Carry skin prick tests routinely to determine if rhinitis is allergic or non-allergic.
5. Perform serum total and specific IgE tests if skin prick tests are not possible, or when a skin prick test together with the clinical history gives equivocal or conflicting results.
6. Laboratory investigations are usually unnecessary.
7. AR treatment encompasses three distinct aspects:
 - a) Avoidance of allergen exposure
 - b) Pharmacotherapy
 - c) Allergen-specific immunotherapy

Urticaria :

1. Diagnosis is based on clinical appearance and the time course of events that led to urticaria.
2. Search for possible underlying causes and/or relevant triggers in patients presenting with relapsing symptoms.
3. Be aware of urticaria after COVID infections.

Allergic contact dermatitis :

1. Diagnosis can be based on the history of :
 - a. Exposure to chemicals, allergic substances, and physical examination findings
 - b. Occupation, hobbies, medications, lifestyle, use of fragrances, and perfumes

2. Definitive treatment is the identification and removal of the offending agent.
3. Educating patients and helping them in identifying their allergic triggers.

Atopic Dermatitis :

1. Patient education about lifestyle changes prevents flare-ups.
2. Ask the patient to bathe with warm water, NOT hot water.
3. Apply a moisturizer at least twice a day.
4. Keep fingernails short to avoid damage to the skin due to scratching.
5. Atopic dermatitis is a clinical diagnosis with no definitive laboratory test.

Asthma :

1. During history taking, ask whether the patient had AR in childhood.
2. Ask about nocturnal or early morning attacks of wheezing and coughing, especially in children.
3. Look for symptoms and signs of AR.
4. If testing for bronchodilatory variability, stop:
 - a. Short-acting β -agonists (e.g., salbutamol) 4 hours before the test
 - b. Long-acting β -agonist 24 hours before the test
 - c. Ultra LABA 36 hours before the test
5. If a spirometry facility is not available, a peak flow meter can be used to measure diurnal variation >20% performed over a span of 2 weeks.
6. Educate the patient about the use of the peak flow meter and, based on the reading treat the patient.
7. Factors to consider during treatment:
 - a) Avoidance of allergens
 - b) Asthma severity
 - c) Drug choice
 - d) Route of drug administration
 - e) Inhaler technique
 - f) Medications adherence
 - g) Modifiable risk factors
 - h) Presence of co-morbidities
8. Patient education about asthma, trigger avoidance, use of peak flow meter, and the proper use of inhalers are important.

Food Allergy :

1. Correlate the food intake timing with patient history and the results of allergy testing.
2. Advise to strictly avoid anything that contains even a minuscule amount of food allergens.
3. Avoid cross-contact by thoroughly cleaning utensils, cookware, glassware, and storage containers.
4. Washing food storage containers and dishes in a dishwasher or hand washing with hot water and liquid

dish soap to remove food allergens.

Drug Allergy :

1. Ask the patient for drug intake history.
2. Allergic drug reactions can be treated with oral antihistaminic drugs, emollients, and if needed topical corticosteroids.
3. The physician must be well versed in the management of life-threatening anaphylaxis, as it is a medical emergency, and immediate initiation of treatment can be lifesaving.
4. Patient education about drug allergy is important:
 - a. Avoid drugs that the patient is allergic to.
 - b. Consult the doctor before taking drugs.
 - c. In case of severe drug reaction, rush for emergency care.
 - d. Carry a card mentioning the drugs he/she is allergic to.

Anaphylaxis :

1. The key advice is to strictly avoid any known triggering allergens as far as possible.
2. A standard needle (25 mm i.e., 1 inch and 23 G) should be used to inject intramuscular adrenaline.
3. Someone suffering from acute anaphylaxis is also likely to be showing signs of clinical shock. If the patient is not having difficulty breathing, but is feeling sick, dizzy, and could be going into shock – they should lie down with their legs raised to help increase the circulation to their vital organs.
4. Reassuring the casualty and positioning them appropriately can make a major difference in their treatment.
5. Patient should also be kept warm and dry.

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