



Allergic Disorders:
*Simplify Allergic Management
in India*

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Message From President and Hon. Secretary-General

Indian Medical Association (IMA), a national voluntary organization of Doctor of Modern scientific allopathy system of medicine is the largest professional association of modern medicine doctors with 3,51,258 members spread over 1700 local branches in all the 640 districts of India. Baptized in the struggle for Independence it serves as the platform for the medical fraternity as an academic forum, trade union as well as the family outlet of doctors apart from being the voice of the fraternity and the people in the issues of Health.

Our objective is to promote and advance medical and allied sciences and their different branches. We aim to promote the improvement of public health and medical education in India. IMA has been publishing guidelines and monographs to update its members on the ever-changing clinical practice. A group meeting was conducted among Chest Physicians, Consulting Physician, General Practitioner, ENT, Dermatologist and Allergologist, where important issues related to the stepwise management of allergy were discussed. This publication attempts to simplify management of allergy in its multifarious manifestations.

We feel immense pleasure in announcing that the final recommendation from the meeting has been derived and has been published and it is accessible to all. We thank all the experts for their participation in developing these recommendations so that these can be utilized by GPs for the diagnosis and stepwise management of Allergy effectively in the Indian scenario.



Dr. Sahjanand Prasad Singh
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Allergic Disorders: *Simplify Allergic Management in India*

Introduction

Allergic diseases are a group of immune-mediated disorders mainly caused by an IgE-dependent immunological reaction to an innocuous environmental antigen (allergen).

According to the site of contact with the allergen, different clinical manifestations may develop in the airways, skin, eyes or gastrointestinal tract.

The frequency of allergic diseases is increased over the last century. Because of their frequency and their impact on the quality of life, new therapeutic approaches for these disorders have been the object of intensive research¹.

Epidemiology

20-30% of the Indian population suffers from at least one allergic disease².

Table 1: Prevalence rate of Allergic Diseases in India

Disease	Prevalence
Allergic rhinitis	20% and 30% ² .
Atopic dermatitis (AD)	11% and 21% ⁶⁻⁷ .
Urticaria	8.8–20% ³ .
Contact dermatitis	4.38% ⁵ .
Asthma	Children 2-20% adults is 2% ⁴ .
Food allergy	1-10% ⁸ .
Drug allergy	1% to 2% of all admissions and 3% to 5% of hospitalized patients ⁹ .

Impact of allergy on QoL and society

- ▶ Some allergic disorders such as allergic rhinitis lead to impaired cognition and hence impaired work and school performance (lower grades in school)¹⁰.
- ▶ Allergic Rhinitis can be severe at night and in the early morning thus impacting the quality of sleep¹⁰.
- ▶ Nasal congestion leads to discomfort, frustration, fatigue, irritability, stress, and impaired quality of life¹⁰.
- ▶ The severity of asthma significantly contributes to poor quality of life¹¹.
- ▶ In disorders such as urticaria or contact dermatitis, pruritus interferes with sleep and further impairs quality of life. The rashes could cause significant embarrassment¹².
- ▶ Anaphylactic food allergy and asthma can lead to anxiety, panic, depression, and mental health issues.
- ▶ Severe allergic diseases (allergic rhinitis, asthma food allergies and atopic dermatitis) have also been associated with anxiety and depressive disorders¹³.

Atopic march

Atopic dermatitis, allergic rhinitis, and asthma are common, frequently appear together, and usually begin in early life, thus posing lifelong burdens for many affected patients. Based on clinical observations and studies of disease prevalence, it has been proposed that the sequential development of atopic dermatitis, asthma and allergic rhinitis is a causal relationship now known as the "atopic march"¹⁴.

Figure 1: Incidence rate of Atopic March over a lifetime

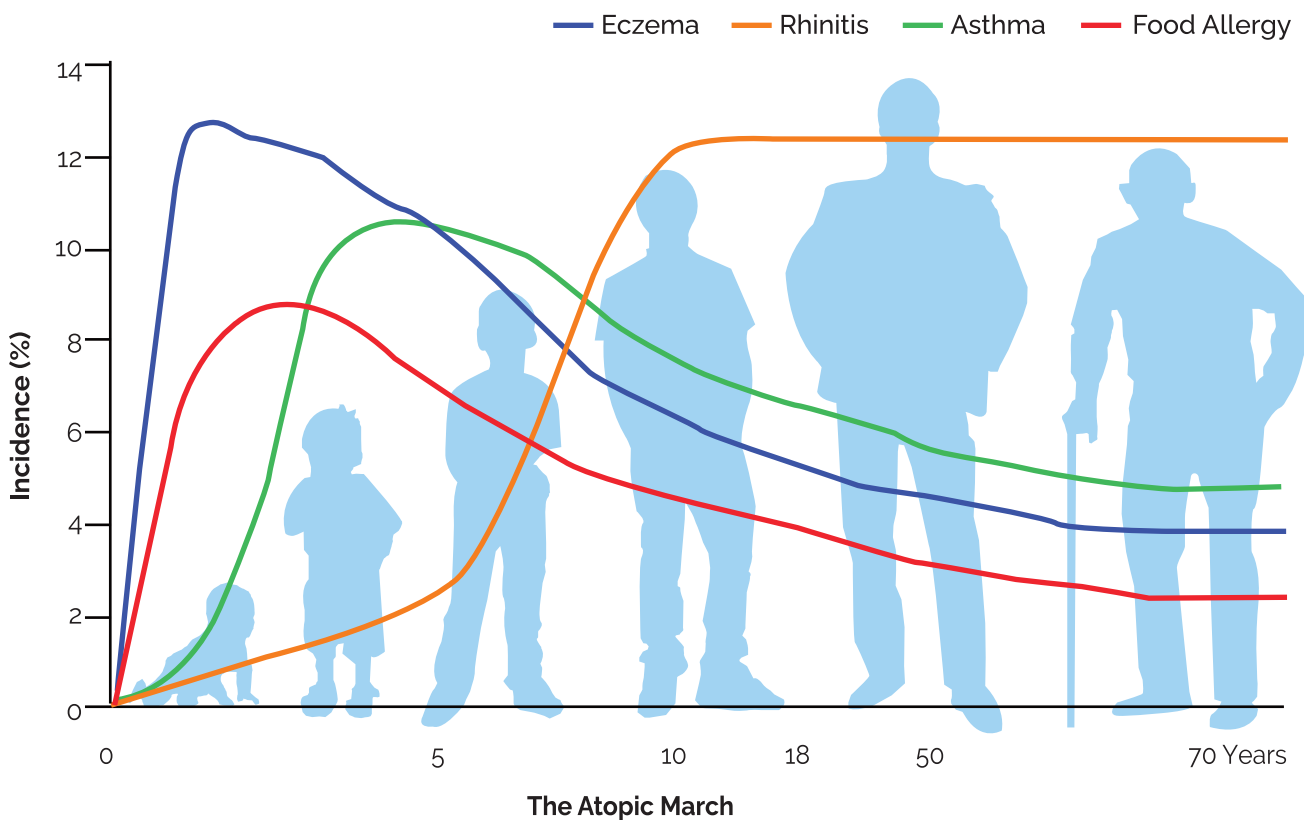


Table 2: Different types of allergic reactions¹⁵

	Type I (Anaphylactic reactions/ acute hypersensitivity/ immediate type)	Type II (Cytotoxic reactions)	Type III (Immunocomplex mediated reaction)	Type IV (Cell-mediated reactions/delayed hypersensitivity)
Immune system involvement	IgE	IgG or IgM	IgG or IgM Immune complex-mediated hypersensitivity	T cell-mediated hypersensitivity
Examples	<ul style="list-style-type: none"> • Bee sting • Local allergic reactions • Eczema • Allergic rhinitis • Food allergies • Drug allergies • Anaphylaxis 	<ul style="list-style-type: none"> • Red blood cell destruction after transfusion of mismatched blood 	<ul style="list-style-type: none"> • Rheumatoid arthritis • Systemic lupus erythematosus 	<ul style="list-style-type: none"> • Allergic contact dermatitis • Type 1 diabetes • Multiple sclerosis • Graft rejection

Allergy disorders and their management

a. Urticaria

Urticaria (hives) is a disorder characterized by erythematous, edematous, itchy, and transient urticarial plaques, covering the skin and mucous membranes³.

Table 3: Etiology

Medications	Penicillin, aspirin, non-steroidal anti-inflammatory drugs, sulfonamides, thiazide diuretics, oral contraceptives, angiotensin-converting enzyme inhibitors. Symptoms of urticaria can be seen within 1–2 h to 15 days after oral intake of the drugs.
Foods	Several foods may cause urticaria within 1–2 h after ingestion. These include milk, eggs, nuts, seafood, chocolate, meat, citrus fruits, grapes, plums, pineapples, bananas, preservatives, and food colors.
Respiratory allergens	Pollen, mold spores, mites, animal dandruff, hairs, and smoking.
Infections	Viral Infections, Respiratory infections such as sinusitis, tonsillitis, dental abscesses, urinary tract infections, hepatitis, and parasitic infections.
Insect bites	Honey bee, wasp, yellow jackets, white faced hornets, red ants and others.
Psychogenic factors	Stress, anxiety, sadness, and depression may trigger urticaria.
Systemic diseases	Thyroid diseases (autoimmune thyroiditis) and rheumatic diseases such as systemic lupus erythematosus, lymphoma, leukemia, and carcinoma.
Physical factors	Urticaria may develop due to pressure, hot, cold, and dermatographism.
Hereditary urticaria	Seen in angioedema and familial cold urticaria.
Idiopathic urticaria	Urticaria without any known cause ³ .
Autoimmune urticaria	A distinct subset of chronic idiopathic urticaria (CIU). About 40-50% of the patients with CIU demonstrate an immediate wheal and flare response to intra-dermally injected autologous serum ¹⁶ .
Urticaria after COVID infections	Urticarial rash may be either generalized or distributed on the trunk ¹⁷ . Six main patterns have been identified namely (i) urticarial rash (ii) confluent erythematous/maculopapular/morbilliform rash (iii) papulovesicular exanthem (iv) chilblain-like acral pattern (v) livedo reticularis/racemosa-like pattern (vi) purpuric "vasculitic" pattern ¹⁸

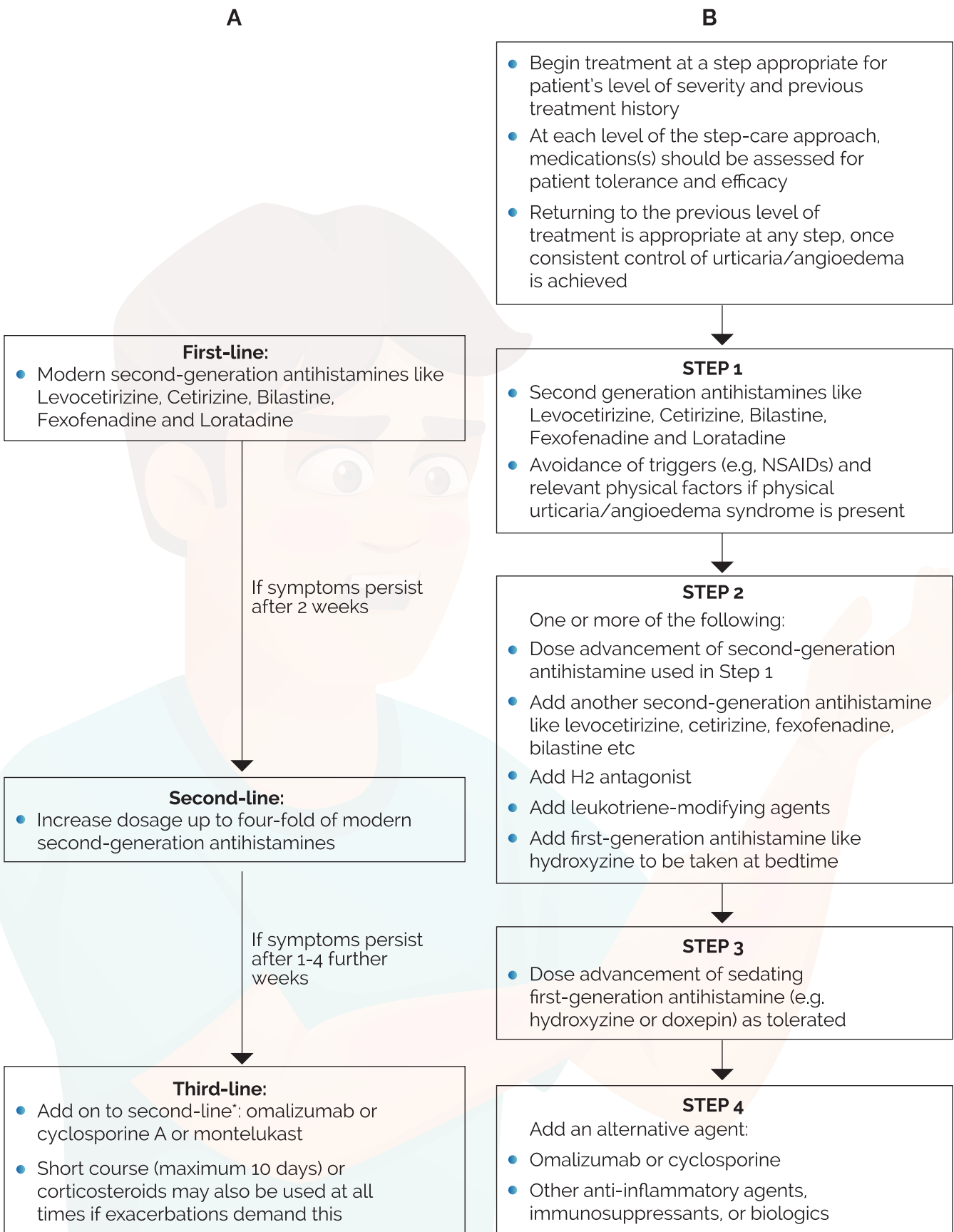
Table 5: Classification

Type	Duration	Characteristic features
Acute urticaria	Less than 6 weeks	
Chronic spontaneous urticaria	More than 6 weeks	Recurrers at least 2 times a week
Chronic inducible urticaria (Chronic physical urticaria)	More than 6 weeks	Subtypes of urticaria according to triggering factors <ul style="list-style-type: none"> • Dermatographic urticaria • Cold urticaria • Heat urticaria • Delayed pressure urticaria • Solar urticaria • Vibration urticaria • Aquagenic urticaria • Contact urticaria • Cholinergic urticaria
Episodic chronic urticaria	Lasts more than 6 weeks	Recurrers at least 2 times a week or sometimes less (Chronic Intermittent Urticaria)

Diagnosis of urticaria

- ▶ Diagnosis is based on clinical appearance and the time course of events that led to urticaria.
- ▶ A search for possible underlying causes and/or relevant triggers in patients who present with relapsing symptoms¹⁹.
- ▶ In patients with infection-related urticaria differential blood count analyses, determination of blood sedimentation rate, and C-reactive protein tests are performed¹⁹.
- ▶ Just 25% of acute urticaria cases become chronic in time³.
- ▶ About 40% of patients with urticaria can develop swelling of their lips/eyelids/genitals/extremities (This is called angioedema).

Figure 2: Treatment



Patient education for urticaria

- ▶ Avoid any known triggers
 - Excessive heat, spicy foods or alcohol.
 - Many types of drugs can trigger hives, including antibiotics²¹.
- ▶ If you get hives all over your body after an insect sting, this may be a sign of a more serious reaction called anaphylaxis. Anaphylaxis must be treated as soon as possible²².
- ▶ Swelling can be a medical emergency
 - Along with hives, some people develop swelling deep in their skin or the moist tissue that lines the mouth/lip, eyelids, or other areas. This swelling is called angioedema. If the angioedema affects the tongue or throat this becomes a medical emergency and the patient must consult their doctor immediately or go to an emergency medical facility²³.



b. Allergic rhinitis

Allergic rhinitis (AR) is one of the most common chronic conditions which is a global health problem that causes significant morbidity worldwide²⁴.

Etiology

- ▶ Common allergens that cause allergic rhinitis include pollen – this type of allergic rhinitis is known as hay fever–, as well as house dust mites, cockroach, mould spores and flakes of skin or droplets of urine or saliva from certain animals.
- ▶ Allergens found in the work environment, such as wood dust, flour dust, or latex²⁵.

Types of allergic rhinitis

- ▶ Seasonal and perennial (throughout the year)²⁶
- ▶ New proposed classification: intermittent and persistent rhinitis²⁷

Figure 3: Intermittent and persistent rhinitis

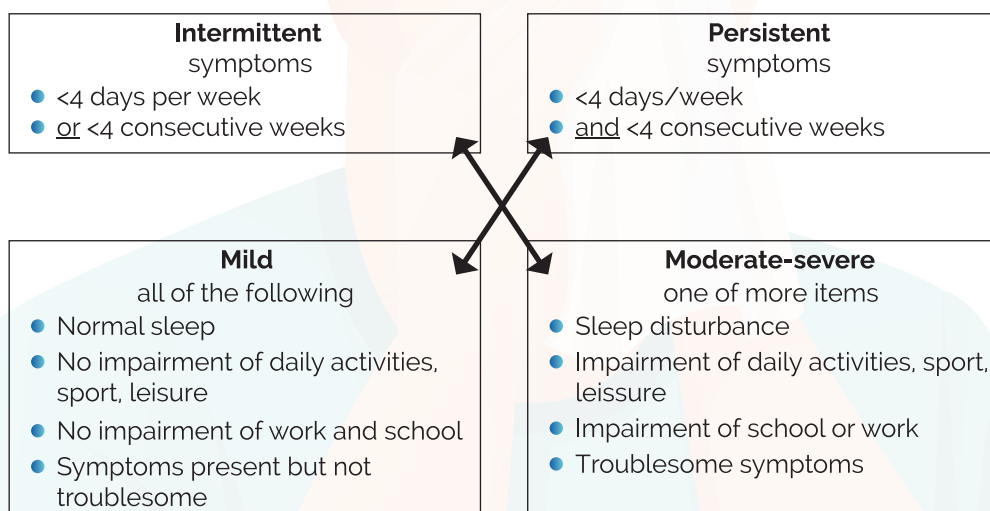


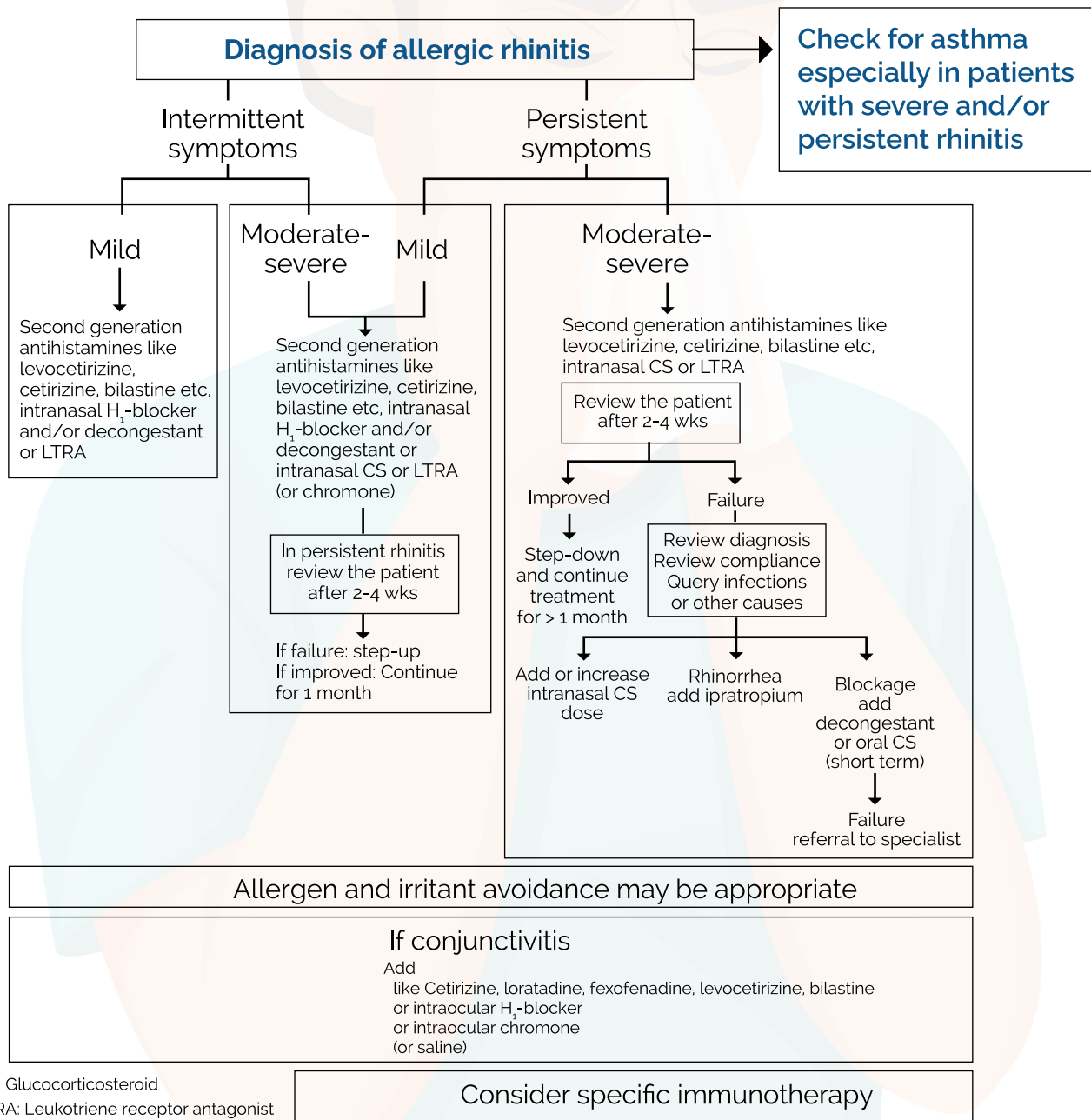
Table 6: Diagnosis of allergic rhinitis

<p>History taking</p>	<ul style="list-style-type: none"> • Ask about the ability to breathe through the nose and to smell. • Ask about the inciting allergen or allergens. • Ask whether symptoms were present since childhood or timing of onset, seasonal variation & progression of symptoms.
<p>Look for key symptoms and signs of rhinitis</p>	<ul style="list-style-type: none"> • Rhinorrhoea with watery nasal discharge. The presence of yellow or green discharge indicates sinusitis or bacterial rhinitis. • Nasal blockage • Nasal crusting • Dennie-Morgan folds are linear wrinkles beneath the lower eyelashes • Allergic shiners are dark circles beneath the lower eyelid • Nasal salute and nasal crease • Coexistence of allergic conjunctivitis with AR • Bleeding (might be associated severe rhinitis/medication misuse) • Sneezing and itching • Hyposmia caused by nasal polyps • Eye symptoms including red eye, lid swelling, and periorbital edema (allergic conjunctivitis) • Cough, wheeze, and breathlessness—asthma or bronchitis may also be present • Snoring and sleep problems • Repeated sniffing and nasal intonation of speech
<p>Physical examination</p>	<ul style="list-style-type: none"> • General examination: Look for atopic dermatitis, signs of allergic rhinitis and for eye signs such as puffiness, redness, watery discharge and/or bulging, as seen in hypothyroidism. • Nasal examination: External appearance, internal examination, preferably with a nasal endoscopy. • Ear examination for otitis media with effusion (also known as glue ear). • Look for presence of asthma by asking patients about wheezing, shortness of breath, and sleep disturbance plus, consider, a spirometry examination.
<p>Suggested Investigations</p>	<ul style="list-style-type: none"> • For every single case of AR perform a peak flow meter test for potential screening of asthma. • Perform spirometry (pulmonary function test) in selected patients where the coexistence of asthma is suspected. • Skin prick tests should be carried out routinely to determine if rhinitis is allergic or non-allergic and identify relevant triggers. • Serum total and specific IgE are performed if skin prick tests are not possible, or when a skin prick test together with the clinical history gives equivocal or conflicting results. • Laboratory investigations are usually unnecessary unless indicated by the patient's clinical history and results of skin prick tests—examples include:

Table 6: Diagnosis of allergic rhinitis

	<ul style="list-style-type: none"> ■ Full blood count, C-reactive protein, immunoglobulin profile, microbiological examination of sputum, and sinus swabs when a chronic infection is suspected. ■ Thyroid function tests if there is an unexplained nasal blockage. ■ Urine toxicology when cocaine abuse is suspected. ■ Nasal secretions - asialotransferrin for cerebrospinal fluid identification.
	<ul style="list-style-type: none"> ● Radiology: A limited computed tomography scan of the sinuses can be helpful in the diagnosis of rhinosinusitis or nasal polyposis

Figure 4: Management (adapted from ARIA guidelines)²⁸



Patient education about allergic rhinitis²⁹

- ▶ Avoid triggers for your attack of allergic rhinitis.
- ▶ Avoid carpets, pet fur where indicated.
- ▶ House dust mites
 - Wash bedding every week in hot water (55°C) and detergent and dry on a hot setting.
 - Use dust mite proof covers on the mattress and pillows
 - If possible, sleep in a room with no carpet, curtains, or upholstered furniture.
- ▶ Don't smoke. Stay away from cigarette smoke. Cigarette smoke is an irritant that can make symptoms worse. Avoid mosquito coils, incense sticks etc due to irritant smoke produced by them.
- ▶ Clean moldy areas with bleach and water. Don't mix bleach with other cleaners.
- ▶ To prevent cockroaches
 - Store food in sealed containers
 - Remove garbage from the home promptly
 - Fix water leaks
 - Use baits
- ▶ To avoid pollen if allergic to them, stay indoors when pollen counts are high (peak season) and wear protective eye wear and face masks when outdoors and avoid travelling in open vehicles.

c. Allergic asthma

Asthma is an episodic reversible chronic airway inflammation. If left untreated it can lead to fixed airway obstruction. Asthma is a serious global health problem as per the GINA guidelines³⁰.

Table 7: Etiology

Triggers	<ul style="list-style-type: none"> • Common cold (viral infection) • Allergens, e.g. house dust mites, pets • Cold weather • Irritants <ul style="list-style-type: none"> → Smoke → Haze → Strong smells, i.e. perfumes, cleaning solutions → Exhaust fumes
History of atopy	<ul style="list-style-type: none"> • Eczema • Allergic rhinitis
Family history	<ul style="list-style-type: none"> • Asthma • Allergic rhinitis • Eczema

Table 8: Classification³²

Intermittent	<ul style="list-style-type: none"> • Symptoms less than once a week • Nocturnal symptoms not more than twice a month • PEF or FEV₁ variability <20% 	<ul style="list-style-type: none"> • Brief exacerbations • FEV₁ or PEF > 80% pred
Mild persistent	<ul style="list-style-type: none"> • Symptoms more than once a week but less than once a day • Exacerbations may affect activity and sleep • Nocturnal symptoms more than twice a month • FEV₁ or PEF > 80% pred 	<ul style="list-style-type: none"> • PEF or FEV₁ variability <20-30%
Moderate persistent	<ul style="list-style-type: none"> • Symptoms daily • Nocturnal symptoms more than once a week • FEV₁ or PEF 60-80% pred 	<ul style="list-style-type: none"> • Exacerbations may affect activity and sleep • Daily use of inhaled short-acting β_2- agonist • PEF or FEV₁ variability >30%
Severe persistent	<ul style="list-style-type: none"> • Symptoms daily • Frequent nocturnal asthma symptoms • FEV₁ or PEF <60% pred 	<ul style="list-style-type: none"> • Frequent exacerbations • Limitation of physical activities • PEF or FEV₁ variability >30%

FEV₁: forced expiratory volume in one second; PEF: peak expiratory flow; % pred: % predicted.

Table 9: Presentation (symptoms)³¹

Common symptoms	<ul style="list-style-type: none"> • Cough • Wheeze • Chest tightness • Shortness of breath • Nocturnal or early morning attacks of wheeze, and cough especially in children. These vary in intensity over time and in severity • Look for symptoms and signs of allergic rhinitis • When taking the history of the patient, ask whether the patient had allergic rhinitis in childhood
Symptom variability	<ul style="list-style-type: none"> • Episodic symptoms • Diurnal symptoms • Symptoms after/during exercise • With extremes of emotions (laughing a lot or crying a lot)

Table 10: Investigations for Asthma³¹

Investigation	Description
Physical examination	<p>A FEV₁ (forced expiratory volume in 1 second)/FVC (forced vital capacity) ratio of <70% is a positive test for obstructive airway disease.</p> <ul style="list-style-type: none"> • Eczema • Allergic rhinitis signs • Use of accessory muscles • Hyperinflation • Audible wheeze or Ronchi on auscultation
<i>Demonstration of airway obstruction</i>	
Spirometry	<p>A FEV₁ (forced expiratory volume in 1 second)/FVC (forced vital capacity) ratio of <70% is a positive test for obstructive airway disease.</p>
<i>Demonstration of airway obstruction variability</i>	
Bronchodilator reversibility	<p>An improvement in FEV₁ of ≥12% and ≥200 mL is a positive bronchodilator reversibility test.</p> <p>When assessing bronchodilatory variability,</p> <ul style="list-style-type: none"> • Short-acting beta-agonist must be stopped 4 hours before the test. • Long action beta-agonist must be stopped 24 hours before the test. • Ultra LABA must be stopped 36 hours before the test. They would hamper the results.
Other methods	<p>An increase in FEV₁ >12% and >200 mL [or peak expiratory flow (PEF) >20%] from baseline after four weeks on inhaled corticosteroids (ICS) is a positive test. The patient must not have respiratory infections.</p>

Table 10: Investigations for Asthma³¹

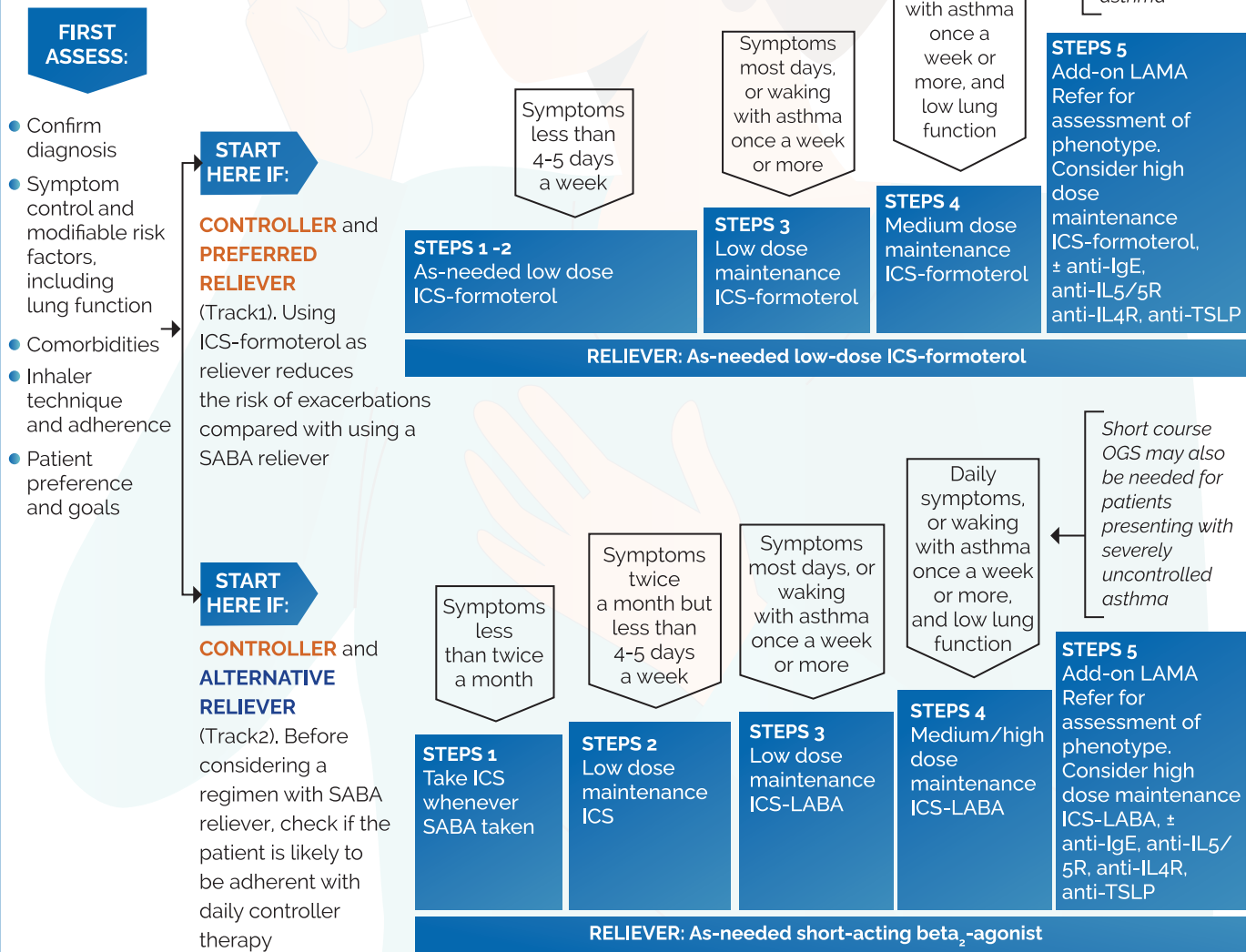
<p>Peak flowcharting</p>	<p>If we do not have PFT facilities, peak flow meter measuring diurnal variation >20% performed over a span of 2 weeks can be considered as asthma.</p> <p>Peak flow monitoring over 2 – 4 weeks. Calculate mean variability. Daily diurnal PEF variability is calculated from twice daily PEFs as [(day's highest – day's lowest)/mean of day's highest and lowest] and averaged over one week.</p> <p>Variability ≥20% or diurnal variation >15% on >3 days/week indicates a positive test.</p>
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Figure 5: Treatment (adapted from GINA guidelines)

STARTING TREATMENT

in adults and adolescents with a diagnosis of asthma

Track 1 is preferred if the patient is likely to be poorly adherent with daily controller. ICS-containing therapy is recommended even if symptoms are infrequent, as it reduces the risk of severe exacerbations and need for OCS.



ICS : inhaled corticosteroid; LABA: long-acting beta₂-agonist; LAMA: long-acting muscarinic antagonist; MART: maintenance and reliever therapy with ICS-formoterol; OCS: oral corticosteroids; SABA: short acting beta₂-agonist. See Box, p. 63 for low, medium and high ICS dosed for adults and adolescents.

Role of antihistaminic drugs in asthma

- ▶ Antihistamines are not a first-line treatment for asthma. However, they can help reduce allergy symptoms, which can sometimes help manage allergic asthma.
- ▶ Antihistamines block the actions of histamine and also have effects on inflammation which is independent of histamine-H(1)-receptor antagonism.
- ▶ Antihistamines have bronchodilatory effects, effects on allergen-, exercise-, and adenosine-monophosphate-challenge testing.
- ▶ Antihistamines prevent allergen-induced non-specific airway hyper-responsiveness.
- ▶ The combination of an antihistamine and a leukotriene receptor antagonist has been shown to have additive effects.
- ▶ Antihistamines have also been shown to delay or prevent the development of asthma in a subgroup of atopic children³³.
- ▶ Oral H1 antihistamines are recommended only in asthma patients with concomitant AR or significant allergic triggers identified for their asthma³⁴.

Patient education about asthma³⁵

- ▶ Avoid triggers, irritants and allergens, some medications (eg non-selective beta blockers), stress.
- ▶ Take medications correctly
- ▶ Understand the difference between "controller" and "reliever" medications
- ▶ Monitor status using symptoms or peak expiratory flow meter
- ▶ Recognize signs that asthma is worsening and take action
- ▶ Follow an Asthma Action Plan

d. Allergic contact dermatitis

- ▶ Contact dermatitis is a common inflammatory skin condition characterized by erythematous and pruritic skin lesions after contact with a foreign substance³⁶.
- ▶ Allergic contact dermatitis is a delayed-type hypersensitivity response by an individual's immune system to a small molecule (less than 500 daltons), or hapten that contacts a sensitized individual's skin.
- ▶ The disorder is more common in women than in men. Common substances implicated are nickel, rubber gloves, hair dyes, textile chemicals, preservatives, fragrances, sunscreens, and photo allergens³⁷.

Classification

- ▶ Irritant contact dermatitis is caused by non-immune-modulated irritation of the skin by a substance, leading to skin changes. (Usatine RP, et al). At least 100 are known contact allergens, perfumes cosmetics, shampoos and other hair products, soaps, moisturizers, and deodorants.
- ▶ Allergic contact dermatitis is a delayed hypersensitivity reaction initiated when a foreign substance comes into contact with the skin; skin changes occur with re-exposure³⁶.

Clinical presentation

- ▶ Erythematous, eczematous, or vesicular dermatitis.
- ▶ Localized, well-demarcated skin eruption most commonly on the hands or face, or it can also be more widespread.
- ▶ Chronic allergic contact dermatitis more commonly presents with lichenification, fissuring, cracking and scaling³⁷.

Diagnosis

Table 11: Diagnosis

History	<ul style="list-style-type: none">• Exposure to chemicals, allergic substances, and physical examination findings³⁶.• Occupation, hobbies, medications, lifestyle, use of fragrances, and perfumes³⁷.
A potassium hydroxide (KOH) preparation	Is useful if tinea or candida infection is suspected because these fungal infections can have erythema and scaling similar to contact dermatitis ³⁷ .
Fungal culture	Is indicated if the KOH preparation has negative results but fungal etiology is still suspected, a fungal culture should be sent for laboratory testing ³⁶ .
Dermoscopy and microscopy	can be used to look for scabies and mites ³⁶ .

Management

Table 12: Management

The definitive treatment of ACD is the identification and removal of the offending agent ³⁷ .
Cool compresses can soothe the symptoms of acute contact dermatitis.
Calamine lotion and colloidal oatmeal baths may help dry and soothe acute, oozing lesions ³⁶ .
Symptomatic management includes oral antihistamines, topical hydrocortisone or more potent topical corticosteroids, and cool water soaks.
Vesicles should not be ruptured as there is a risk of infection.
The use of moisturizers is a recommended adjunct ³⁷ .
Antihistamines are used for the relief of pruritus associated with allergic contact dermatitis, they are commonly used ³⁶ . Antihistamines such as hydroxyzine and cetirizine are recommended to control pruritus ³⁸ .
If ACD involves a delicate area such as skin folds or eyelids, topical calcineurin inhibitors or PDE4 inhibitors may also be effective.
Upon identification of the allergen, strict avoidance is necessary to prevent a recurrence.
For severe cases, topical immunomodulators like tacrolimus may be beneficial. Some patients may benefit from phototherapy using UV-A plus psoralen.
Rarely in severe cases, one may require immunosuppressive agents like mycophenolate ³⁷ .

Patient education for allergic contact dermatitis³⁷

- ▶ Educating patients on allergic contact dermatitis (ACD) involves assisting the patient in identifying their allergic triggers.
- ▶ Patients must then be provided with practical behavioral modifications to help decrease the inflammatory response of this disease.
- ▶ Advise patients to keep a "diary" of when the symptoms appear, get worse or improve, how long they last, do they occur after certain activities, or exposure to a specific environment or chemical

e. Atopic dermatitis

- ▶ Atopic dermatitis (also known as atopic eczema) is a chronic, pruritic inflammatory skin disease, with a relapsing course, often seen in children but can also occur in adults.
- ▶ Atopic dermatitis has a relapsing course and is often associated with
 - Elevated serum immunoglobulin (IgE) levels
 - A personal or family history of type I allergies
 - Allergic rhinitis, and asthma
 - Food allergies³⁹

Etiology⁴⁰

- ▶ Woollen clothing
- ▶ Heat, sweating, hot water
- ▶ Several infections such as staphylococcal infections
- ▶ Contact urticaria: a reaction following skin exposure to a food, for example, citrus fruits or tomatoes. The skin around the mouth is often the site of such a reaction.
- ▶ Stress aggravates eczema

Clinical presentation⁴¹

Table 13: Clinical presentation

<p>Essential features; must be present</p>	<ul style="list-style-type: none"> ● Pruritus ● Eczema (acute, subacute, chronic): <ul style="list-style-type: none"> ▶ Typical morphology and age-specific patterns* ▶ Chronic or relapsing history <p><i>*Patterns include:</i> Facial, neck and extensor involvement in infants and children; Current or prior flexural lesions in any age group; Sparing of groin and axillary regions.</p>
<p>Important features; seen in most cases, adding support to the diagnosis:</p>	<ul style="list-style-type: none"> ● Early age of onset ● Atopy <ul style="list-style-type: none"> ▶ Personal and/or family history ▶ IgE reactivity ● Xerosis
<p>Associated features; These clinical associations help to suggest the diagnosis of AD but are too non-specific to be used for defining or detecting AD for research and epidemiologic studies:</p>	<ul style="list-style-type: none"> ● Atypical vascular responses (e.g., facial pallor, white dermographism, delayed blanch response) ● Keratosis pilaris / pityriasis / alba / hyperlinear palms / ichthyosis ● Ocular / periorbital changes ● Other regional findings (e.g., perioral changes / periauricular lesions) ● Perifollicular accentuation / lichenification / prurigo lesions

Note: Sleep disturbance is also common due to significant itch associated with AD.

Diagnosis

Atopic dermatitis is a clinical diagnosis with no definitive laboratory test. Approximately 80% of patients with atopic dermatitis are diagnosed and treated in the primary care setting⁶.

Table 14: American Academy of Dermatology Diagnostic Criteria for Atopic Dermatitis

<p>Essential features: Must be present for diagnosis</p>	<ul style="list-style-type: none"> • Chronic or relapsing history • Eczema (acute, subacute, chronic) • Pruritus • Typical morphology and age-specific patterns*
<p>Important features: support the diagnosis (observed in most cases)</p>	<ul style="list-style-type: none"> • Atopy (personal or family history) • Early age at onset • Immunoglobulin E reactivity • Xerosis
<p>Associated features: suggestive of the diagnosis but nonspecific</p>	<ul style="list-style-type: none"> • Atypical vascular responses (facial pallor, white dermographism) • Keratosis pilaris, alba, hyperlinear palms, or ichthyosis • Ocular or periorbital changes • Perifollicular accentuation, lichenification, or prurigo lesions

*_Patterns include: facial, neck and extensor involvement in infants and children; current or previous flexural lesions in any group; and sparing of the groin and axillary regions.

Adapted with permission from Eichenfield LF, Tom WL, Chamlin SL, at. Guidelines of care for the management of atopic dermatitis: section 1, Diagnosis and assessment of atopic dermatitis, J Am Acad Dermatol. 2014;70(2):341

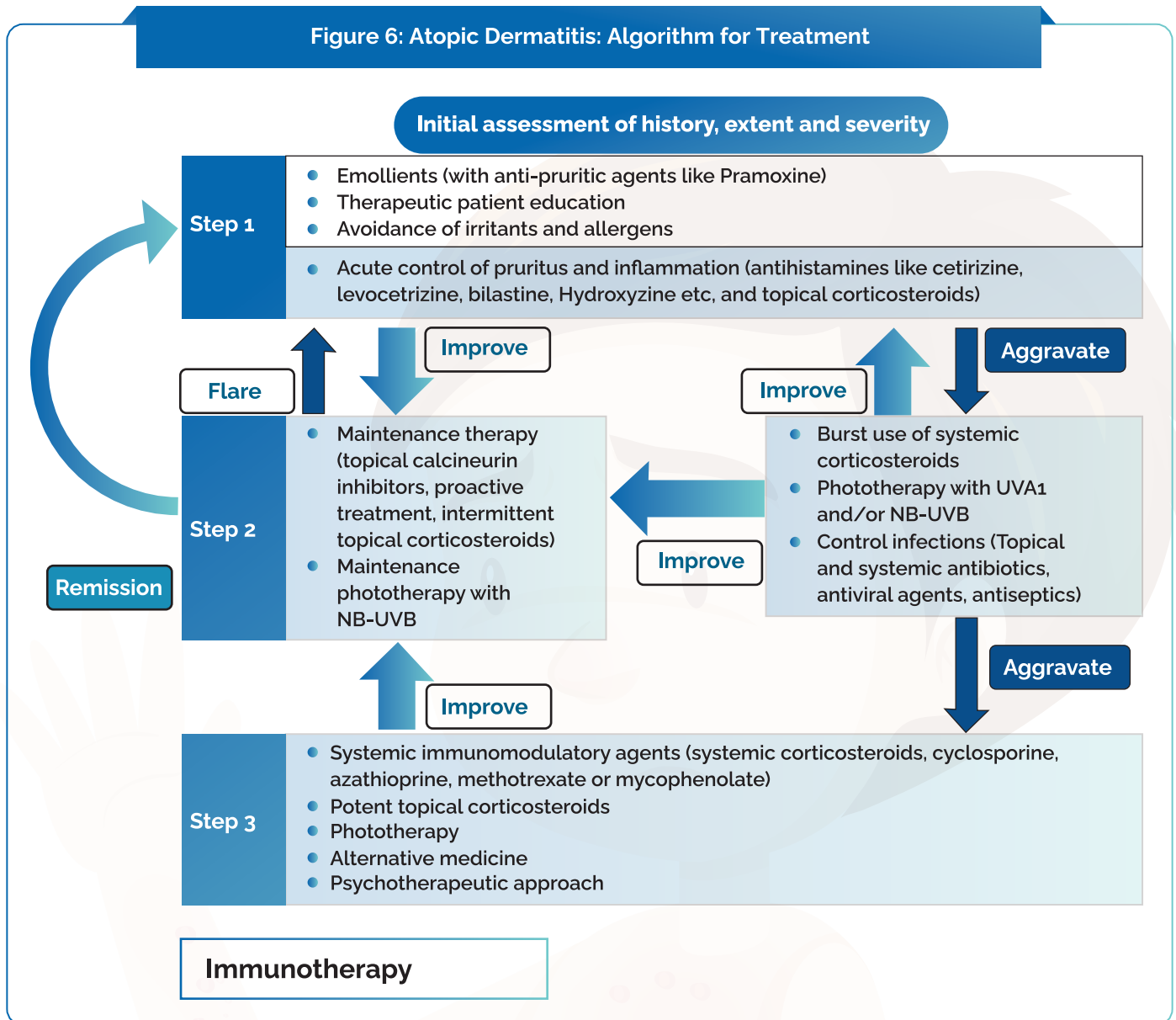
Tests that may be performed to arrive at the diagnosis of Atopic dermatitis

- ▶ Skin allergy testing (in vivo)
- ▶ Blood specific allergy testing (in vitro)

Treatment of atopic dermatitis⁴²

Atopic dermatitis can be well controlled. Some patients will experience a chronic course of the disease. Many children undergo remission between the ages of 2-7 years.

Figure 6: Atopic Dermatitis: Algorithm for Treatment



Patient education for atopic dermatitis⁴³

- ▶ Bathe with warm water, NOT hot water
- ▶ After bathing gently pat the skin dry
- ▶ Apply a moisturizer at least twice a day
- ▶ Keep finger nails short to avoid damage to skin due to scratching
- ▶ When washing clothes do not use excess detergent or bleach or fabric softeners and use adequate amount of water to wash these off completely.

f. Drug allergy

Drug allergy encompasses a spectrum of immunologically-mediated hypersensitivity reactions with varying mechanisms and clinical presentations. This type of adverse drug reaction (ADR) not only affects patient quality of life, but may also lead to delayed treatment, unnecessary investigations, and even mortality. Given the myriad of symptoms associated with the condition, diagnosis is often challenging⁴⁴.

Clinical features of drug hypersensitivity reactions⁴⁵

Table 15: Drug hypersensitivity reactions

Reaction	Clinical manifestations
Delayed drug exanthem	Fine macules and papules that occur days after drug initiation and resolve a few days after discontinuing the medication; lack of other systemic symptoms.
IgE-mediated	Combination of urticaria, angioedema, vomiting, diarrhea, cough, wheeze, hypotension, and/or syncope one to six hours after starting a medication; usually requires prior sensitization.
Serum sickness-like reaction	Rash (usually urticarial), fever, arthralgias, lymphadenopathy one to three weeks after starting a medication; could be earlier with sensitization.
SJS/TEN	Mucosal involvement, fever, cutaneous target and bullous lesions (SJS: < 10% epidermal detachment; SJS/TEN overlap: 10%–30% epidermal detachment; TEN: > 30% epidermal detachment); possible involvement of liver, kidney, lungs.
DRESS	Fever, eosinophilia, lymphadenopathy, liver dysfunction, possible renal dysfunction, multiple different cutaneous eruptions possible; starts up to 12 weeks after starting a medication and may persist for weeks or months after stopping the medication
Allergic contact dermatitis	Dermatitis in area of cutaneous contact that evolves over days; requires prior sensitization
Drug-induced lupus erythematosus	Cutaneous: photodistributed erythematous plaques Systemic: sudden onset myalgias, fever, arthralgias, malaise several weeks after drug initiation
Fixed drug eruption	Hyperpigmented plaques that recur at the same site
Other	Hematologic (cytopenia), hepatic (hepatitis, cholestatic jaundice), renal (interstitial nephritis), pulmonary (pneumonitis, fibrosis), vasculitis

Classification of allergic drug reactions: Mechanisms, clinical manifestations, and timing of reactions⁴⁴.

Table 16: Different types of allergies and its age-wise prevalence

Immune reaction	Mechanism	Clinical manifestations	Timing of reaction
Type I (IgE-mediated)	Drug-IgE complex binding to mast cells with a release of histamine, inflammatory mediators	Anaphylaxis*, urticaria*, angioedema*, bronchospasm*	Minutes to hours after drug exposure
Type II (cytotoxic)	Specific IgG or IgM antibodies directed at drug-hapten coated cells	Anemia, cytopenia, thrombocytopenia	Variable
Type III (immune complex)	Tissue deposition of drug-antibody complexes with complement activation and inflammation	Serum sickness, vasculitis, fever, rash, arthralgia	1 to 3 weeks after drug exposure
Type IV (delayed, cell mediated)	MHC presentation of drug molecules to T cells with cytokine and inflammatory mediator release; may also be associated with activation and recruitment of eosinophils, monocytes, and neutrophils	Contact sensitivity skin rashes, organ-tissue damage	2 to 7 days after drug exposure

*These reactions may also be non-immunologically mediated

Figure 7: Treatment⁴⁶

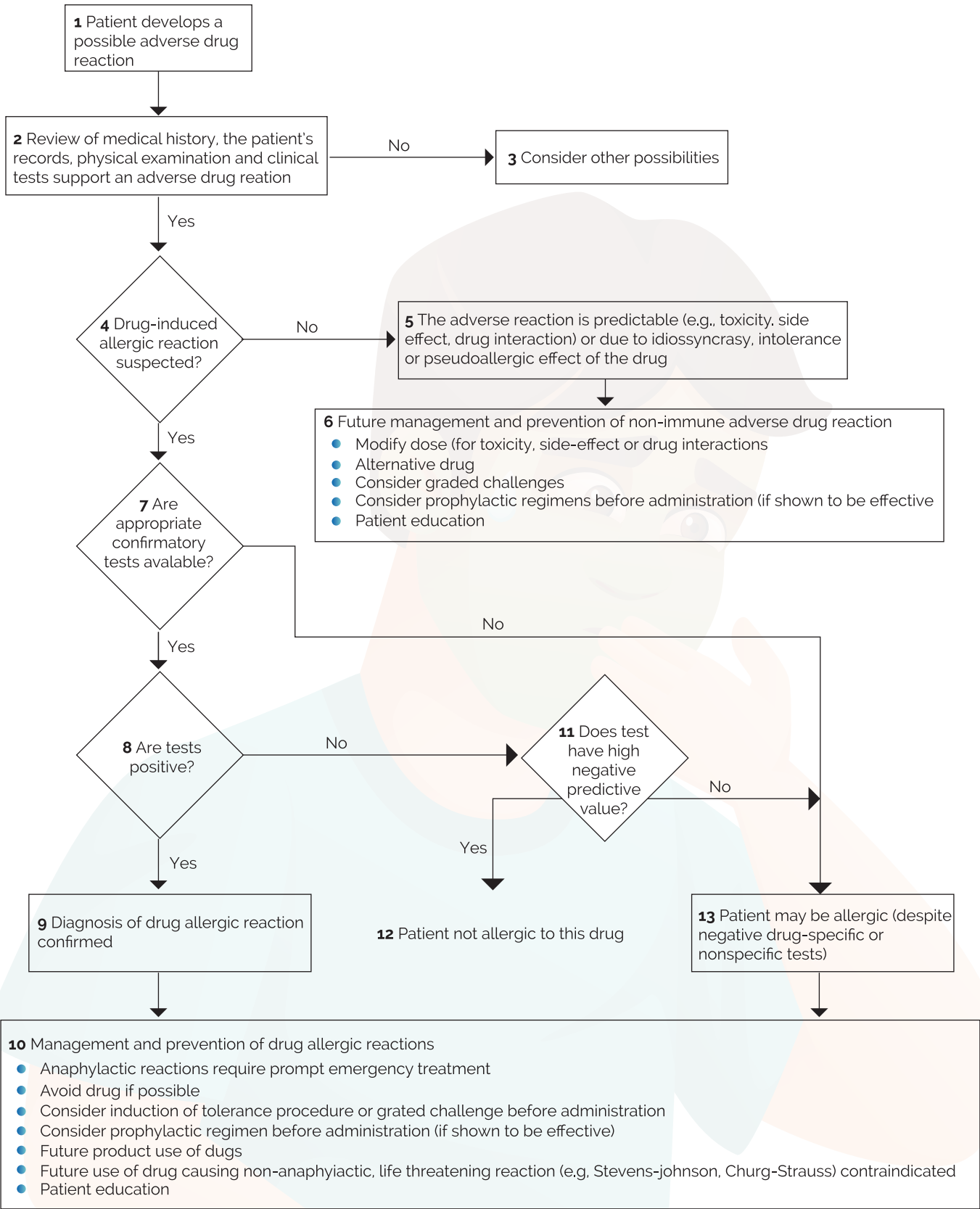


Table 17: Treatment for Drug-Induced Skin Reactions

Reaction	Treatment
Exanthematous drug eruptions	Antihistamines
Urticaria, angioedema, anaphylaxis	Antihistamines Glucocorticoids, systemic: prednisone 0.5-1 mg/kg/day po for 3-5 days Montelukast (angioedema) Epinephrine (severe cases)
Allergic contact dermatitis	Topical corticosteroids: low-potency (areas of thin skin), mid-potency, high-potency
Drug contact dermatitis	Systemic corticosteroids: prednisone 1-2 mg/kg/day po, with slow taper
Fixed drug eruption	Watchful waiting Topical corticosteroids: low-potency, mid-potency Antihistamines
Erythema multiforme	Antihistamines NSAIDs (if arthralgia present) Systemic corticosteroids: low-potency, mid-potency
Irritant contact dermatitis	Gentle cleansing Moisturizers Topical corticosteroids: low-potency, mid-potency
Photosensitivity: Phototoxic reaction	Sunblock (preventive) Cool compresses NSAIDs Systemic corticosteroids (severe reactions): prednisone 40-60 mg/day po for 2-3 days
Photoallergic reaction	Topical corticosteroids: low-potency, mid-potency
Pseudoallergy and color changes: Hyperpigmentation Melasma	Topical hydroquinone Topical tretinoin
Pseudoallergy	Antihistamines

Patient education for drug allergy⁴⁷

Tell the patient

- ▶ To avoid use of drugs that the patient is allergic to
- ▶ Consult the doctor before taking drugs
- ▶ In case of severe drug reaction, rush to the hospital for emergency care
- ▶ Carry a card mentioning the drugs he/ she is allergic to

g. Food allergy

Food allergy is an adverse immunologic response to a specific food/food component that be reproduced on exposure to a given food. It must be distinguished from food intolerance, which is s a non-IgE immune reaction.

Etiology:

Food allergens that may cause allergic reactions in some people

Nuts e.g. peanuts, pistachios, cashew nuts and others.	Milk	Eggs	Fish	Soya	Wheat
Sesame	Preservatives	Food colors	Any other food		

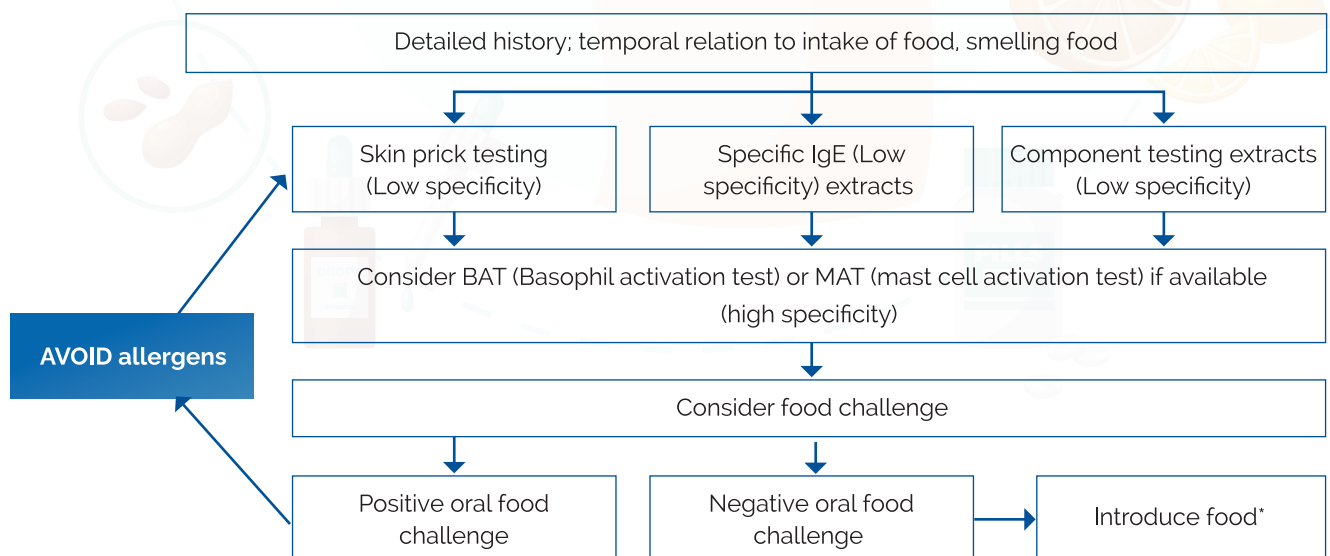
Clinical manifestations

Table 18: Clinical manifestations pertaining to various organ systems

Skin	Rash, pruritus, erythema, urticaria/hives, angioedema
Respiratory	Sneezing, rhinitis, wheezing, coughing, difficulty in breathing
Cardiovascular	Hypotension, dizziness
Gastrointestinal	Abdominal pain, nausea, vomiting, diarrhea
Neurological	Change in behavior, confusion, loss of consciousness
Life-threatening anaphylaxis	

Diagnosis of food allergy⁴⁸

Figure 8: Diagnosis of food allergy

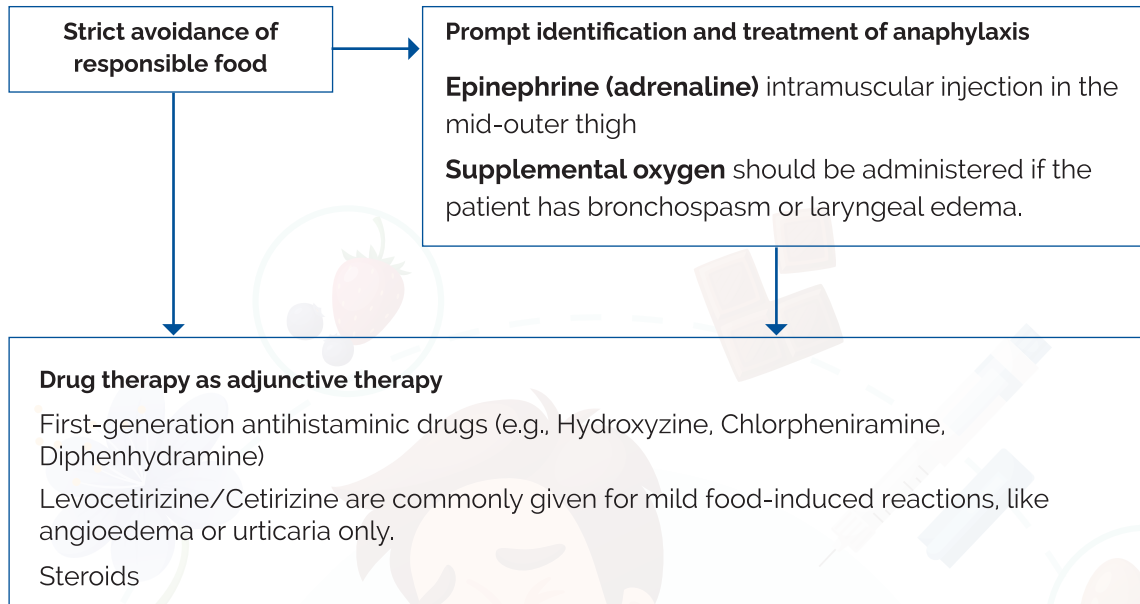


*If there is a strong history of an anaphylactic reaction, food should be introduced only after a supervised food challenge.

*It is important to correlate the food intake timing with the patient history and the results of allergy testing.

Management of food allergy⁴⁹

Figure 9: Management of food allergy



Patient education for food allergy⁵⁰

- ▶ Advise people with food allergies must strictly avoid eating or drinking anything that contains even a minuscule amount of a food allergen
- ▶ Some people who have a reaction related to exercise also need to avoid exercise for few hours before eating particular foods.
- ▶ Inhaling tiny food particles (as a result of steaming, boiling, frying, grating, shedding, or grinding) can potentially trigger an allergic reaction in highly sensitive people. Thus, people who are very sensitive should avoid situations in which aerosolized food could be inhaled (for example, being in close proximity to boiling or steaming milk or shellfish or frying fish or eggs)
- ▶ Avoiding cross-contact requires thoroughly cleaning utensils, cookware, glassware, storage containers, and other food preparation materials used with a food allergen before the item is used to prepare or serve "safe" meals.
- ▶ Washing food storage containers and dishes in a dishwasher or hand washing with hot water and liquid dish soap is generally adequate to remove food allergens.

h. Anaphylaxis

Anaphylaxis is a sudden-onset life-threatening systemic hypersensitivity reaction, which is considered to be the most severe manifestation of allergy. Anaphylaxis is a systemic, severe immediate hypersensitivity reaction caused by immunoglobulin (Ig) E-mediated immunological release of mediators of mast cells and basophils⁵¹.

Common triggers for reactions⁵¹

Individuals can react to absolutely anything. However, some common causes include foods such as those below:

Table 19: Common triggers⁵¹

Food causes	Non-food causes
<ul style="list-style-type: none">• Peanuts• Tree nuts (e.g. almonds, walnuts, cashews, and Brazil nuts)• Sesame• Fish• Shellfish• Dairy products• Egg	<ul style="list-style-type: none">• Wasp or bee stings• Natural latex (rubber)• Penicillin or any other drug or injection• Exercise can also trigger a delayed allergic reaction following exposure to an allergen• Idiopathic anaphylaxis (no clear identifiable trigger)

Common symptoms include:

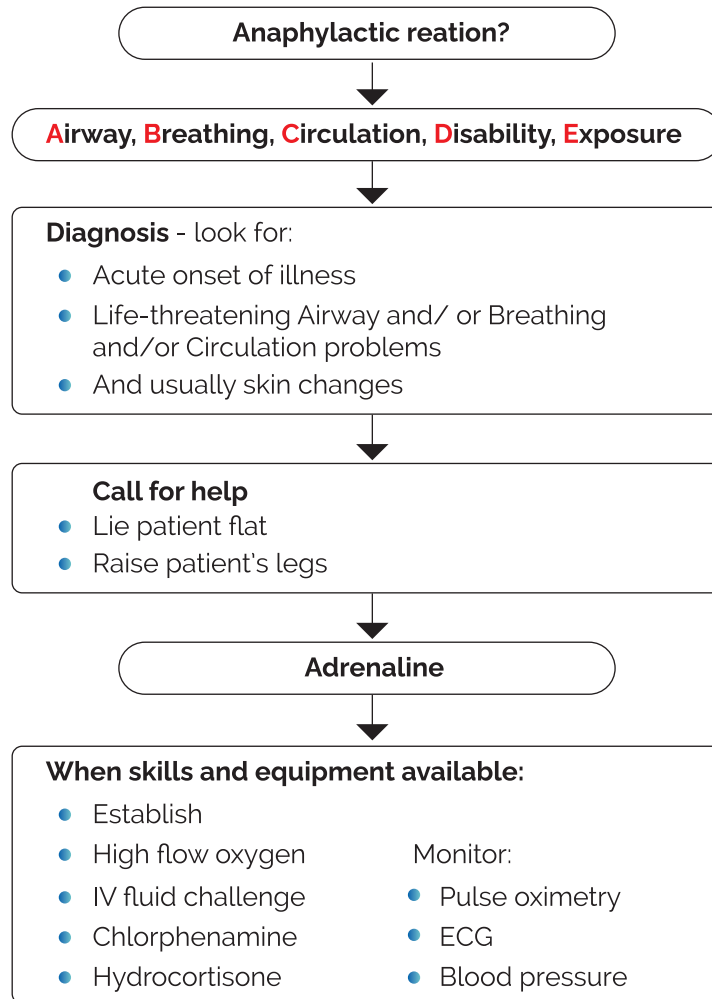
- ▶ Generalized flushing of the skin
- ▶ A rash or hives anywhere on the body
- ▶ A feeling of anxiety or 'sense of impending doom'
- ▶ Swelling of throat and mouth and difficulty in swallowing or speaking
- ▶ Alterations in heart rate – usually a speeding up of the heart
- ▶ Severe asthma attack which isn't relieved by their inhaler
- ▶ Acute abdominal pain, violent nausea, and vomiting
- ▶ A sudden feeling of weakness followed by collapse and unconsciousness

A patient is unlikely to experience all of the above symptoms⁵¹.

Treatment of anaphylaxis⁵¹

- ▶ The key advice is to strictly avoid any known triggering allergens as far as possible.
- ▶ If someone is having a mild allergic reaction involving only the skin or upper respiratory system, an antihistamine tablet or syrup can be very effective. However, the medication will take at least 15 minutes to work.
- ▶ 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.
- ▶ Adrenaline (also known as epinephrine) acts quickly to constrict blood vessels, relax smooth muscles in the lungs to improve breathing, stimulate the heartbeat and help to stop swelling in the larynx & airways as well as around the face and lips.
- ▶ Antihistamines, steroids and bronchodilators can be used subsequently after adrenaline has been administered.

Figure 10: Anaphylactic reaction algorithm, with thanks to the Resuscitation Council (UK)



Adrenaline dosage if drawing up⁵¹

Adrenaline (give IM)

IM doses of 1:1000 adrenaline (repeat after five minutes if no better)

- ▶ Adult 500 micrograms IM (0.5 mL)
- ▶ Child more than 12 years: 500 micrograms IM (0.5 mL)
- ▶ Child 6-12 years: 300 micrograms IM (0.3 mL)
- ▶ Child less than six years: 150 micrograms IM (0.15 mL).

The incidence of acute severe anaphylaxis following vaccination is extremely rare: about 1:1 million.

Patients with an allergy to egg or gelatine may be more likely to react to the flu vaccine and other vaccines containing derivatives of these substances.

The preferred needle length for an IM injection⁵¹

A standard needle (25 mm i.e 1 inch and 23 G) should be used to inject intramuscular adrenaline.

The best site for an intramuscular injection of adrenaline for the treatment of an anaphylactic reaction is the antero-lateral aspect of the middle third of the thigh &. An option is the deltoid muscle in the upper arm.

The needle needs to be long enough to ensure that the adrenaline is injected into muscle. The current Resuscitation Council (UK) guidance states that a 25 mm length needle is best and suitable for all ages.

Patient positioning for anaphylaxis⁵¹

Someone suffering from acute anaphylaxis is also likely to be showing signs of clinical shock. Reassuring the casualty and positioning them appropriately can make a major difference to their treatment. They should also be kept warm and dry.

If someone is very short of breath, they should be encouraged to sit in an upright position to help their breathing; putting something under their knees to help increase their circulation can be very helpful – into the 'lazy W' position.

If they are not having difficulty breathing, but are 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. Encourage them to turn their head to one side if they are likely to vomit. They should be covered to keep them warm and kept in this position until the paramedics arrive.

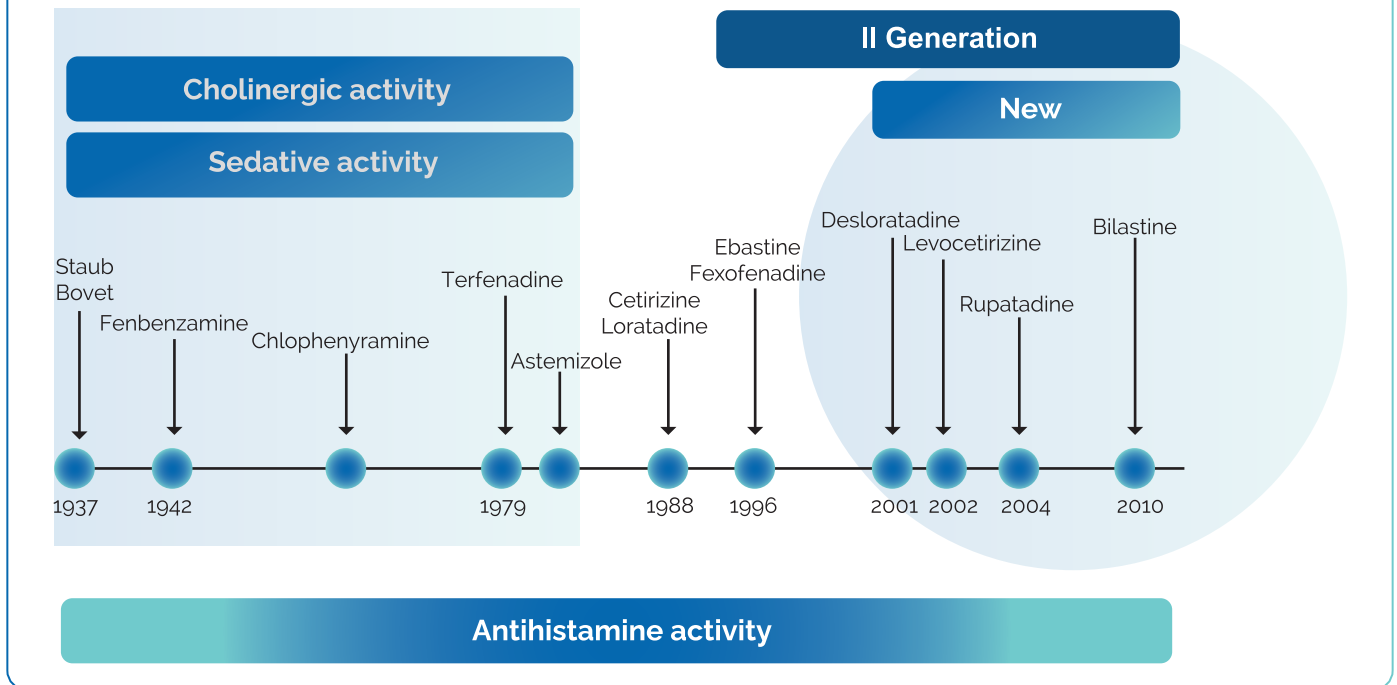
Do not get them up until they have been medically assessed.

Treat for shock if the patient is showing symptoms of shock and is not having breathing problems.

Role of antihistaminic drugs in allergic disorders

Mechanism of action of antihistaminic drugs

Figure 11: Different types of allergies and its age-wise prevalence



Endogenous histamine is released during an allergic reaction, resulting in increased vascular permeability and shift of fluid from capillaries to the surrounding tissues. This leads to swelling seen with allergic reactions. Antihistamines stop this effect by acting as antagonists at the H-1 receptors and can help relieve symptoms of allergy⁵².

Possible mechanisms by which antihistamines could suppress cough due to upper airway cough syndrome (UACS):

- ▶ Direct inhibition of the peripheral afferent nerves that cause cough.
- ▶ An indirect peripheral action for inhibiting pharyngeal or laryngeal mechanoreceptors that elicit cough.
- ▶ Direct central inhibitory action on the Histamine H1 receptors in the central nervous system.
- ▶ Indirect central inhibitory action on Histamine H1 receptors in the central nervous system which regulate nasal mucus secretion⁵³.

b. Brief on antihistamine classification⁵⁴**Table 20: Antihistamine classification**

	First generation	Second generation
Alkylamines	Chlorpheniramine, Pheniramine Clemastine, Cyproheptadine, Diphenhydramine, Promethazine	Acrivastine
Piperazines	Hydroxyzine	Cetirizine, Levocetirizine
Piperidines	Cyproheptadine, Ketotifen	Astemizole, Desloratadine, Fexofenadine, Loratadine, Mizolastine, Olopatadine, Terfenadine, Bilastine
Ethanolamines	Dimenhydrinate, Diphenhydramine, Doxylamine	—
Phenothiazines	Promethazine	—
Others	Doxepin	Azelastine

c. Antihistamines

Table 21: Hydroxyzine⁵⁵

Hydroxyzine is used for relieving symptoms of chronic pruritus due to dermatological and non-dermatological causes. It binds to H1 receptors & Muscarinic, Alpha-adrenergic, Dopamine, and Serotonin receptors, Sedative and anxiolytic effect along with potent anti-histaminic action makes it first line treatment in acute and chronic pruritus

CDSCO approved Indications:

- ▶ For the management of pruritus due to allergic conditions such as chronic urticaria and atopic and contact dermatosis, and in histamine-mediated pruritis

Dosage:

- ▶ Adults—25 milligrams (mg) up to 3 or 4 times a day.
- ▶ Children:
 - 12 months to 6 years old: 1 mg/kg/day up to 2.5 mg/kg/day in divided doses
 - Over 6 years old 1 mg/kg/day up to 2 mg/kg/day in divided doses

Dosage forms available:

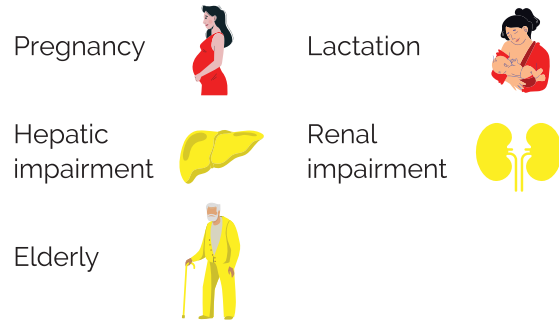


Precautions:

Contraindicated in patients with:

- ▶ Early pregnancy
- ▶ Prolonged QT interval.
- ▶ Patients who have shown a previous hypersensitivity to any component of this medication.

In Special Patient Populations:



Note: Yellow: Use with caution; Red: No

Disclaimer

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Table 22: Cetirizine⁵⁶

Cetirizine is fast acting antihistamine with symptom control seen within 20mins of oral ingestion. Allergic Rhinitis and Urticaria symptoms at night can be effectively managed by Cetirizine thus improving the nighttime sleep quality and reducing the early morning symptoms.

CDSCO approved Indications:

- ▶ For the management of Allergic Rhinitis and Chronic urticaria





Precautions:

- ▶ Patients with a known hypersensitivity to cetirizine hydrochloride or any of its ingredients, levocetirizine, or hydroxyzine.

Dosage:

- ▶ 12 Years and Older: 5 or 10 mg once daily depending on symptom severity, not to exceed 10 mg per day
- ▶ Children 6 to 11 Years: 5 or 10 mg once a day, not to exceed 10 mg per day
- ▶ Children 2 to 6 Years 2.5 mg once a day.

In Special Patient Populations:

Pregnancy		Lactation	
Hepatic impairment		Renal impairment	

Note: Green: Yes; Yellow: Use with caution; Red: No

Dosage forms available:

Tablet  Syrup  Drops 

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Table 23: Levocetirizine⁵⁷

Levocetirizine has high bioavailability, high affinity, and occupancy of the H1 receptor due to selective and specific binding of the receptors. This attribute allows for longer duration of action with greater magnitude of allergy relief.

CDSCO approved Indications:

- ▶ For the treatment of allergic rhinitis and chronic urticaria

Dosage:

- ▶ Allergic Rhinitis
Children 6 Months to 2 Years of Age
1.25 mg once daily
12 years of age and Adults: 5mg once daily
Children 6 to 11 years of age
2.5 mg once daily
- ▶ Chronic Urticaria
Adults and children 12 years of age and older
5 mg once daily.
Children 6 to 11 years of age
2.5 mg once daily.
Children 6 months to 5 years of age
1.25 once daily.

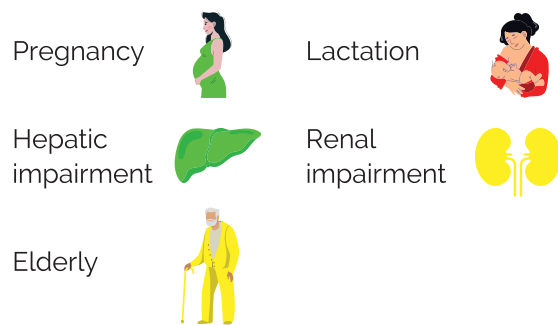
Dosage forms available:



Precautions:

- ▶ Patients with a known hypersensitivity to Levocetirizine or any of its ingredients.
- ▶ Patients with end-stage renal disease at less than 10 mL/min creatinine clearance or patients undergoing hemodialysis.

In Special Patient Populations:



Note: Green: Yes; Yellow: Use with caution; Red: No

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Table 24: Fexofenadine⁵⁸

Fexofenadine is clinically effective in the treatment of seasonal allergic rhinitis and chronic idiopathic urticaria for which it is a suitable option for first-line therapy. Comparative data suggest that fexofenadine is as effective as loratadine or cetirizine in the treatment of seasonal allergic rhinitis.

CDSCO approved Indications:

- ▶ In the treatment of relief of symptoms associated with seasonal allergic rhinitis and chronic idiopathic urticaria in children 2 years of age and older as well as adults.

Dosage:

- ▶ Adults- 120mg or 180 mg daily
- ▶ Children:
 - 30mg for relief of seasonal allergic rhinitis in children (6-12yrs)
 - 60mg-120 mg tab for relief of chronic idiopathic urticaria in 12yrs age and older children

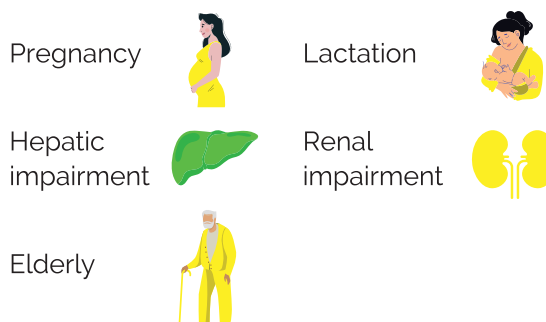
Dosage forms available:



Precautions:

- ▶ Patients with known hypersensitivity to any of its ingredients.
- ▶ Fexofenadine should not be taken closely in time with aluminium and magnesium containing antacid.

In Special Patient Populations:



Note: Green: Yes; Yellow: Use with caution

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Table 25: Bilastine⁵⁹

Bilastine is one of the newer generations of antihistamines. It reportedly does not cause sedation, has quick onset of action and long duration of action and high affinity to H₁ receptor. Bilastine does not have any negative effect even in extreme driving conditions as assessed by the Formula One (F1) high-speed simulator-driving test and it does not cause sleepiness or impaired performance on tasks related to flying

CDSCO approved Indications:

- ▶ For Symptomatic treatment of allergic rhino-conjunctivitis (seasonal and perennial) and urticaria.

Dosage:

- ▶ Adults and adolescents (12 years of age and over)- 20 mg bilastine once
- ▶ 6 years to 11 years may be prescribed the 10 mg orodispersible tablets or oral solution
- ▶ For chronic spontaneous urticaria in adults- 40mg






Dosage forms available:



Precautions:

- ▶ The tablet should be taken one hour before or two hours after intake of food interferes with its absorption.
- ▶ Do not drink fruit juice (grapefruit juice in particular) during the hour before you take your dose or for two hours afterwards
- ▶ Co-administration of Bilastine and P-glycoprotein inhibitors should be avoided in patients with moderate or severe renal impairment

In Special Patient Populations:

Pregnancy 	Lactation 
Hepatic impairment 	Renal impairment 
Elderly 	

Note: Green: Yes; Orange: No data available

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d. Combination of antihistamine and LTRA

- ▶ Leukotriene receptor antagonists have particular benefits for patients with exercise-induced asthma.
- ▶ Montelukast is an effective drug in allergic rhinitis to decrease nasal inflammation and limit nasal congestion, sneezing, and rhinorrhea.
- ▶ They are indicated as monotherapy but have been widely recommended as an adjunct to antihistamines or intranasal corticosteroids.
- ▶ These drugs primarily help with congestion and are particularly useful in asthmatics where they may have the double benefit of improving lower airway disease⁶⁰.
- ▶ Montelukast is more effective than placebo in treating the overall symptoms of allergic rhinitis while the combined therapy of montelukast and an oral antihistamine is superior to either montelukast or an oral antihistamine alone⁶¹.
- ▶ Both antihistamines and antileukotrienes have been found to be useful when used alone in allergic rhinitis and asthma.
- ▶ Combination of both drugs showed a synergistic effect in treating seasonal allergic rhinitis. In persistent allergic rhinitis, montelukast, levocetirizine, desloratadine, and the montelukast/antihistamine combinations significantly improved nasal symptoms during the first 24 hours, but improvement at the end of 6 weeks was significantly greater than that achieved on the 1st day of therapy in patients treated with montelukast alone or in combination therapy with the antihistamine⁶⁰.
- ▶ The U.S. Food and Drug Administration (FDA) has given warnings about rare behaviour and mood-related changes with montelukast including but not limited to agitation, anxiety, restlessness, sleep disturbance, bad dreams, and depression. However, The Sentinel study, which studied asthma patients 6 years and older, and other observational studies did not find an increased risk of mental health side effects with montelukast compared to inhaled corticosteroids (ICS)⁶².

When to refer to a specialist?

Table 26: When to refer to a specialist?

Allergic disorder	Cause for referral
Asthma	<ul style="list-style-type: none"> ▶ Persistent uncontrolled asthma or frequent exacerbations, or low lung function despite correct inhaler technique. ▶ Symptoms suggesting complications ▶ Uncontrolled asthma ▶ Severe asthma ▶ Persistent asthma⁶³
Allergic rhinitis	<ul style="list-style-type: none"> ▶ Presence of nasal polyps ▶ Patient is experiencing moderate-severe symptoms, recurrent otitis media, coexisting asthma, recurrent sinusitis, or symptoms that are not responding to treatment. ▶ If patients have chronic symptoms and do not want to take daily medications or if skin testing is necessary to confirm an unclear allergy diagnosis. ▶ Sublingual immunotherapy is considered as a treatment option⁶⁴.
Atopic dermatitis	<ul style="list-style-type: none"> ▶ Mild or moderate AD not responding to treatment after 2 months. ▶ Severe or poorly controlled AD despite management recommendations (topical steroids, wet wrap therapy, and oral antihistamines)³⁹.
Urticaria	<ul style="list-style-type: none"> ▶ Persistent or severe symptoms ▶ Chronic symptoms affecting work/sleep/study ▶ Patients require immunomodulating therapies⁶⁵ ▶ All cases of Anaphylaxis must be referred to an Allergy Specialist for further evaluation and treatment

Current barriers in allergy management

- ▶ Shortage of allergy specialists.
- ▶ Limited access to allergen immunotherapy and biologics.
- ▶ Limited access to basic and post-graduate training in allergic diseases.
- ▶ Inappropriate/inaccurate blood tests or unproven diagnostic methods that confuse patients and their doctors.

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