

INTRODUCTION TO ALLERGIC DISORDER IN PEDIATRIC

PRESENTED BY :

YAZAN YASEEN

AHMAD JASER

ISSA OBIEDAT

AHMAD MOHAYAR

FARES ALSHARIF

SUPERVISED BY:

Dr. ALA'A AL-DALA'IEN

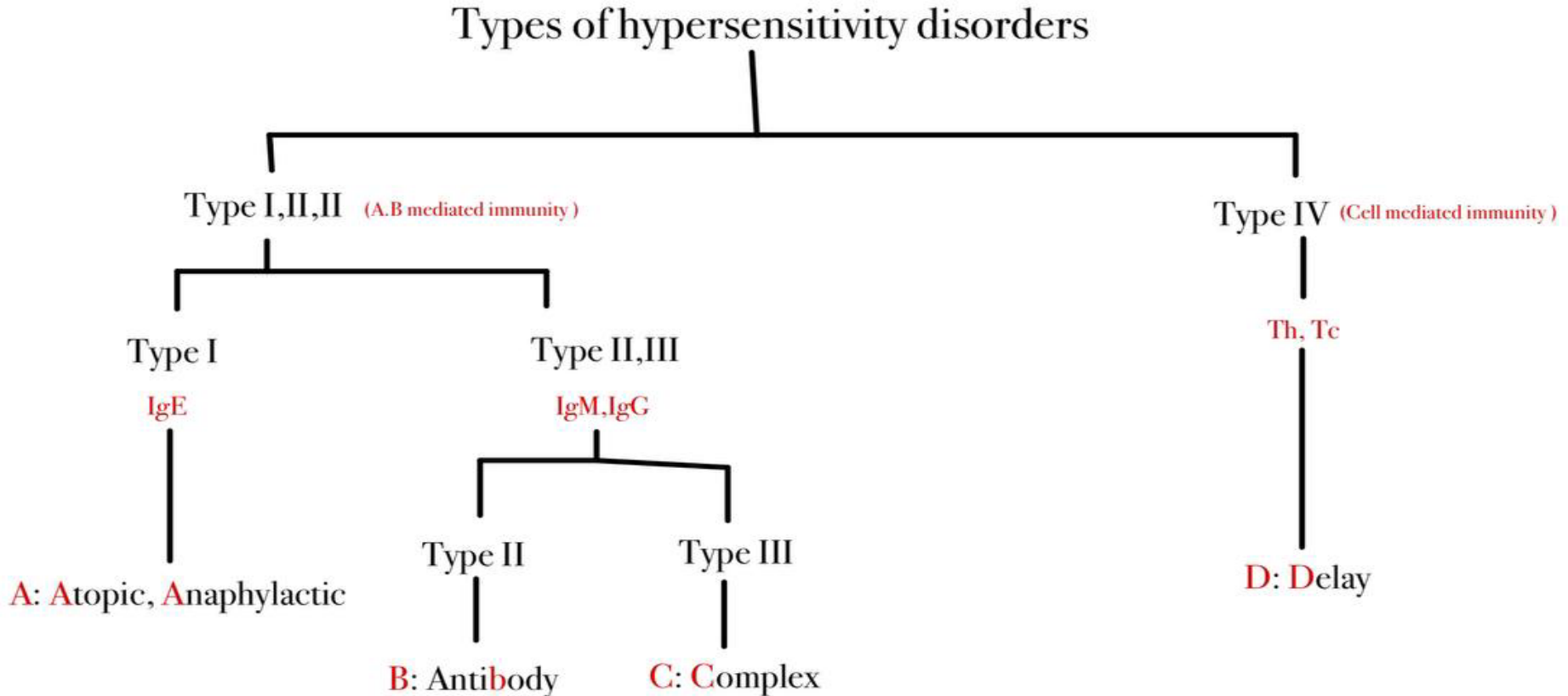


INTRODUCTION

An allergy is an exaggerated immune response to a typically harmless substance, known as an allergen. In individuals with allergies, the immune system mistakenly identifies the allergen as a threat, triggering the production of immunoglobulin E (IgE) antibodies. This response leads to the release of histamines and other chemicals, causing symptoms that can range from mild (such as sneezing and itching) to severe (such as anaphylaxis). Common allergens include pollen, pet dander, certain foods, and insect stings.

Hypersensitivity refers to undesirable reactions produced by the normal immune system, including allergies and autoimmunity. These reactions may be damaging, uncomfortable, or occasionally fatal and classified into four groups, based on the mechanism of tissue
Inflammation:

Types of hypersensitivity reactions:



• Types of hypersensitivity reactions: •

Type I (Immediate) Hypersensitivity

Commonly called allergy

Mediated by IgE antibodies produced by plasma cells in response to stimulation of Th2 cells by an antigens.

The antigens that stimulate it are called allergens (i.e. House dust, Pollens, Cosmetics, Insects, Clothing and Drug)

Exposure may be ingested, inhalation, injection or direct contact.

Type I hypersensitivity reactions can be systemic (e.g., systemic anaphylaxis) or localized to a specific target tissue or organ (e.g., allergic rhinitis, asthma).

• Types of hypersensitivity reactions: •

Type II (Cytotoxic) Hypersensitivity

Cytotoxic

Type II hypersensitivity involves IgG or IgM antibody-mediated

IgM or IgG immunoglobulin react with cell-surface antigens to activate the complements system and produce direct damage of the sell surface.

Transfusion reactions and hemolytic disease of the newborn are examples of type II hypersensitivity

• Types of hypersensitivity reactions: •

Type III (ICM) Hypersensitivity

Type III (Immune Complex-Mediated) Hypersensitivity

Type III hypersensitivity is also known as immune complex hypersensitivity.

The reaction may take 3-10 hours after exposure to the antigen (as in Arhus reaction).

The reaction may be general (e.g., serum sickness) or may involve individual organs including or other organs.

Antigens causing immune complex mediated injury are:

Exogenous

Endogenous

• Types of hypersensitivity reactions: •

Type IV (Cell Mediated) Hypersensitivity

Type IV (Delayed or Cell-Mediated) Hypersensitivity

Delayed hypersensitivity is a function of T Lymphocytes, not antibody.

It starts hours (or Days) after contact with the antigen and often lasts for days.

It can be transferred by immunologically committed (Sensitized) T cells, not by serum.

Principal pattern of immunologic response to variety of intra cellular microbiologic agents

i.e.: Mycobacterium Tuberculosis, Viruses, Fungi, Parasites

TABLE 77.1

Gell and Coombs Classification of Hypersensitivity Disorders

TYPE	INTERVAL BETWEEN EXPOSURE AND REACTION	EFFECTOR MOLECULE	TARGET OR ANTIGEN	EXAMPLES OF MEDIATORS	EXAMPLES
I Immediate Late phase	<30 min 2–12 hr	IgE	Pollens, food, venom, drugs	Histamine, tryptase, leukotrienes, prostaglandins, platelet-activating factor	Anaphylaxis, urticaria, allergic rhinitis, allergic asthma
II Cytotoxic antibody	Variable (min–hr)	IgM, IgG, IgA	Red blood cells, platelets	Complement	Hemolytic anemia, thrombocytopenia, Goodpasture syndrome
III Immune complex	1–3 wk after drug exposure	Antigen-antibody complexes	Blood vessels, liver, spleen, kidney, lung	Complement, anaphylatoxin	Serum sickness, hypersensitivity pneumonitis
IV Delayed type	2–7 days after drug exposure	Lymphocytes	<i>Mycobacterium tuberculosis</i> , chemicals	Cytokines (IFN- γ , TNF α , GM-CSF)	TB skin test reactions, contact dermatitis, graft-vs-host disease

GM-CSF, Granulocyte-macrophage colony-stimulating factor; IFN- γ , interferon- γ ; TB, tuberculosis; TNF α , tumor necrosis factor- α .

• Allergies to be covered:

- Allergic rhinitis
- Atopic dermatitis
- Urticaria and Angioedema
- Insect bites
- Food allergy
- Anaphylaxis

• Allergic Rhinitis: •

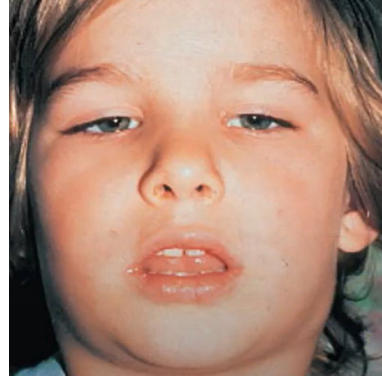
Allergic rhinitis (AR) is a common chronic disease affecting 20–30% of children. AR is an inflammatory disorder of the nasal mucosa marked by nasal congestion, rhinorrhea, and itching, often accompanied by sneezing and conjunctival inflammation.

• Symptoms of allergic rhinitis:

- Recurrent episodes of sneezing
- Pruritus, rhinorrhea
- Nasal congestion and lacrimation
- Snorting throat clearing
- Postnasal drip.
- Nasal obstruction unilateral or bilateral

• Sequelae of allergic rhinitis:

• Elongated facies

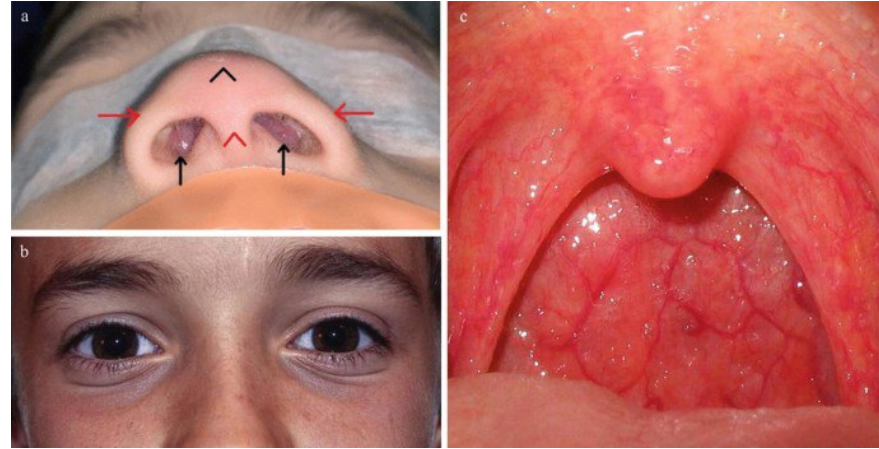


- Allergic shiners, allergic salute

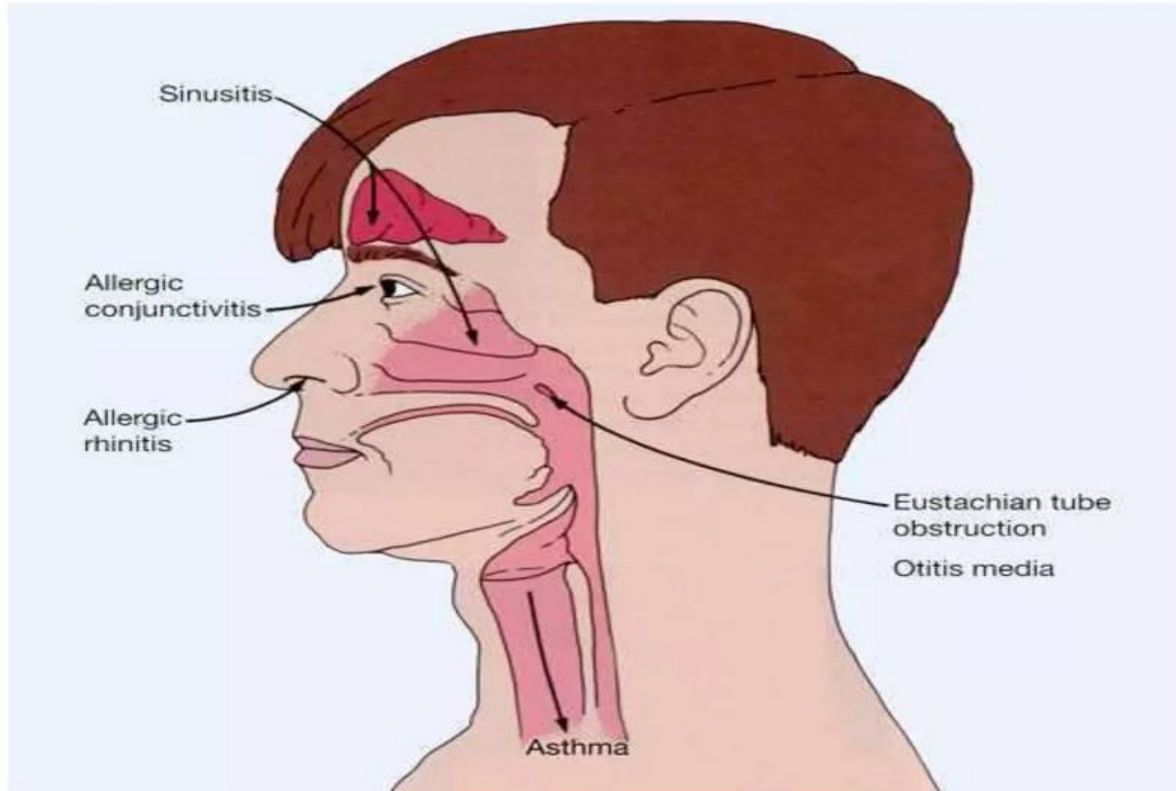


Sequelae of allergic rhinitis:

- Nose :Septal deviation, polyps, drainage, turbinate hypertrophy, hypo-nasality.
- Mouth :Cobble stoning of oropharynx
- Chest: wheezing



Related Anatomic Structures Compromised by Allergic Rhinitis



• Classification of allergic rhinitis:

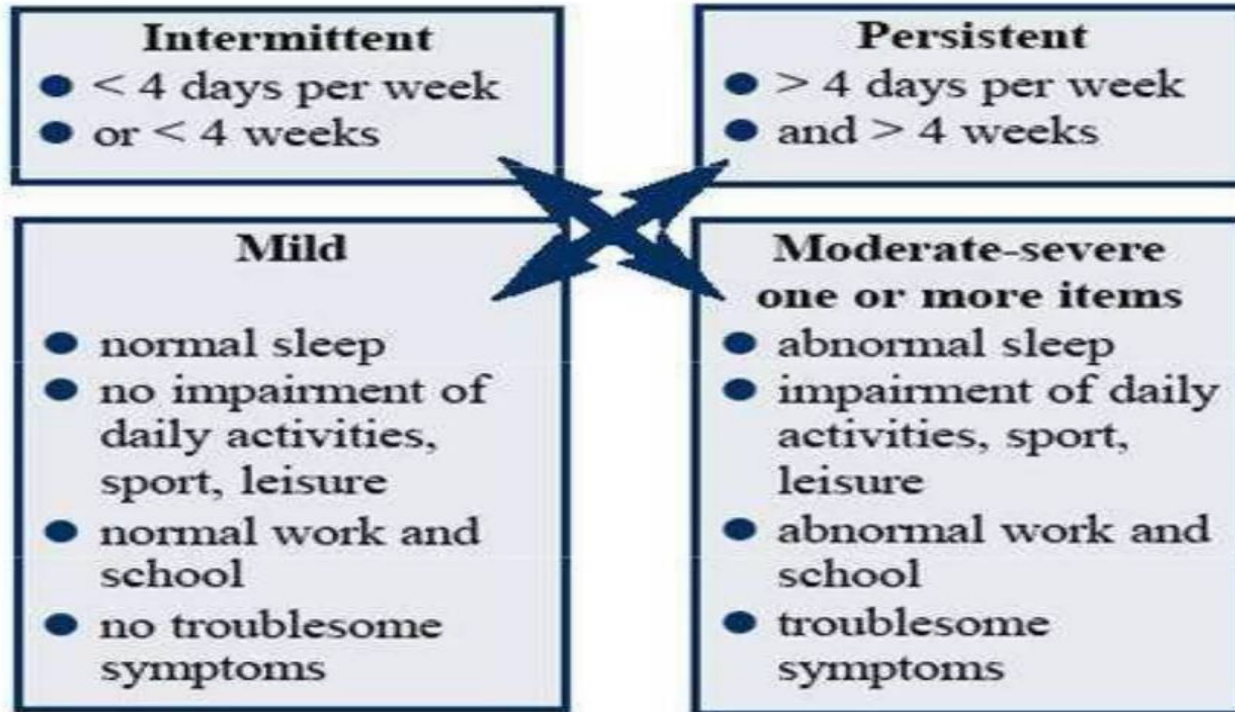
- Intermittent allergic rhinitis (acute) :

Symptoms present for less than 4 days a week, or for less than 4 consecutive weeks.

- Persistent allergic rhinitis (chronic) :

Symptoms present for more than 4 days a week and for more than 4 consecutive weeks

Severity Of Allergic rhinitis



Allergic Rhinitis And Quality Of Life:

- Sleep loss or disturbance
- Increased daytime sleepiness
- Learning problems
- Reduction in work productivity

Diagnosis:

- The 3 most common tests used to confirm the diagnosis:
 - 1) Skin testing
 - 2) Nasal smear
 - 3) In vitro testing for serum levels of specific IgE antibodies.

Prevention:

- Avoidance Of Allergens
- Removing a pet from the house
- Covering pillows and mattresses
- Washing bedding with hot water
- Vacuuming mattresses and pillows. No dry dusting

Pharmacotherapy

Drug type	Itch / sneezing	Discharge	Blockage	Impaired smell	Preparation
Antihistamines	+++	++	+	-	Fexofenadine Cetirizine
Anticholinergics	-	+++	-	-	Ipratropium
Decongestants	-	+++	++	-	Xylometazoline Oxymetazoline
Mast Cell Stabilizers	+	+	-	-	Sodium cromoglycate

• Urticaria and Angioedema:

- Urticaria (hives) is a vascular reaction of the skin characterized by wheals surrounded by a red halo or erythema.
- Cardinal symptom is PRURITUS
- Caused by swelling of the upper dermis
- Up to 20% of the population experience urticaria at some point in their lives

Rash in urticaria



• Angioedema: •

Angioedema can be caused by the same pathogenic mechanisms as urticaria, but the pathology is in the deep dermis and subcutaneous tissue.

- Swelling is the major manifestation
- Commonly affects the face or a portion of an extremity
- May be painful or burning, but not pruritic
- May last several days

Angioedema



Source: Usatine RP, Smith PA, Mayhew EJ, Chumley H: The Color Atlas of Family Medicine, Second Edition. www.accesmedicine.com
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• Common cause of acute urticarial:

- Idiopathic
- Upper respiratory streptococcal infections, helminthes
- Food reactions
- Shellfish, nuts etc.
- Drug reactions (penicillin, sulfonamide, NSAIDs)
- IV administration Blood products, contrast agents

• Chronic urticaria: •

- Idiopathic: over 50% of chronic urticaria
- Physical urticarias: many patients with chronic urticaria have physical factors that contribute to their urticaria
- These factors include pressure, cold, heat, water (aquagenic), sunlight (solar), vibration, and exercise
- Cholinergic urticaria is triggered by heat and emotion

• Dermatographism:

- Most common form of physical urticaria
- Sharply localized edema or wheal within seconds to minutes after the skin has been rubbed
- Affects 2-5% of the population



• Clinical findings: •

- Lesions typically appear over the course of minutes, enlarge, and then disappear within hours
- Individual wheals rarely last >12hrs
- Erythema blanches with pressure
- Urticaria may be acute or chronic
- Acute = new onset urticaria < 6 weeks
- Chronic = recurrent urticaria (most days) > 6 weeks
- Most urticaria is acute and resolves

• Diagnosis: •

- Urticaria is a clinical diagnosis
- A detailed history and physical examination
- If a physical urticaria is suspected, a challenge test with the respective trigger may be performed
- IgE-mediated food allergy is far more likely to present with acute urticaria
- A detailed food diary or dietary modification may reveal foods (or additives) that cause fluctuations in symptoms of chronic urticaria
- Allergy testing is not routinely performed in patients with chronic urticaria

Treatment

ANTI-HISTAMINE

•a) 1st Generation

Diphenhydramine

Hydroxyzine

Chlorpheniramine

b) 2nd Generation

Cetirizine

Loratadine

Fexofenadine

Epinephrine. intramuscularly - rarely needed

• Cyclosporine has been effective in some adults with chronic urticaria but its use is limited by hypertension and/or nephrotoxicity

● Hereditary angioedema ●

Hereditary angioedema (HAE) is an autosomal dominant disease due to a deficiency of C1-esterase inhibitor. The genetic defect may be caused by spontaneous mutation since approximately 25% of cases occur in patients without any family history.

The disease is estimated to affect approximately 10,000 persons in the United States. It is characterized by unpredictable, recurrent attacks of episodic swelling that involves the face, peripheral extremities, genitalia, abdomen, oropharynx, and pharynx. Episodes are often triggered by trauma. Asphyxiation from laryngeal attacks is a significant cause of mortality. Patients with HAE rarely have urticaria associated with angioedema, and the swelling is not relieved with antihistamines or oral corticosteroids. Most patients (85%) have type I disease, which is due to decreased production of C1-esterase inhibitor. A minority of patients (15%) have type II disease, which is due to production of dysfunctional C1-esterase inhibitor. A low C4 level serves as an initial screening test. Patients with reduced C4 should have quantitative and functional levels of C1-esterase inhibitor measured. C2 levels are low during an acute attack. HAE with normal C1 inhibitor patients have normal laboratory evaluation of C1-esterase inhibitor. These patients are more typically females. Treatment for HAE is divided into on-demand treatment for acute attacks and prophylaxis. Prophylactic C1 inhibitor concentrate has advantage over other prophylactic therapies in terms of availability, effectiveness, and side effects. Bradykinin is an important mediator in the pathophysiology of HAE, and newer treatments are aimed at blocking this mediator.

Food allergy:

Adverse reactions to foods consist of any untoward reaction following the ingestion of a food or food additive and are classically divided into

- food intolerances which are adverse physiologic responses
- food allergies which are adverse immunologic responses
- When allergens are encountered in the GI system, they activate an immune response. The allergic cascade is activated and response is seen.

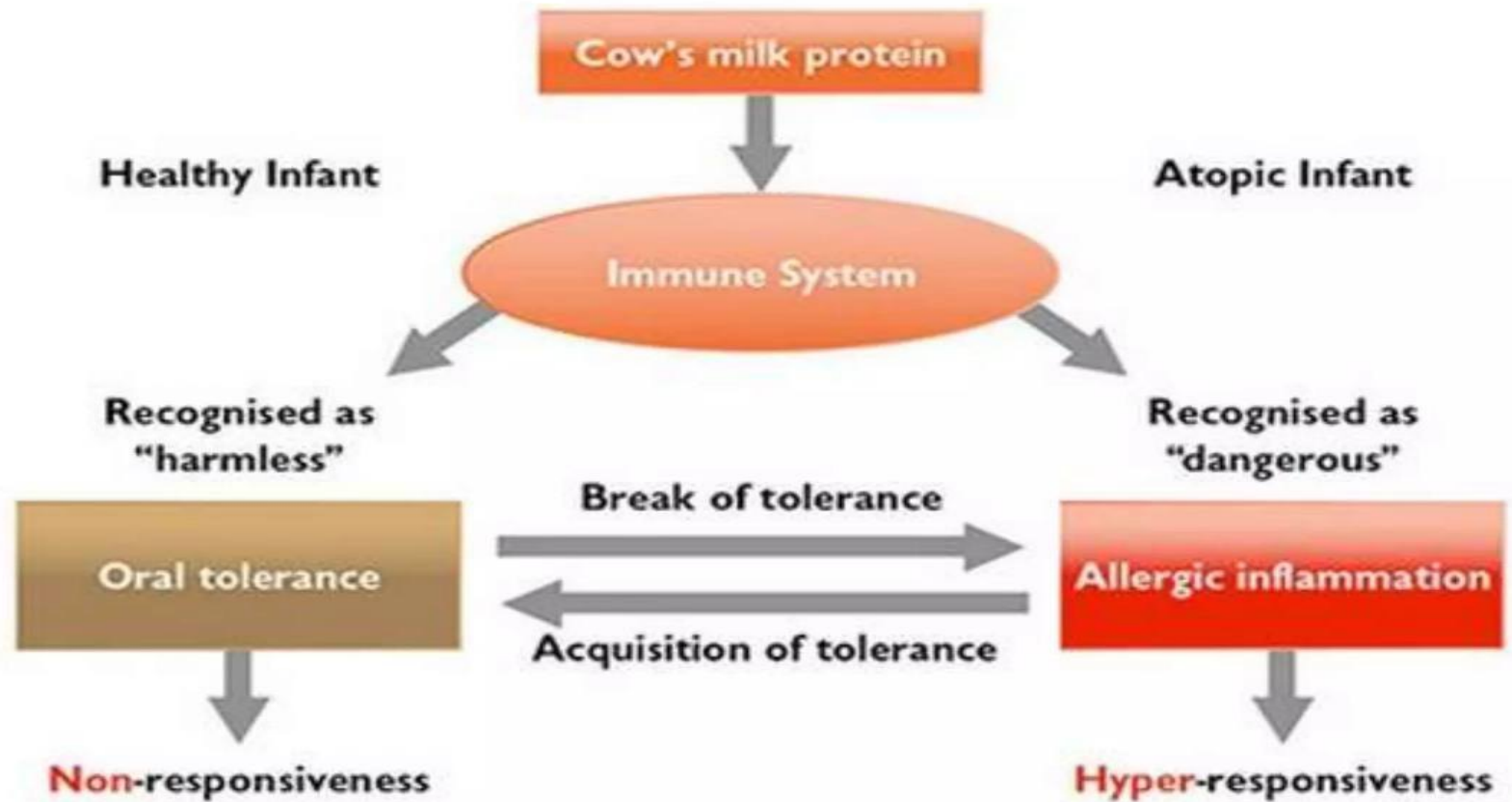
Common food allergens

- Peanuts
- Sea food
- Cow's milk
- Egg
- Wheat
- Soy products
- Fruits



**FOOD
ALLERGENS**





Clinical feature:

• Gastrointestinal :

1) Food protein-induced enterocolitis syndrome (FPIES) typically manifests in the first several months of life as irritability, intermittent vomiting and protracted diarrhea

2) Food protein-induced proctocolitis

presents in the first few month of life as blood-streaked stools in otherwise healthy infants

3) Food protein-induced enteropathy

often manifests in the first several months of life as diarrhea, often with steatorrhea and poor weight gain

4) Eosinophilic gastroenteropathies may

appear from infancy through adolescence, more frequently in boys manifests as chronic gastroesophageal reflux, intermittent emesis, food refusal, abdominal pain, dysphagia, irritability, sleep disturbance, and failure to respond to conventional reflux medications

Clinical feature:

- Oral allergy syndrome
- Skin Manifestations

(Atopic dermatitis, Acute urticaria and angioedema)

- Perioral dermatitis & perioral flushing
- Respiratory manifestations: Food induced rhinoconjunctivitis
- Anaphylaxis

Treatment:

- Appropriate identification and elimination of foods responsible for food hypersensitivity reactions are the only validated treatments for food allergies.



Anaphylaxis

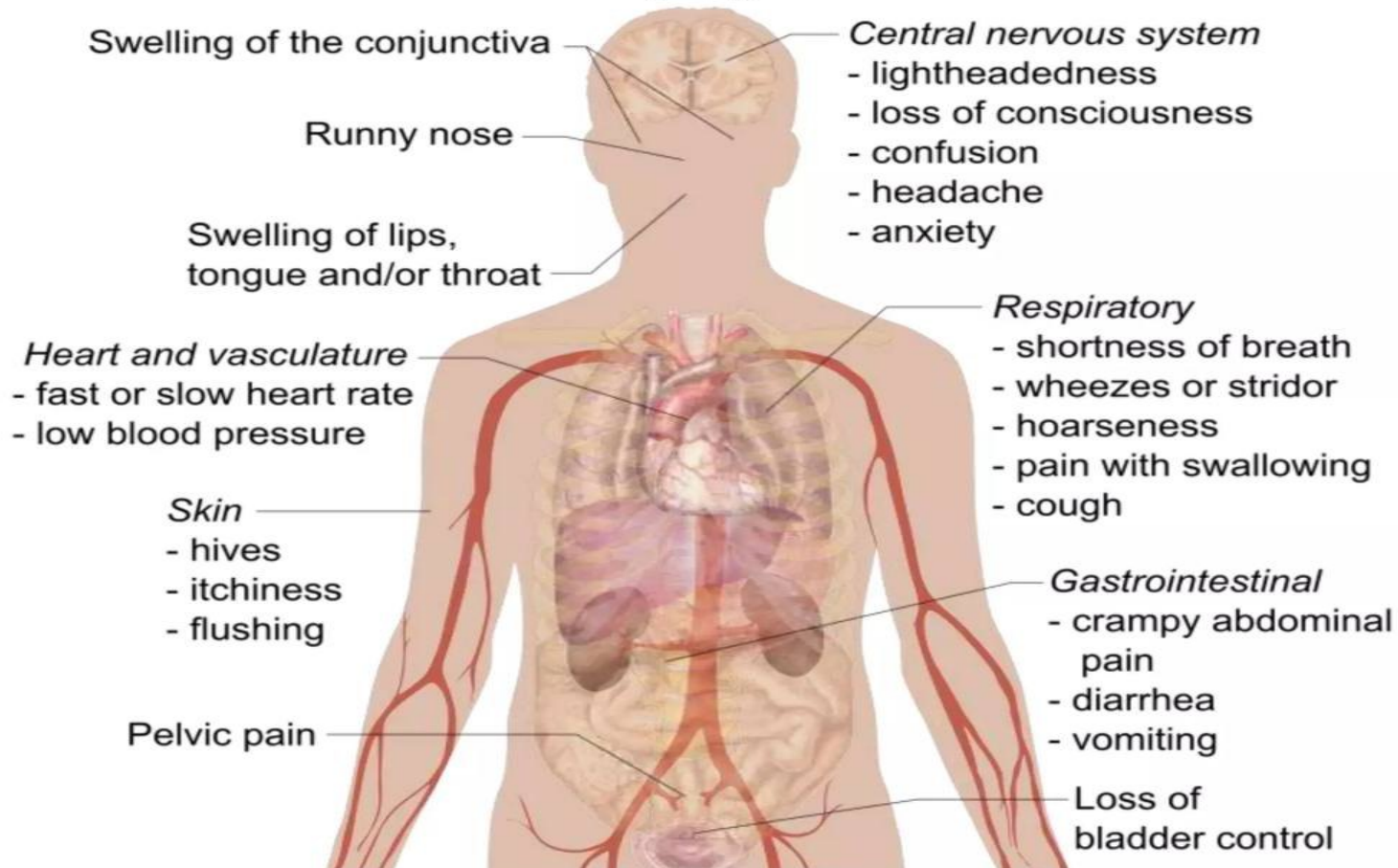
- Anaphylaxis is defined as a serious allergic reaction that is rapid in onset and may cause death.
- Anaphylaxis in children, particularly infants, is underdiagnosed.
- Anaphylaxis occurs when there is a sudden release of potent biologically active mediators from mast cells and basophils leading to symptoms

Common Causes of Anaphylaxis

- Foods
- Insect venom
- Latex
- Medication
- Immunotherapy
 - insect venom
 - inhalant allergies



Signs and symptoms of **Anaphylaxis**



4- Diagnosis of anaphylaxis:

- Anaphylaxis is highly likely when any 1 of the following 3 criteria is fulfilled:

1. Acute onset of an illness (minutes to several hours) with involvement of the skin and/or mucosal tissue

AND AT LEAST 1 OF THE FOLLOWING:

- a. Respiratory compromise

- b. Reduced BP or associated symptoms of end-organ dysfunction

2. Two or more of the following that occur rapidly after exposure to a likely allergen for that patient (minutes to several hours):

- a. Involvement of the skin/mucosal tissue

- b. Respiratory compromise

- c. Reduced BP or associated symptoms

- d. Persistent gastrointestinal symptoms

Anaphylactic reaction?

Assess: Airway, Breathing, Circulation, Disability, Exposure

Diagnosis - look for:

- Acute onset of illness
- Life-threatening features ¹
- And usually skin changes
- +/- Exposure to known allergen
- +/- Gastrointestinal symptoms

Call for help

Lie patient flat and
raise legs (if breathing not impaired)

Adrenaline

When skills and equipment available:

- A.** Establish airway
 - B.** High flow oxygen
 - C.** IV fluid challenge ³
- Chlorphenamine ⁴
Hydrocortisone ⁵

Monitor:

- Pulse oximetry
- ECG
- Blood pressure

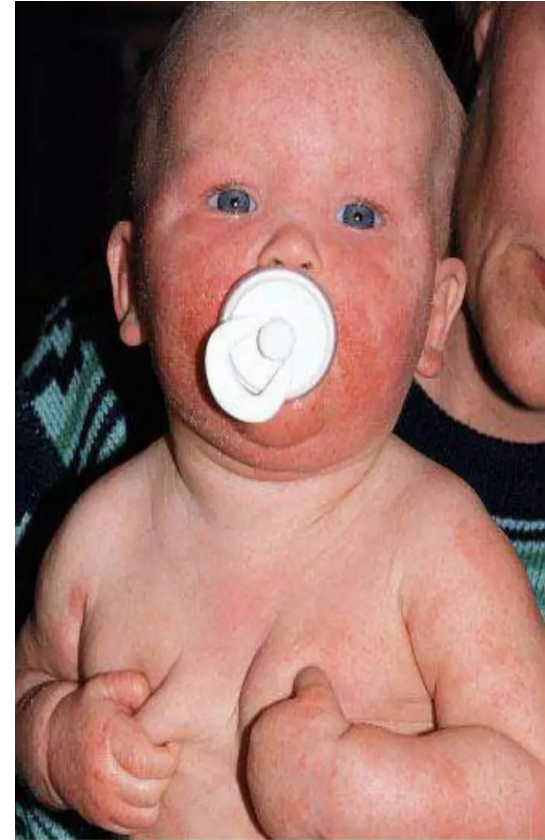
Atopic Dermatitis:

- Chronic Relapsing Skin Disease
- Most commonly during early infancy and childhood
- AD remains a clinical diagnosis
- Pruritus is a consistent feature
- Family history of atopic disease (asthma, allergic rhinitis, atopic dermatitis)
- Etiology:
 - Complex integration of environmental and genetic factors
 - Wool, harsh detergents are particularly irritating
 - Emotional stress can lead to flares
 - Exclusive breast feeding for first 3 months of life is associated with lower incidence rates of atopic dermatitis during childhood in children with a family history of atopy
 - In healthy people, the skin acts as a protective barrier against external irritants, moisture loss, and infection.
 - Proper function of the skin depends on adequate moisture and lipid content, functional immune responses, and structural integrity.
 - Severely dry skin is a hallmark of AD.

This results from a combination of the skin's barrier function, which is defective in AD, and an overactive immune system that produces inflammatory responses.

Clinical feature:

- Vary with the age
- **Infancy:**
- Ill-defined scaling, erythematous patches and confluent, edematous papules and vesicles are typical.
- Scalp and face are most often involved
- When crawling : extensor surfaces especially knees are involved



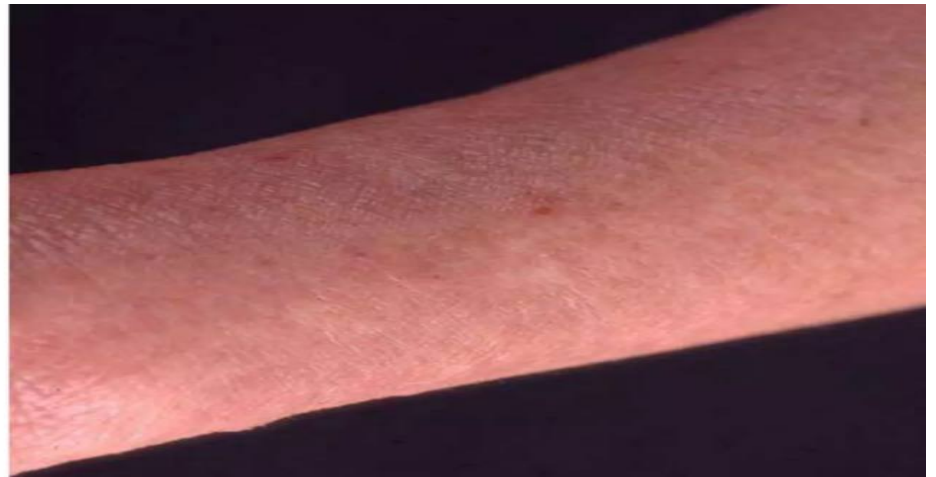
In Childhood:

- Lesions are drier, less eczematous, involve flexural areas & neck
- Scaling, fissured & crusted hands become troublesome
- Infraorbital folds (Morgan lines)



Chronic or chronically relapsing:

- Pruritic, erythematous papulovesicular eruptions that progress to scaling lichenified dermatitis is common.



Diagnosis:

- Radioallergosorbent tests (RASTs) or skin tests may suggest dust mite allergy.
- Eosinophilia and increased serum IgE levels may be present but are nonspecific.

Treatment

- Reduction of trigger factors
- Bland emollients, mild non alkali soaps
- Scented soaps and oil can be irritating
- Cotton clothing is preferable to wool and synthetics
- Topical steroids
- Systemic steroids for severe, acute flares
- Calcineurin inhibitors: tacrolimus, pimecrolimus: no skin atrophy, therefore, useful on face and neck
- Antihistamines helpful in breaking itch-scratch cycle

1- SKIN PRICK/ SCRATCH TEST:

A skin prick test, also called a puncture or scratch test, checks for immediate allergic reactions to as many as 40 different substances at once. This test is usually done to identify allergies to pollen, mold, pet dander, dust mites and foods. In adults, the test is usually done on the forearm. Children may be tested on the upper back.

Allergy skin tests aren't painful. This type of testing uses needles (lancets) that barely penetrate the skin's surface. You won't bleed or feel more than mild, momentary discomfort.

PROCEDURE:

- After cleaning the test site with alcohol, the nurse draws small marks on your skin and applies a drop of allergen extract next to each mark. He or she then uses a lancet to prick the extracts into the skin's surface. A new lancet is used for each allergen.



RESULT:

- About 15 minutes after the skin pricks, the nurse observes your skin for signs of allergic reactions. If you are allergic to one of the substances tested, you'll develop a raised, red, itchy bump (wheal) that may look like a mosquito bite. A nurse will then measure the bump's size.
- After the nurse records the results, he or she will clean your skin with alcohol to remove the marks.



Radio-Allergosorbent Test (RAST)

- RADIO-ALLERGOSORBENT TEST (RAST):
- It's a blood test used to determine to what substances a person is allergic.
- This test is different from a skin allergy test, which determines allergy by the reaction of a person's skin to different substances.
- Both of these tests have similar diagnostic values in terms of sensitivity and specificity.

METHOD OF RAST:

- The RAST is a radioimmunoassay test to detect specific IgE antibodies to suspected or known allergens for the purpose of guiding a diagnosis about allergy.
- Radioimmunoassay (RIA) is a very sensitive in vitro assay technique used to measure concentrations of antigens (for example, hormone levels in the blood) by use of antibodies.
- If a person exhibits a high level of IgE directed against pollen, the test may indicate the person is allergic to pollen (or pollen-like) proteins. A person who has outgrown an allergy may still have a positive IgE years after exposure.
- The suspected allergen is bound to an insoluble material and the patient's serum is added.
- The serum contains antibodies to the allergen, which will bind to the allergen.
- Radiolabeled anti-human IgE antibody is added where it binds to those IgE antibodies already bound to the insoluble material.
- The unbound anti-human IgE antibodies are washed away.
- The amount of radioactivity is proportional to the serum IgE for the allergen.

● DIRECTIONS For RAST:

- RASTs are often used to test for allergies when;
- I. A physician advises against the discontinuation of medications that can interfere with test results or cause medical complications.
- II. A patient suffers from severe skin conditions such as widespread eczema or psoriasis.
- III. A patient has such a high sensitivity level to suspected allergens that any administration of those allergens might result in potentially serious side effects.

The **RAST** is scored on a scale from
0 to 6:

RAST rating	IgE level (IU/ml)	comment
0	< 0.35	ABSENT OR UNDETECTABLE ALLERGEN SPECIFIC IgE
1	0.35 – 0.69	LOW LEVEL OF ALLERGEN SPECIFIC IgE
2	0.70 – 3.49	MODERATE LEVEL OF ALLERGEN SPECIFIC IgE
3	3.50 – 17.49	HIGH LEVEL OF ALLERGEN SPECIFIC IgE
4	17.50 – 49.99	VERY HIGH LEVEL OF ALLERGEN SPECIFIC IgE
5	50.00 – 100.00	VERY HIGH LEVEL OF ALLERGEN SPECIFIC IgE
6	> 100.00	EXTREMELY HIGH LEVEL OF ALLERGEN SPECIFIC IgE

Thank You

A close-up, high-angle shot of a hand holding a silver fountain pen, writing the words "Thank You" in a fluid, cursive script on a light-colored, textured surface. The pen is positioned at the end of the word "You", with the nib just finishing the final flourish. The lighting is soft and even, highlighting the texture of the paper and the metallic sheen of the pen.