

Child with Allergies or Allergic Reactions

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Abstract Incidence of allergic disorders in children has increased significantly over time due to environmental and life-style changes. These include allergic rhinitis, atopic dermatitis, allergic conjunctivitis, food allergies, bronchial asthma, drug allergies, insect bites and anaphylaxis; most being IgE-mediated type 1 hypersensitivity reactions to common environmental and food antigens. Although most of them are self-limiting, they may adversely affect the quality of life and sometimes become life-threatening as well. These conditions are more likely to get underestimated, or over-diagnosed as recurrent infections. Hence a careful history and physical examination by attending pediatrician are necessary to differentiate it from infections. Diagnostic tests have limited value in identifying the inciting allergen. Management includes avoidance of the inciting allergens (if known), combined with symptomatic relief provided by a combination of pharmacological agents, *e.g.*, antihistamines, anticholinergics, chromones, leukotriene-modifying agents, topical and systemic steroids. Further, specialist consultation needs to be sought, for children with recurrent or persistent symptoms. The scope of this manuscript does not include bronchial asthma.

Keywords Allergy · Allergic reactions · Anaphylaxis · Children

Introduction

Allergy or atopy is a condition of increased reactivity to common environmental and food antigens which in recent decades, has increased multi-fold due to indoor and outdoor air pollution, exposure to tobacco smoke; and changing host factors, *e.g.*, obesity. There is a strong familial predisposition to atopy, with 60% heritability found in twin studies of asthma and atopic dermatitis. Risk of allergy in a child approaches 50% with one allergic parent, and 66% with both parents being allergic. Complex genetic factors like regulation of IgE synthesis, eosinophil and mast cell responses, innate immune response and barrier function in specific target organs (*i.e.*, skin, lungs and gut) are involved. Atopic individuals may have manifestations limited to one or more specific organs like nose, lungs, skin, eyes and gut, or may present with systemic features.

Goals of Assessment in an Urgent Care Facility

- Identify children with a serious allergies and provide immediate stabilization
- Identification and treatment of benign causes
- Parental guidance and counselling

Etiology and Pathogenesis

Allergies are type 1 hypersensitivity reactions, triggered by allergens which are almost always proteins. These induce Immunoglobulin E (IgE) antibodies leading to type 1 hypersensitivity reaction on subsequent exposure to the same allergen. IgE-mediated reactions can be classified into three reaction patterns. The ‘Early Phase’ response occurs immediately

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in the target organ after exposure to the allergen. Mast cell degranulation and release of preformed mediators occurs during the first 30 min and then resolves in 1–3 h. The increased local vascular permeability causes tissue swelling, pruritis, rash, sneezing, acute abdominal pain and wheezing, depending on the organ involved.

‘Late Phase’ response occurs within hours of exposure, peaking by 6–12 h and resolves by 24 h. It is due to recruitment of circulating inflammatory cells to tissues by cytokines leading to sustained nasal block, persistent wheezing and skin rash. In the third phase of chronic allergic reaction, tissue inflammation persists for years, resulting in tissue remodeling, thickening of airway walls and submucosal tissues (bronchial asthma) and lichenification of skin (atopic dermatitis).

Clinical Presentation

Clinical presentation depends on the target organ and the allergen involved. Patients often suffer from more than one allergic disease *e.g.*, a child may suffer from both atopic dermatitis and allergic rhinitis. Common allergic reactions presenting to an Urgent Care Centre are as follows:

Allergic Rhinitis (AR)

Allergic inflammation of nasal mucosa is characterised by mucosal congestion, nasal discharge and itching, associated with episodes of sneezing. It is highly prevalent in children and affects their quality of life and school performance. It is classified into a) Intermittent AR (IAR) [symptoms for <4 d per wk lasting for <4 consecutive wk] and b) Persistent AR (PAR) [symptoms are for >4 d per wk lasting for >4 consecutive wk]. Both are further classified as mild or moderate to severe. Mild disease will not hamper sleep, daily routine work, sports, school activities, whereas moderate/severe disease will cause impairment in one or more of these [1].

PAR is caused by allergens present perennially, *e.g.*, cockroaches, animal dander and house dust mites. Children with AR may have associated allergic conjunctivitis, serous otitis media, atopic dermatitis, adeno-tonsillar hypertrophy and sinusitis. These children have a three-fold increased risk of developing bronchial asthma at a later age. They usually have paroxysms of sneezing, snorting and repeated throat clearing. Nasal polyps, turbinate hypertrophy and typically thin and clear nasal secretions are seen in allergic rhinitis. Pale to purple nasal mucosa is characteristic of allergic rhinitis as opposed to beefy red in non-allergic causes of rhinitis. Children have ‘allergic salute’ (rubbing of nose upwards with the palms) due to nasal itching and nasal discharge. It helps in relieving itching and nasal obstruction. ‘Nasal crease’ is a horizontal crease on the nose due to such repeated manoeuvre. Children may also have continuous open mouth breathing.

‘Allergic cluck’ is produced when tongue is placed against the palatal roof in an attempt to scratch it. These signs can be useful pointers for diagnosis.

Allergic Conjunctivitis

Allergic conjunctivitis may occur as a single entity or in association with other allergic disorders. It occurs due to continuing exposure to airborne allergens, and is usually bilateral. Affected patients present with eye itching, conjunctival congestion with chemosis. Forceful rubbing of eyes with side of fists and thumbs is frequently seen. Eye discharge can be watery, frequently described as ‘stringy’ or ‘ropy’. Symptoms are usually seasonal, less frequently perennial and triggered by pollens or fungal spores. Vernal keratoconjunctivitis is a chronic severe bilateral inflammation of upper tarsal conjunctiva, associated with giant papillae, described as ‘cobble stoning’. Atopic keratoconjunctivitis is seen in children with atopic dermatitis in whom there is inflammation of the lower tarsal conjunctiva [2].

Atopic Dermatitis

Atopic dermatitis, also called eczema, is frequently associated with atopic march, which is development of allergic rhinitis and/or bronchial asthma in later life. It is a common chronic inflammation of skin, involving 10–30% of children worldwide [3]. Repetitive scratching leads to excoriation marks. Dry skin (xerosis), is common. ‘Dennis Morgan folds’ are prominent infraorbital folds of skin extending from inner canthus, parallel to lower lid margin. Hyperlinearity, *i.e.*, prominent skin creases of palms and soles is a characteristic finding. Keratosis pilaris, wherein hair follicles plugged by keratin are seen as skin colored papules is found. Erythematous squamous plaques, lichenification/ thickening of skin is seen in chronic atopic dermatitis.

Food Allergies

Adverse reactions to food can be food intolerance (adverse physiologic response to a food) or food allergy (adverse immunologic responses– IgE-mediated or non-IgE mediated). Cow’s milk, peanuts, eggs, fish, soy and wheat are common food allergens. Symptoms may be related to gut (oral itching, vomiting, diarrhea, abdominal cramps), skin (urticaria, angioedema, itching), respiratory tract (wheezing, sneezing, laryngeal edema, stridor) or cardiovascular (hypotension, syncope, dysrhythmias) [4]. Elimination of and reproducible reaction after challenge with a specific food item raises its suspicion. Timely identification and elimination of food item from the diet is the treatment. Exclusive breast feeding for

first 6 mo along with delayed introduction of potential allergens in the diet may help prevent the development of allergies later in life.

Urticaria

Urticaria and angioedema are IgE-mediated reactions. Acute urticaria lasts <6 wk while chronic lasts >6 wk. The causes and mechanisms and treatment strategies are different for both. A typical urticarial lesion is transient, erythematous blanchable rash that is pruritic and does not leave any residua. Lesions associated with purpura, burning instead of itching, non-blanchable, lasting >24 h and leaving residual scar points to an underlying systemic vasculitis.

Acute urticaria may be secondary to foods, medications, insect stings, infections (bacterial, viral, fungal or parasitic), contact allergy (latex, pollen, caterpillars, *etc.*) or transfusion reactions. However, chronic urticaria may be related to physical factors (cold, heat, vibration, dermatographism *etc.*), autoimmune diseases (systemic lupus erythematosus, juvenile idiopathic arthritis, *etc.*), neoplasms (lymphoma, mastocytosis, leukemia), hereditary angioedema, *etc.* [5]. In children with angioedema, drug association must be excluded, *e.g.*, angiotensin inhibitors and non-steroidal anti-inflammatory drugs. Routine laboratory tests are not cost-effective in chronic urticaria, unless there are clinical surrogates of autoimmune diseases.

Drug Reactions

Unpredictable drug reactions are dose independent, are not related to its pharmacological actions and occur in patients who are genetically predisposed. These include allergic (hypersensitivity) and idiosyncratic reactions which can vary from trivial macular rash or abdominal pain to life-threatening anaphylactic shock.

Reactions to Insect Bites

Insect venoms contain numerous proteins which have allergenic potential. Most insect stings cause local tissue reaction and do not represent an allergic response. Systemic allergic response is IgE-mediated and is usually due to stings of the order Hymenoptera [*e.g.*, honey bee, bumble bee (bhanvaraa), wasp, hornet, yellow jacket, harvester ants] and rarely from ticks, spiders and scorpions.

These reactions are categorised on the basis of their severity: Simple local reactions involve limited swelling and pain and lasts <24 h. Large local reactions involve larger areas (>10 cm) around the sting site. Generalised

cutaneous reactions progress in minutes and include urticaria, angioedema and itching beyond the site of the sting. Systemic reactions include symptoms of anaphylaxis. Serum sickness, also seen rarely, is due to delayed reaction to insect sting.

Anaphylaxis

Anaphylaxis has been defined by the World Allergy Organisation as ‘a serious allergic reaction that is rapid in onset and might cause death’ [6]. Anaphylaxis in community setting is mostly due to food allergy, whereas in hospital setting it is due to drugs, latex or blood products. In young children and infants, it is often missed or diagnosed late due to their inability to communicate symptoms, *e.g.*, itching, feeling of warmth, nasal congestion, pre-syncope, headache, *etc.*

Diagnosis of anaphylaxis is made when any one of the following three criteria are met [7]—

1. Acute onset of symptoms (within minutes or several hours) with skin and/or mucosal tissue involvement such as generalized hives, pruritus, flushing, swollen lips, tongue, or uvula and at least one of the following:
 - 1.1 Respiratory symptoms, such as rhinitis, hoarseness, dyspnea, wheezing, stridor, decreased peak expiratory flow rate (PEFR) or oxygen saturation.
 - 1.2 Reduced blood pressure or multi-organ system failure, such as hypotonia (collapse), syncope, or incontinence.
2. Two or more of the following symptoms that occur after contact with a suspected allergen (within minutes or several hours)
 - 2.1 Skin and submucosal membrane involvement, such as generalized hives, pruritus, flushing, swollen lips, tongue, or uvula.
 - 2.2 Respiratory symptoms, such as rhinitis, hoarseness, dyspnea, wheezing, stridor, decreased peak expiratory flow rate (PEFR) or oxygen saturation.
 - 2.3 Reduced blood pressure or multi-organ system failure, such as hypotonia (collapse), syncope, or incontinence.
 - 2.4 Gastrointestinal tract involvement, such as abdominal pain, nausea, or vomiting.
3. Reduced blood pressure that occurs after contact with a known allergen (within minutes or several hours)
 - 3.1 For infants and children, systolic blood pressure lower than normal value according to age or decrease in systolic blood pressure of more than 30% of baseline.

- 3.2 For adults, systolic blood pressure less than 90 mmHg or decrease in systolic blood pressure more than 30% of baseline.

Approach to a Patient with Allergy

Clinical History

A complete history and thorough examination are vital. Description of symptoms with respect to onset, seasonal predilection, duration, exposure to common allergens, previous treatments and response to the same should be noted. Perennial allergies are due to indoor allergens such as dust mite, cockroaches, animal dander, *etc.* A thorough environmental survey needs to be done to identify potential source of allergen and cause of allergy. Heavy carpets and curtains serve as reservoir for fungi, dust, dust mites and animal dander. Exposure to indoor smoke, cigarette smoke, paint fumes, strong perfumes, kerosene, sawdust *etc.* should be enquired. Recurrent symptoms on ingesting a specific food item should arouse the suspicion of food allergy. Travel history, exacerbation or relief of symptoms after travel should be noted.

Physical Examination

Anthropometry is important, as chronic illness and intake of systemic corticosteroids can adversely affect the growth of the child. General examination should be conducted for nasal obstruction, mouth breathing, allergic stigmata like the allergic salute, nasal crease, allergic shiners (bluish-gray discoloration of skin beneath the lower eyelids, due to venous stasis) and Dennie-Morgan folds. Eyes should be examined for erythema and chemosis. Ear should be seen for serous otitis media and lobes and post auricular area, for atopic eczema. Children with signs of chronic upper airway obstruction like snoring and mouth breathing should be examined for adeno-tonsillar hypertrophy. Post nasal drip may be there in children with recurrent throat clearing and snorting. Examination should also look for angioedema, swelling of tongue, stridor (in cases of acute anaphylactic reactions) and presence of wheeze.

Investigations

Investigations can be divided into in vitro and in vivo tests:

In Vitro Tests

Peripheral blood eosinophilia (>500 eosinophils/ μL) and nasal and bronchial smear eosinophilia using Hansel stain are

diagnostic as well as prognostic in allergic disorders. Although elevated total serum IgE levels may be more sensitive to detect such patients, allergen-specific IgE levels, as detected by Radioallergosorbant test (RAST), are more specific.

In Vivo Tests

Allergen skin testing using a prick/puncture technique is the most important primary procedure for the diagnosis of allergic disorders. Specific food challenges after a period of elimination help to clinch the diagnosis of food allergies.

Principles of Treatment of Allergic Diseases

The principles of management of allergic disorders include avoidance of exposure to the offending allergen, environmental control measures and pharmacological management of the acute and chronic symptoms of the allergies. In some patients, immunotherapy may be considered.

Parents must be counselled regarding the importance of appropriate environmental control measures like avoidance of furred pets, regular checking of attics and basements for water leaks and moulds, repair of moisture-prone areas, sealing cracks in the walls, avoiding wall to wall carpeting, heavy curtains, upholstery, regular washing of the bedding, reducing the clutter and indoor humidity in the house. During the spring or pollen season, outdoor activities may be restricted. Windows should be kept shut during the pollen season and high efficiency particulate air filters may be useful during such season.

Pharmacotherapy

Antihistamines

Orally administered antihistamines have good systemic absorption and tissue penetration. First generation antihistamines (*e.g.*, promethazine, chlorpheniramine, diphenhydramine, hydroxidine *etc.*) are lipophilic, cross the blood brain barrier and have central nervous system (CNS) side-effects such as sedation and impaired cognition. Additionally, they cause drying of mucosa, constipation and urinary retention due to anticholinergic effects. They need to be administered 3–4 times daily. Second generation antihistamines (*e.g.*, cetirizine, fexofenadine, loratadine *etc.*) are non-sedating or less sedating and most have a once-a-day dosing that is more convenient for children. These are first-line agents in treatment of allergic rhinitis, allergic conjunctivitis and urticaria [8]. Topical antihistamines are also available for management of allergic conjunctivitis and rhinitis, *e.g.*, olopatadine eye drops, azelastine eye drops and nasal spray.

Adrenergic Agents

Systemic Agents Adrenaline is the drug of choice in anaphylaxis. Children with known food hypersensitivity and previous anaphylactic reactions to drugs should ideally carry auto-injectors of adrenaline with them. α -receptor mediated vasoconstriction helps correct hypotension and relieve mucosal edema while β -receptor mediates bronchodilation. Pseudoephedrine and phenylephrine are the oral adrenergics that may be used in rhinitis provided the children are >6 y of age, and do not have diabetes and hypertension.

Topical Agents Topical adrenergic agents like oxymetazoline, tetrahydrozoline, xylometazoline are available as nasal drops and nasal spray. These are recommended for short duration to provide symptomatic relief of nasal obstruction in allergic rhinitis. However due to high risk of rebound congestion, their use should be restricted to 2–3 d.

Chromones

Chromones (*e.g.*, Cromolyn sodium and nedocromil sodium) inhibit the release of mast cell granules and block the early and late allergic response when administered prior to allergen exposure. They have a good safety profile even on long term use. Bioavailability through oral route is only 1%. Local application of these drugs are useful in allergic rhinitis and allergic conjunctivitis.

Glucocorticoids

As a potent anti-inflammatory agent, it is useful in the management of all allergic disorders. Systemic agents are administered orally or parenterally while topical preparations are available as nasal sprays, ophthalmic gels, eyedrops, topical ointments and inhalers. Topical steroid preparations include budesonide, clobetasol, betamethasone, fluticasone, mometasone, ciclesonide *etc.*

Leukotriene-Modifying Agents

They exhibit anti-inflammatory effects by blocking leukotriene receptors or their production. Monteleukast and zafirlukast are useful adjuncts in the management of allergic rhinitis, that does not respond to antihistamines.

Treatment of Specific Conditions

Anaphylaxis

Anaphylaxis is a medical emergency requiring immediate management with oxygen, intravenous fluids, systemic

adrenaline, antihistamines and hydrocortisone. Once adequacy of airway, breathing and circulation is ensured, intravenous adrenaline infusion forms mainstay of therapy. Alternatively, intramuscular adrenaline (0.01 mg/kg; max 0.3–0.5 mg) can also be given and may be repeated 2–3 times at an interval of 5–15 min [7]. Intraosseous infusion may be another good alternative. Due to the risk of recurrence of hypotension within 4–6 h of anaphylaxis, patients should at least be observed for 6 h in the Urgent Care Clinics or emergency rooms.

Allergic Rhinitis

Intermittent mild symptoms may be treated with oral antihistamines, preferably second generation ones. Children with persistent, moderate to severe symptoms are best treated with intranasal steroids. For moderate disease, intranasal corticosteroids alone suffice, however for more severe cases, addition of topical histamines (intranasal azelastine) may be beneficial. Nasal saline irrigation is helpful in clearing the nasal secretions [1].

Allergic Conjunctivitis

Treatment consists of avoidance of the antigen and use of artificial tears to irrigate and dilute the allergen. Topical antihistamines like olapatadine, azelastine, ketotifen along with systemic antihistamines form the first line of therapy. Topical decongestants like naphazoline act as adjunctive therapy. Topical steroids should be used cautiously as these preparations may cause cataract and glaucoma [2].

Acute Urticaria

First generation antihistamines (hydroxyzine, diphenhydramine) are commonly used. They are effective but sedating. Non-sedating antihistamines like cetirizine, fexofenadine and loratadine, can also be tried. Leukotriene antagonists may be considered when antihistamines fail even after 2–4 wk [5]. Short course of oral steroids may be considered for very severe urticaria.

Food Allergy

Avoidance of the triggering food is the primary step in the management of food allergy. Symptomatic management with antihistamines is helpful to manage symptoms of flushing and itching.

Contributions AMDR did the literature search and drafted the manuscript. AKB guided the framework of the manuscript and did a critical review and approved the version to be published. Dr. Muralidharan Jayashree will act as guarantor for this paper.

Compliance with Ethical Standards

Conflict of Interest None.

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