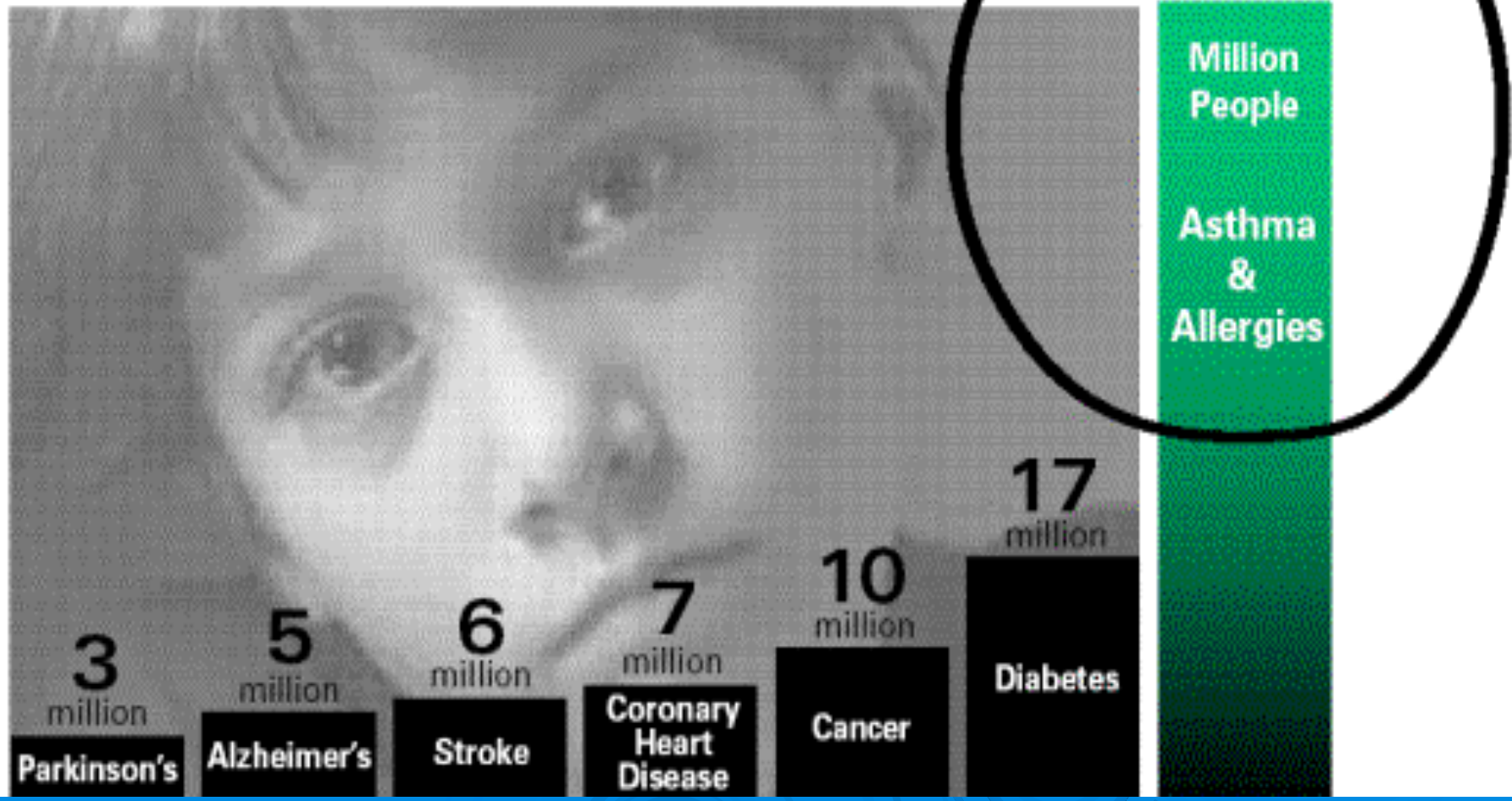
بسم الله الرحمن الرحيم

COMMON PEDIATRIC ALLERGIES

Lectures Reference

1. ALFRAYH AT KSU
2. CV ALFRAYH
3. COURSES
4. GUIDELINES FOR PEDIATIC CLERKSHIP
5. SHORTNESS OF BREATH
6. EXAMINATION OF THE RESPIRATORY SYSTEM
7. COMMON PEDIATRIC ALLERGIES
8. PDF AND POWERPOINT

Asthma and allergies strike 1 out of 4 Americans



PREVALENCE OF ATOPY AND ASTHMA IN PRIMARY SCHOOL CHILDREN IN AUSTRALIA

Asthma diagnosed	31.0%
Hay Fever	38.4%
Eczema	24.8%

- Allergic disease is the 5th leading chronic disease among all ages
- 3rd common chronic disease among children under 18 years old; up to one child in three is affected
- Trends indicate that by 2015, half of all Europeans may be suffering from an allergy

20 – 30 percent of total Indian population suffer from one or other allergic condition

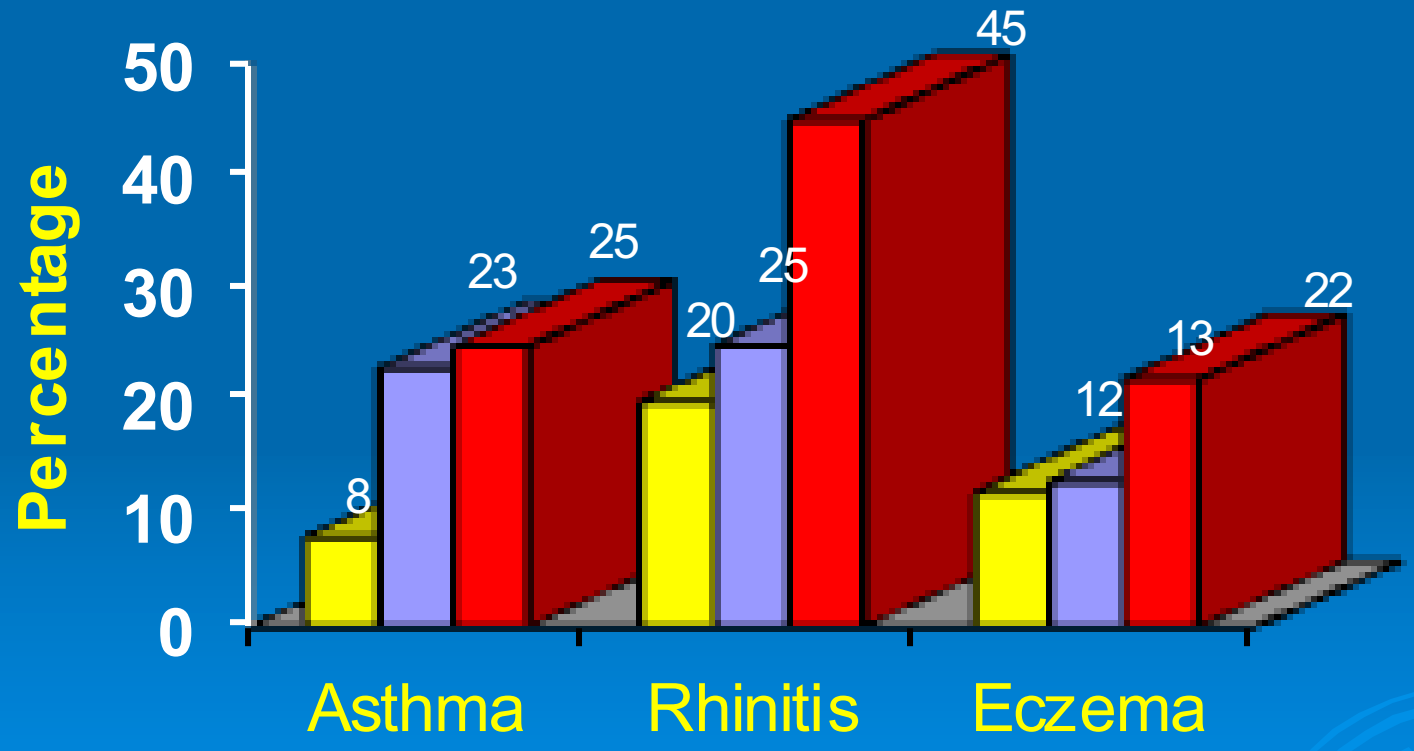
Allergic Rhinitis and Asthma: the Global Burden

Syed Mohammad Moazzam Aarif, Ahmed Ali Al-Mohammed

International Journal of Students' Research

Volume 5 Issue 1 Year 2015 www.ijsronline.com

Prevalence of Asthma, Rhinitis and Eczema in Saudi Arabia



1986: n=2123, 1995: n=1008, 2001:n=1014

Middle Bar indicates Physicians' diagnosed Asthma

Red Bar indicates highly suspected asthma

Asthma Prevalence among Saudi Children <5 years of age was 24%

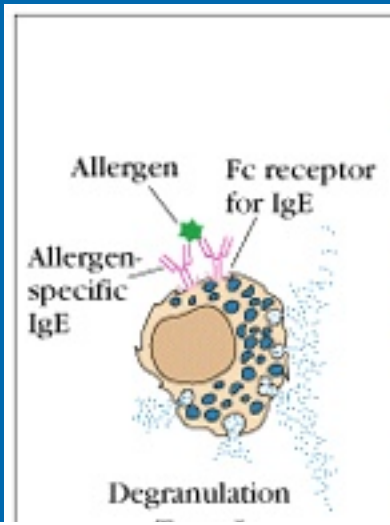
Prevalence Of Asthma Among Saudi Children In Makkah, Saudi Arabia

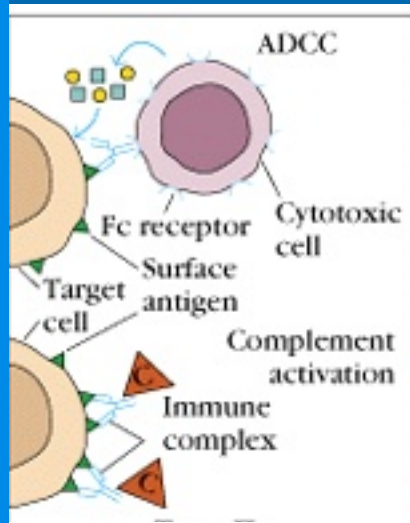
Salman A. Al-Harthi, Abdulrahman S. Al-Wagdani, Abdulrahman Y. Sabbagh, Adel M. Al-Ghamdi, Ibrahim H. Abu-Duruk.
Umm Al-Qura University, College of Medicine, Makkah, Saudi Arabia

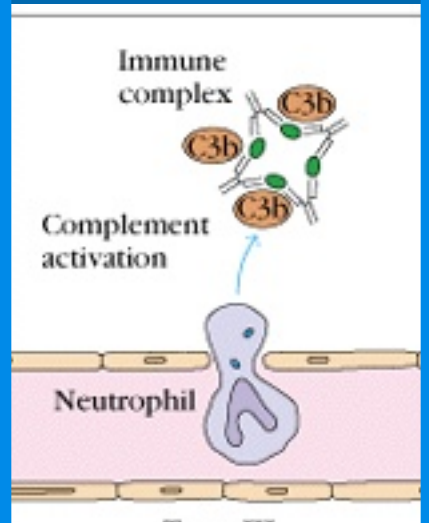
International Journal of Advanced Research (IJAR)
Journal Homepage: - www.journalijar.com Article DOI: 10.21474/IJAR01/2872 DOI URL: http://dx.doi.org/10.21474/IJAR01/2872

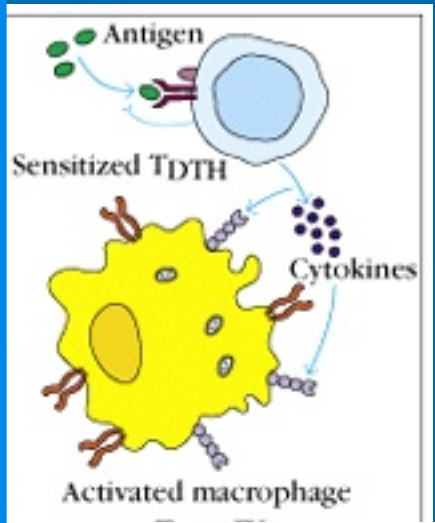
HYPERSENSITIVITY

GeLL and Coombs classification of hypersensitivities.





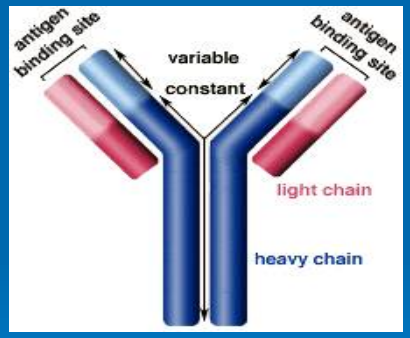


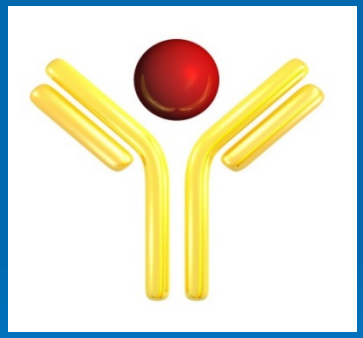


AllergyType I	Type II	Type III	Type IV
IgE Mediated	IgG/IgM Mediated	IgG Mediated	T cell
Classic	rbc lysis	Immune complex Disease	Delayed Type Hypersensitivity

Humoral – Antibody (Extracellular Response)

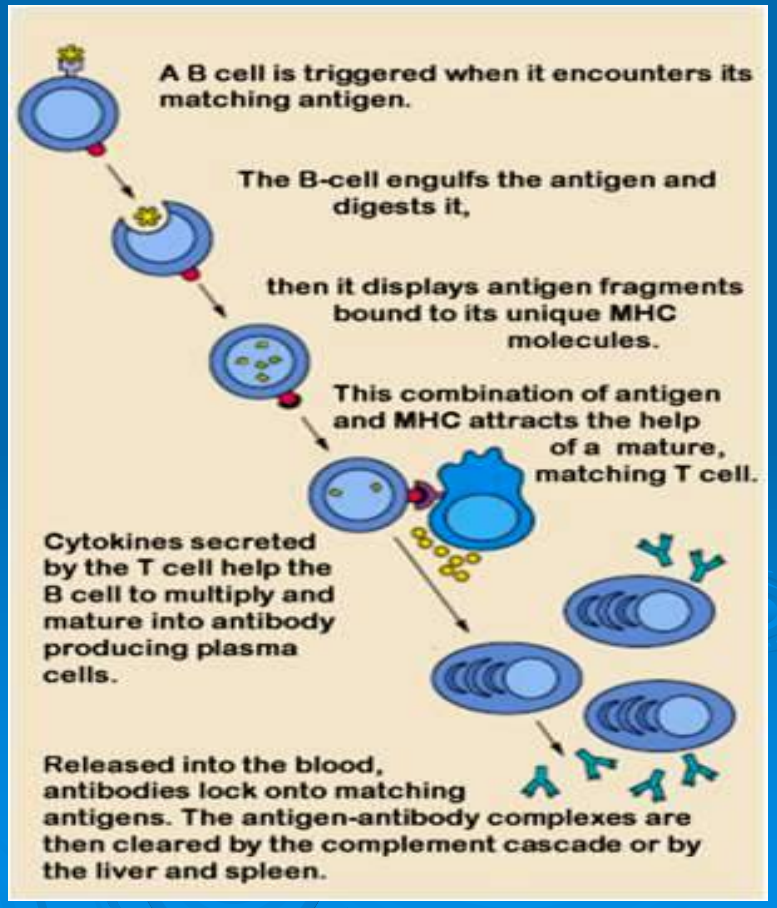
- B cells
- Plasma Cells - produce antibodies



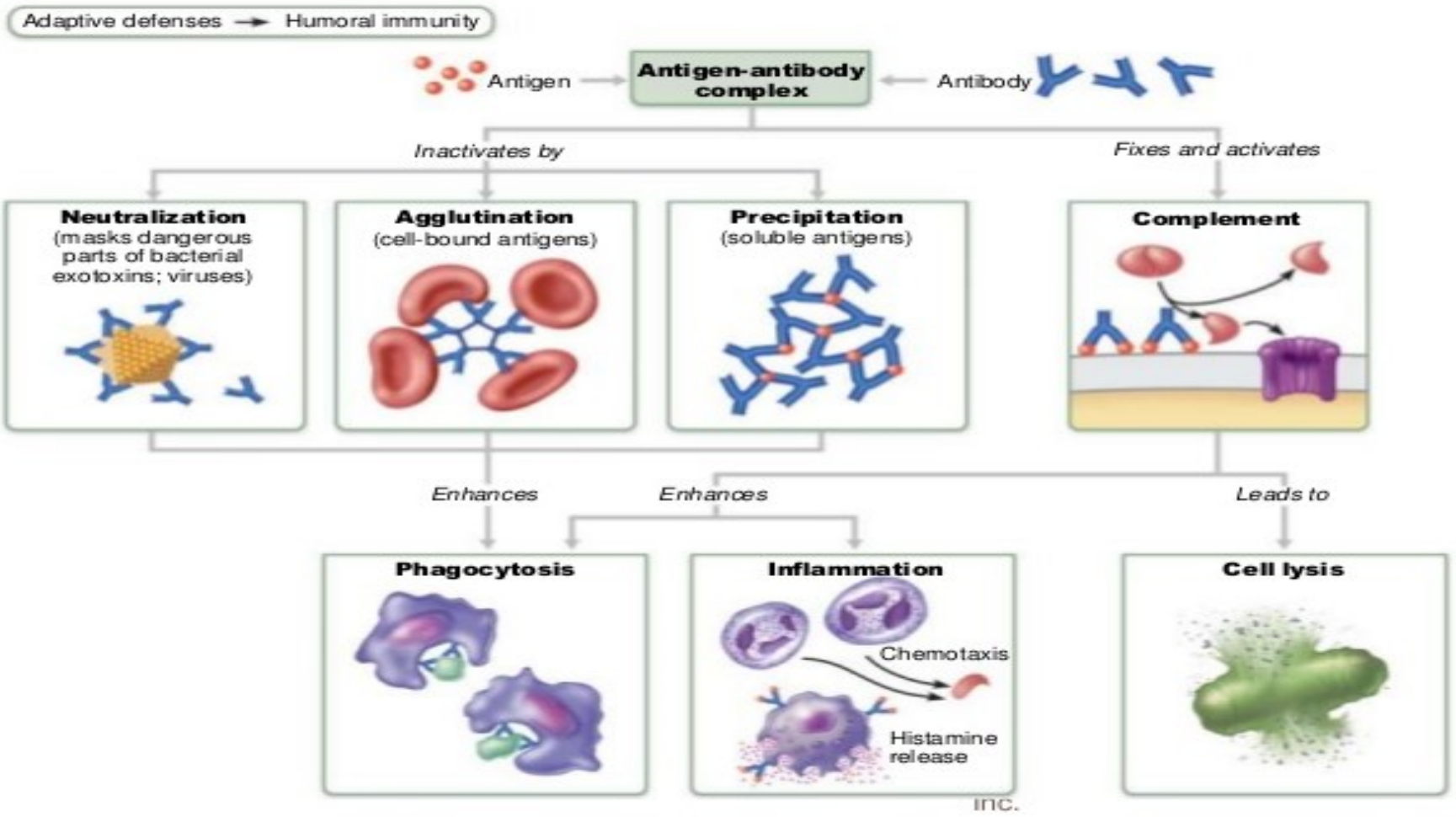


Antibody-antigen Complex

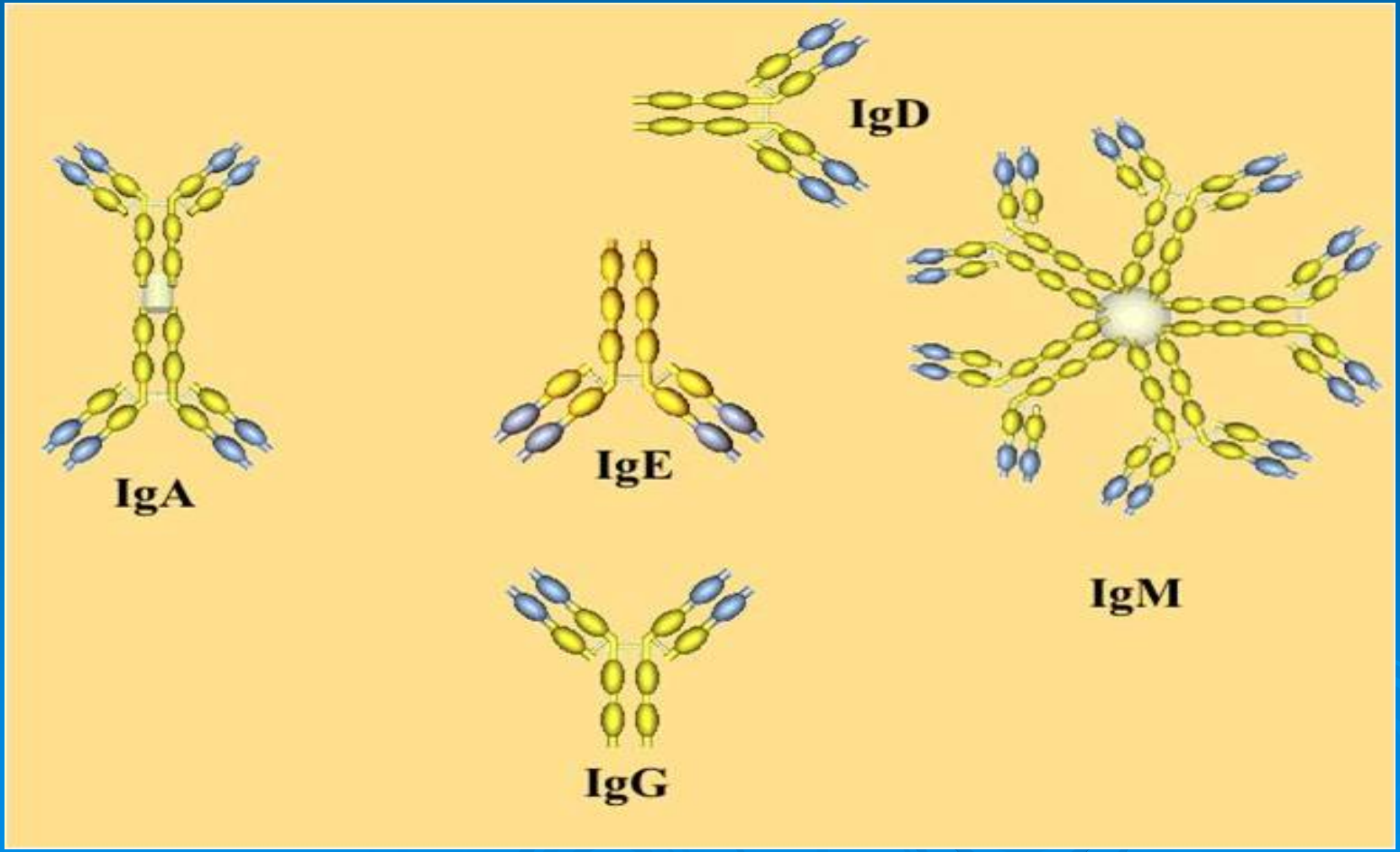
- Helper T Cells
- Memory Cells



Antigen-Antibody Complex Functions



Classes of Antibodies

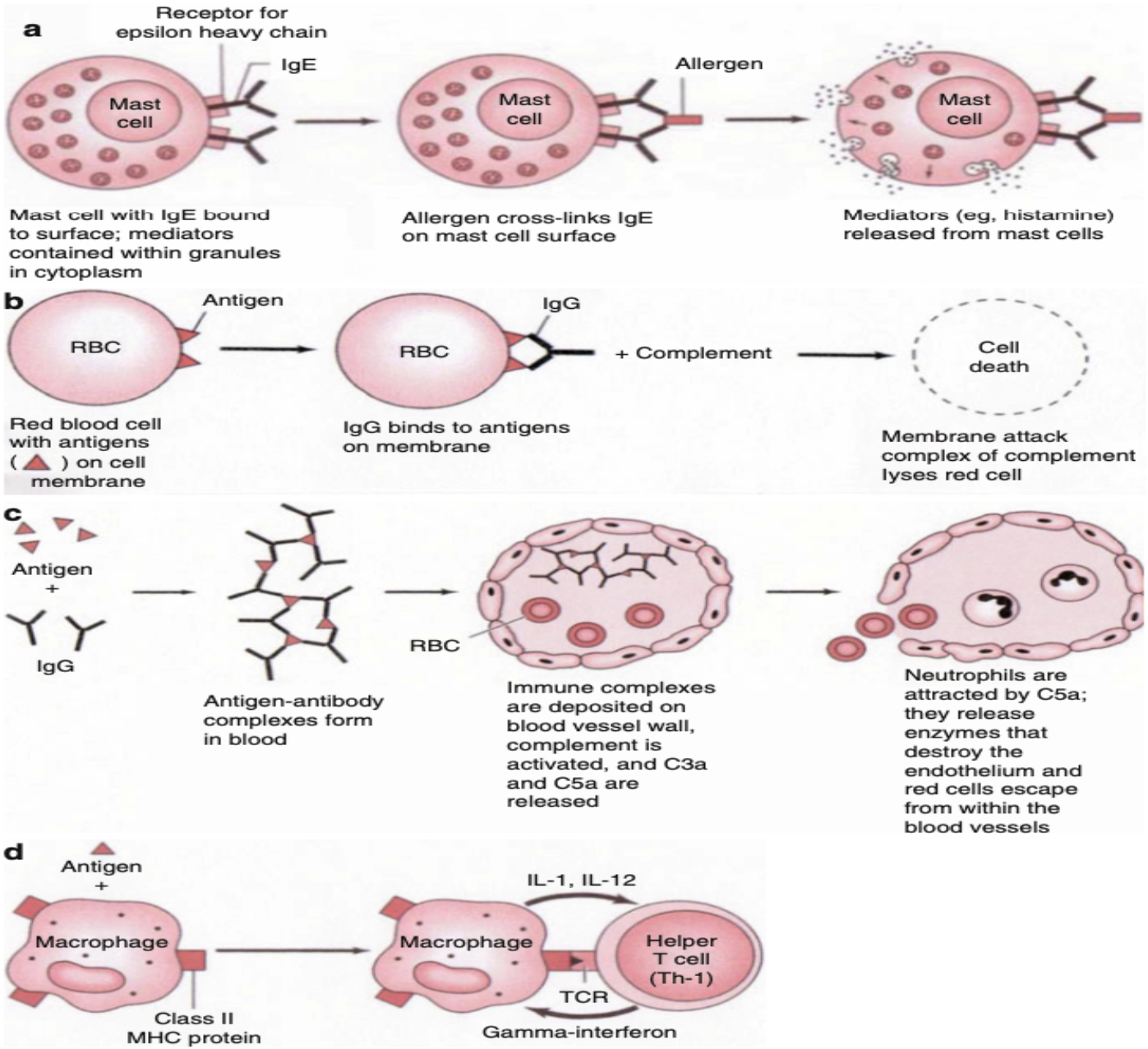


Classes of Antibodies

IgA	Antibodies are dimmers – contain two Y shaped structures. Found in mucosal areas, such as the gut, respiratory tract and urogenital tract. Also found in saliva, tears, and breast milk. They attack microbes and prevents colonization by pathogens before they reach the blood stream so it is most important antibody in local immunity
IgD	Functions mainly as an antigen receptor on B cells that have not been exposed to antigens. It has been shown to activate basophils and mast cells to produce antimicrobial factors.
IgG	In its four forms, provides the majority of antibody-based immunity against invading pathogens. It makes up about 75 % of all human antibodies and is the body's major defense against bacteria. The only antibody capable of crossing the placenta to give passive immunity to fetus. It is the most versatile of antibodies because it carries out functions of the other antibodies as well.
IgE	Binds to allergens and triggers histamine release from mast cells and basophils, and is involved in allergy. Also protects against parasitic worms.
IgM	Expressed on the surface of B cells and in a secreted form with very high avidity. Eliminates pathogens in the early stages of B cell mediated (humoral) immunity before there is sufficient IgG.

Type	Reactions	Mechanism	Onset of action	Examples
Type I immediate hypersensitivity or anaphylactic	IgE mediated	Degranulation of mast cells and release of histamine and other mediators	Minutes to hours	Urticaria, allergic rhinitis, food allergy
Type II antibody-mediated hypersensitivity	Non-IgE (IgG or IgM) mediated	Interaction of antibody with cell surface antigens leading to complement activation and lysis or phagocytosis	Days	Hemolytic anemia, Hashimoto's thyroiditis, transfusion reaction
		Autoimmune reactions		
		Antibody-mediated cytotoxicity		
Type III immune complex-related hypersensitivity	Immune complex mediated	Formation of immune complex and deposition on various sites such as blood vessels	10–21 days	Serum sickness; systemic lupus erythematosus (SLE)
Type IV cell mediated	Cell mediated	Secreted cytokines from CD4+ and CD8+ cells activate macrophages leading to inflammation and tissue injury	2–4 or more days	Mantoux reaction, allergic contact dermatitis
		Direct killing of affected cells by CD8+ T cells		

- Type I: Immediate hypersensitivity or anaphylactic.
- Type II: Antibody-mediated hypersensitivity.
- Type III: Immune Complex-mediated hypersensitivity.
- Type IV: Cell-mediated hypersensitivity.


a
Receptor for epsilon heavy chain
IgE
Mast cell
Allergen
Mast cell
Mast cell
Mast cell with IgE bound to surface; mediators contained within granules in cytoplasm
Allergen cross-links IgE on mast cell surface
Mediators (eg, histamine) released from mast cells
b
Antigen
RBC
IgG
RBC
+ Complement
Cell death
Red blood cell with antigens (▲) on cell membrane
IgG binds to antigens on membrane
Membrane attack complex of complement lyses red cell
c
Antigen
+
IgG
Antigen-antibody complexes form in blood
RBC
Immune complexes are deposited on blood vessel wall, complement is activated, and C3a and C5a are released
Neutrophils are attracted by C5a; they release enzymes that destroy the endothelium and red cells escape from within the blood vessels
d
Antigen
+
Macrophage
Class II MHC protein
IL-1, IL-12
Macrophage
Helper T cell (Th-1)
TCR
Gamma-interferon

TYPE I Hypersensitivity
Classic allergy

- Mediated by IgE attached to Mast cells.

- The symptoms resulting from allergic responses are known as **anaphylaxis**.
  - Includes: Hay fever, asthma, eczema, bee stings, food allergies.

Allergens

- Allergens are antigens that can stimulate a type I hypersensitivity response.
- Allergens bind to IgE and trigger degranulation of chemical mediators.

Allergens

TABLE 16-1 COMMON ALLERGENS ASSOCIATED WITH TYPE I HYPERSENSITIVITY

Proteins
- Foreign serum
- Vaccines

Plant pollens
- Rye grass
- Ragweed
- Timothy grass
- Birch trees

Drugs
- Penicillin
- Sulfonamides
- Local anesthetics
- Salicylates

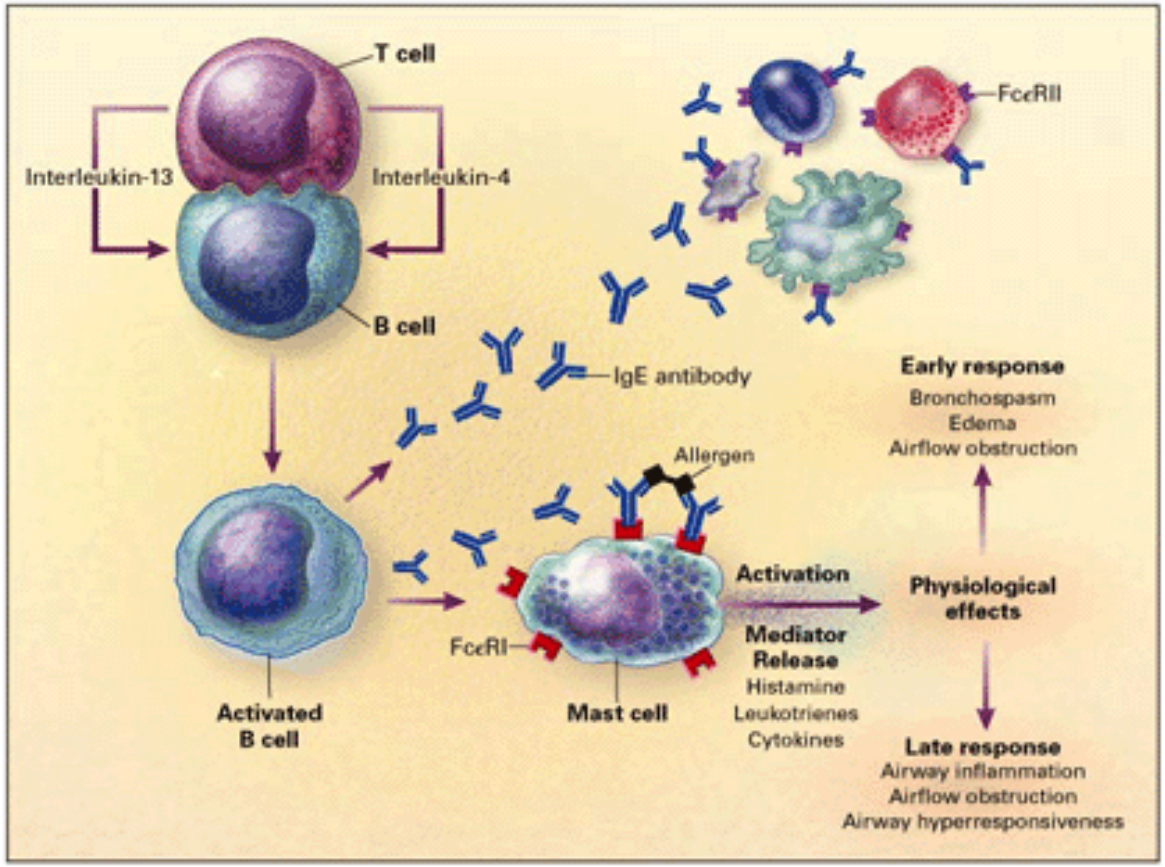
Foods
- Nuts
- Seafood
- Eggs
- Peas, beans
- Milk

Insect products
- Bee venom
- Wasp venom
- Ant venom
- Cockroach calyx
- Dust mites

Mold spores

Animal hair and dander

Mechanisms of allergic response
Sensitization
Th2/B cell interaction



IL-4

IL-4R

CD40

Drive B cell Activation and IgE isotype switch.

Mechanisms of allergic response

Sensitization

- The IgE can attach to Mast cells by Fc receptor, which increases the life span of the IgE.
- Half-life of IgE in serum is days whereas attached to FcεR it is increased to months.

Mechanisms of allergic response

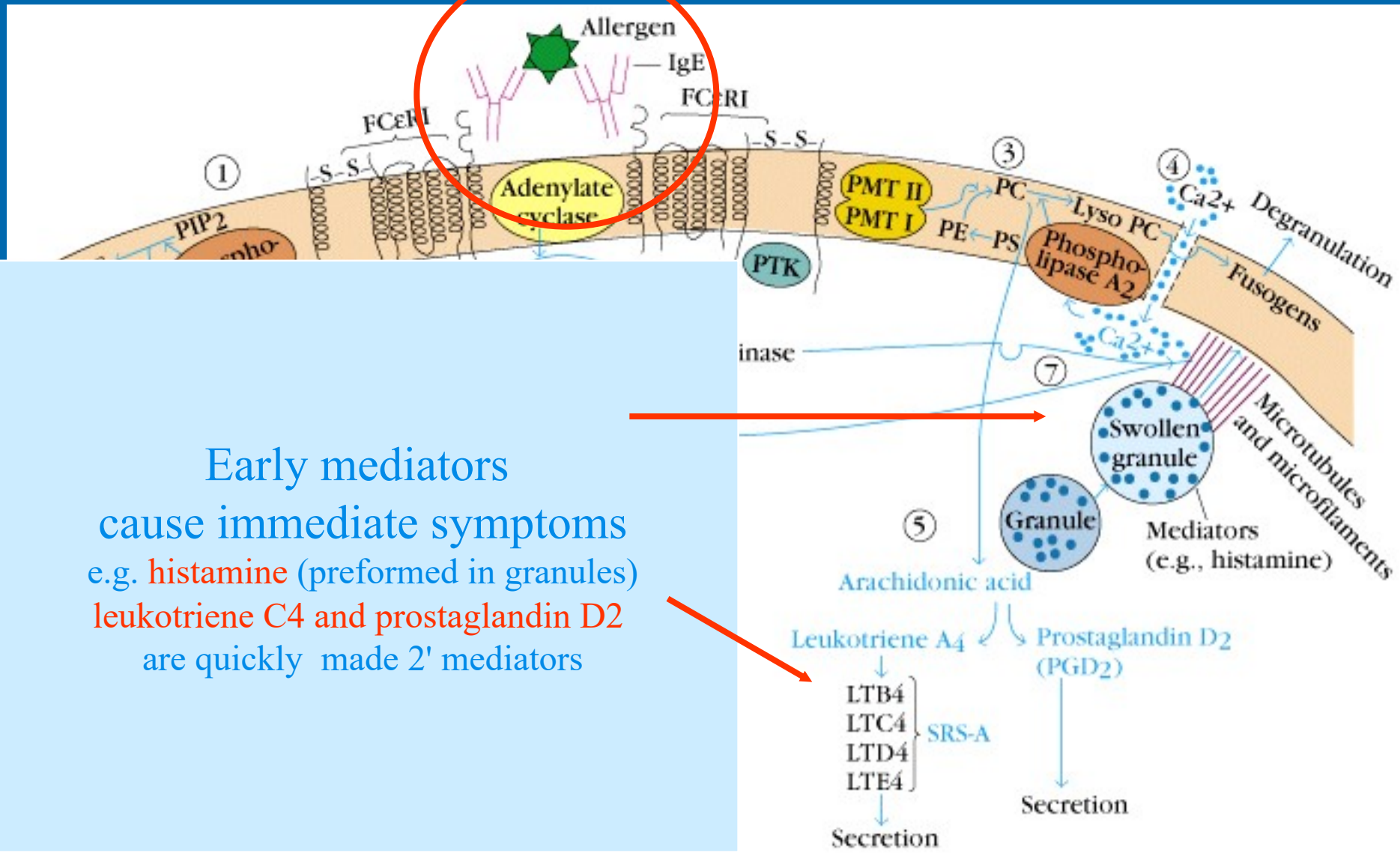
Fc ε receptors (FcεR)

FcεR1

- high affinity IgE receptor found on
  - mast cells/basophils/activated eosinophils.

- Allergen binding to IgE attached to FcεR1 triggers release of granules from cell.

FcεRI Triggers Release of Mediators



Early mediators
cause immediate symptoms
e.g. histamine (preformed in granules)
leukotriene C4 and prostaglandin D2
are quickly made 2' mediators

Mediators of Type I Hypersensitivity
Immediate effects

- Histamine
  - Constriction of smooth muscles.
    Bronchiole constriction = wheezing.
    Constriction of intestine = cramps-diarrhea.
  - Vasodilation with increased fluid into tissues causing increased swelling or fluid in mucosa.
  - Activates enzymes for tissue breakdown.
- Leukotrienes
- Prostaglandins

Mediators of Type I Hypersensitivity

Primary Mediators

Pre-formed mediators in granules

- Histamine
- Cytokines TNF-α, IL-1, IL-6.
- Chemoattractants for Neutrophils and Eosinophils.
- Enzymes
  - tryptase, chymase, cathepsin.
  - Changes in connective tissue matrix, tissue breakdown.

Type I Hypersensitivity Secondary mediators Mediators formed after activation

- Leukotrienes

Prostaglandines

- Th2 cytokines- IL-4, IL-5, IL-13, GM-CSF

Continuation of sensitization cycle

- Mast cells control the immediate response.
- Eosinophils and neutrophils drive late or chronic response.

- More IgE production further driven by activated Mast cells, basophils, **eosinophils.**

Continuation of sensitization cycle

Eosinophils

- Eosinophils play key role in late phase reaction.
- Eosinophils make
  - enzymes,
  - cytokines (IL-3, IL-5, GM-CSF),
  - Lipid mediators (LTC4, LTD4, PAF)
- Eosinophils can provide CD40L and IL-4 for B cell activation.

Localized anaphylaxis

Target organ responds to direct contact with allergen.

- Digestive tract contact results in vomiting, cramping, diarrhea.
- Skin sensitivity usually reddened inflamed area resulting in itching.
- Airway sensitivity results in sneezing and rhinitis OR wheezing and asthma.

Systemic anaphylaxis

- Systemic vasodilation and smooth muscle contraction leading to severe bronchiole constriction, edema, and shock.

- Similar to systemic inflammation.

Delayed type hypersensitivity Th1 cells and macrophages

- DTH response is from:
  - Th1 cells release cytokines to activate macrophages causing inflammation and tissue damage.
  - Continued macrophage activation can cause chronic inflammation resulting in tissue lesions, scarring, and granuloma formation.
- Delayed is relative because DTH response arise 24-72 hours after exposure rather than within minutes.

Stages of Type IV DTH

Sensitization stage

- Memory Th1 cells against DTH antigens are generated by dendritic cells during the sensitization stage.
- These Th1 cells can activate macrophages and trigger inflammatory response.

Stages of Type IV DTH
Effector stage

- Secondary contact yields what we call DTH.
- **Th1** memory cells are activated and produce cytokines.
  - IFN-γ, TNF-α, and TNF-β which cause tissue destruction, inflammation.
  - IL-2 that activates T cells and CTLs.
  - Chemokines- for macrophage recruitment.
  - IL-3, GM-CSF for increased monocyte/macrophage

Stages of Type IV DTH
Effector stage

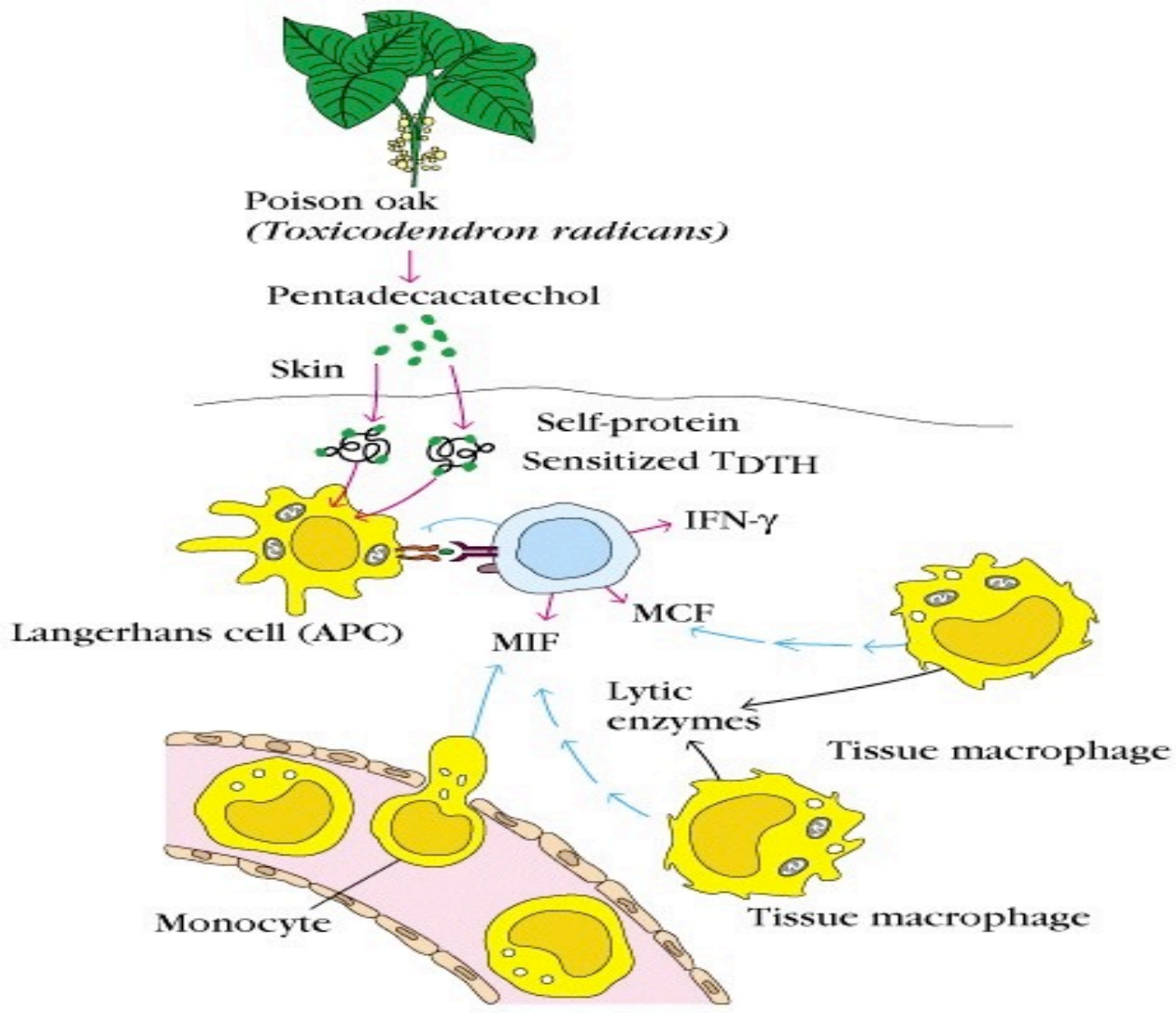
Secondary exposure to antigen

- Inflamed area becomes red and fluid filled can form lesion.
  - From tissue damage there is activation of clotting cascades and tissue repair.
- Continued exposure to antigen can cause chronic inflammation and result in granuloma formation.

Type IV DTH
Contact dermatitis

- The response to poison oak is a classic Type IV.
  - Small molecules act as haptens and complex with skin proteins to be taken up by APCs and presented to Th1 cells to get sensitization.
  - During secondary exposure Th1 memory cells become activated to cause DTH.

Contact dermatitis



Delayed type hypersensitivity (DTH)

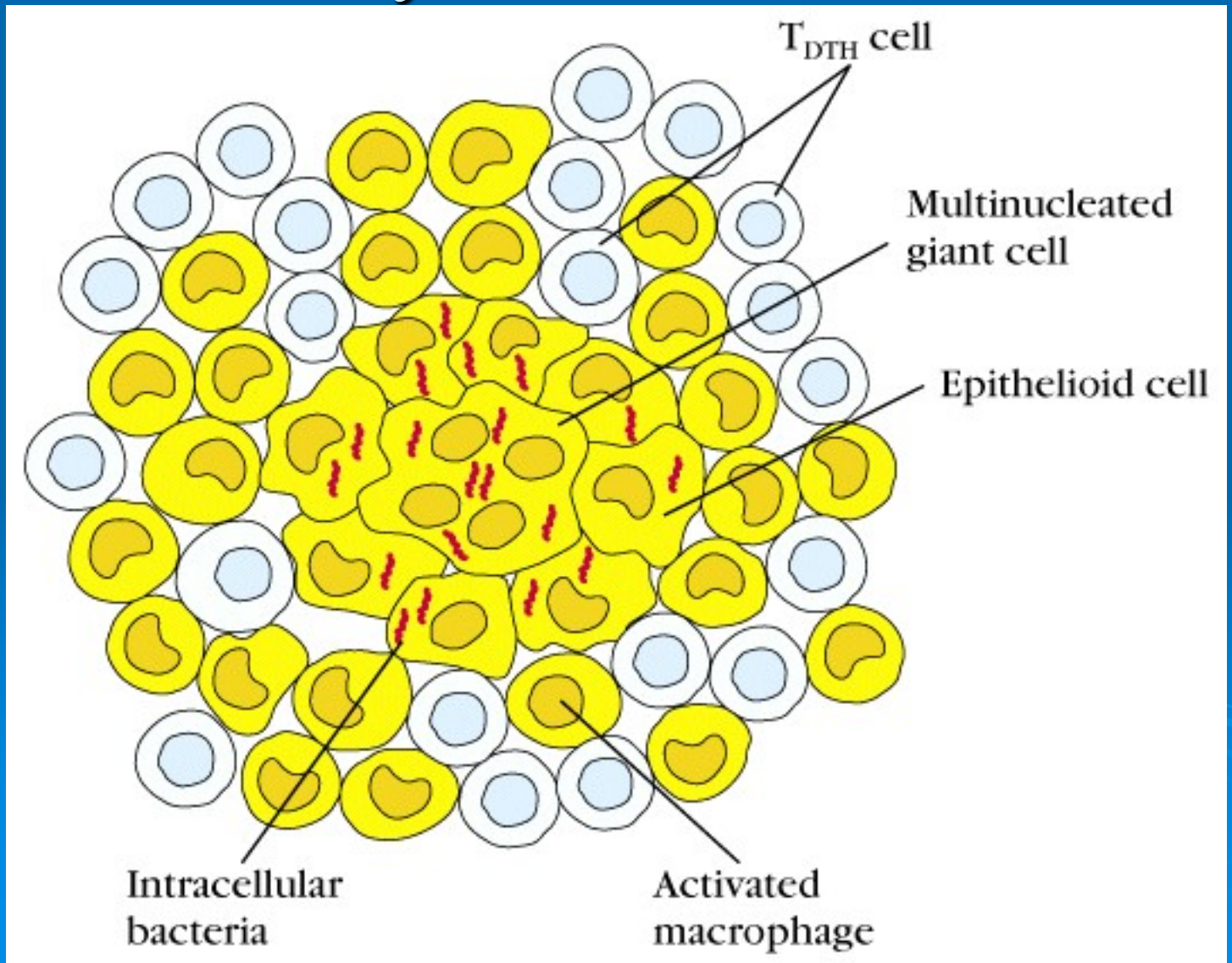
TABLE 14-3 INTRACELLULAR PATHOGENS AND CONTACT ANTIGENS THAT INDUCE DELAYED-TYPE HYPERSENSITIVITY

Intracellular bacteria	Intracellular viruses
Mycobacterium tuberculosis	Herpes simplex virus
Mycobacterium leprae	Variola (smallpox)
Listeria monocytogenes	Measles virus
Brucella abortus	Contact antigens
Intracellular fungi	Picrylchloride
Pneumocystis carinii	Hair dyes
Candida albicans	Nickel salts
Histoplasma capsulatum	Poison ivy
Cryptococcus neoformans	Poison oak
Intracellular parasites	
Leishmania sp.	

DTH is a type of immune response classified by **Th1 and macrophage** activation that results in tissue damage.

DTH can be the result of Chronic infection or Exposure to some antigens.

Granuloma Formation from DTH Mediated by Chronic Inflammation



Drug reactions can be any Type of Hypersensitivity

TABLE 16-5 Penicillin-induced hypersensitive reactions

Type of reaction	Antibody or lymphocytes induced	Clinical manifestations
I	IgE	Urticaria, systemic anaphylaxis
II	IgM, IgG	Hemolytic anemia
III	IgG	Serum sickness, glomerulonephritis
IV	T_{DTH} cells	Contact dermatitis


BERMUDA

RYE


ATRIPLEX (RUGHL)

Amaranthus SP

سندار ، عرف الديك ، قطيفة

Amaranthus SP

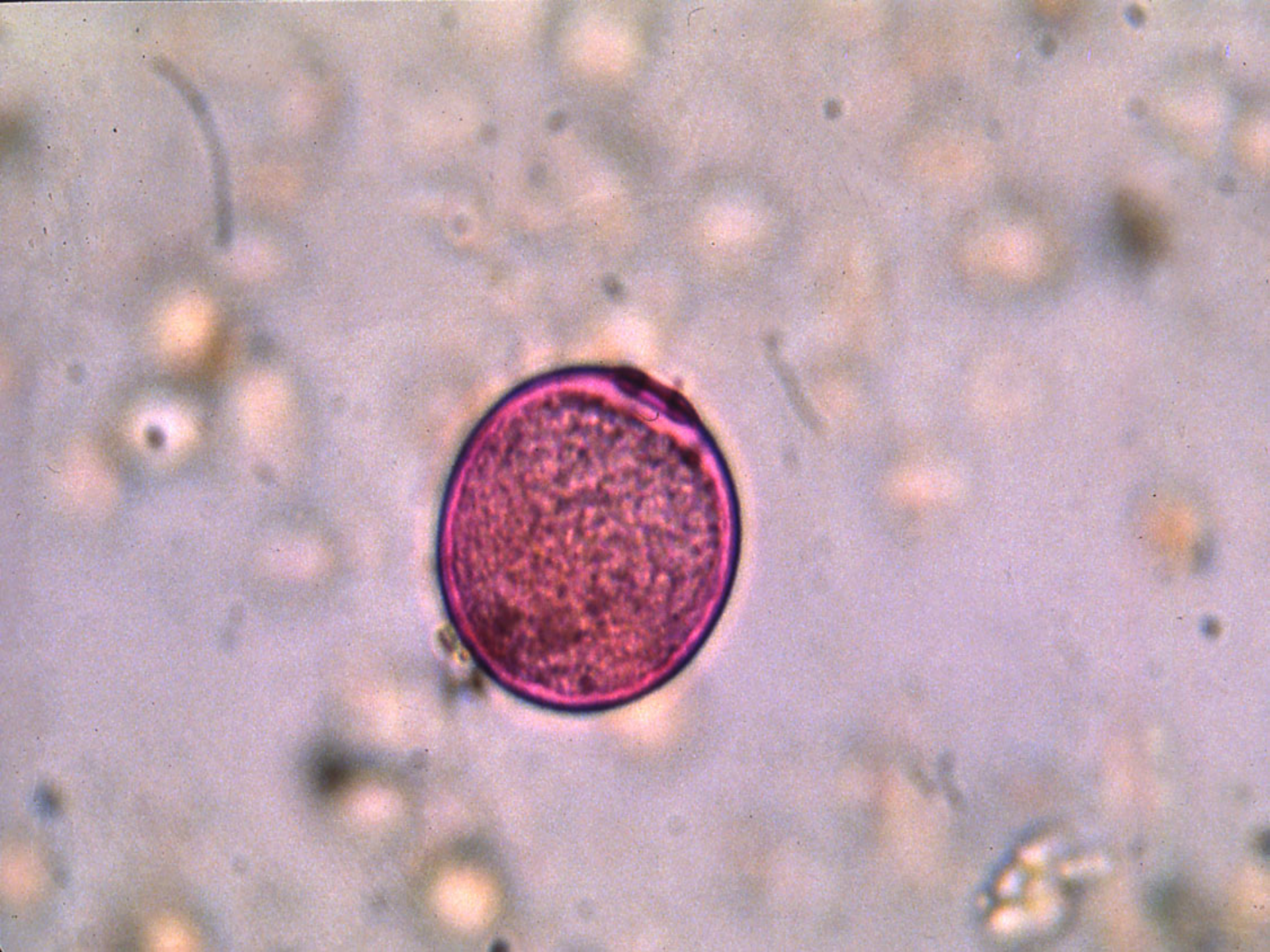
سندار عرف الديك ، قطيفة


Amaranthus Viridis (Orf Al-Deek, Cendar)

Salsola SPP. (Herm)


Chenopodium Album (Etra)

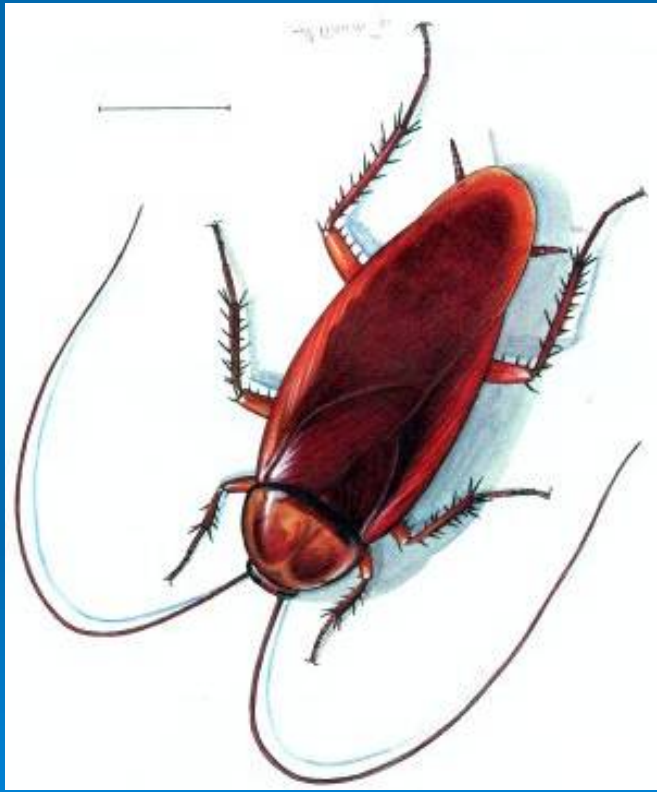

PROSOPIS




Cat

DOGS

COCKROACH



AMERICAN COCKROACH


DUSTMITE

ALLERGIC RHINITIS

Health Effects of Allergic Rhinitis

- Social inconvenience
- Sleep disturbances/obstruction
- Learning difficulties
- Impaired maxillary growth
- Dental problems
- Infection: nose and sinuses
- Co-morbidities: conjunctivitis, asthma, rhinosinusitis, otitis media

The history is the most important element in the evaluation of allergy. Key features of the history are:

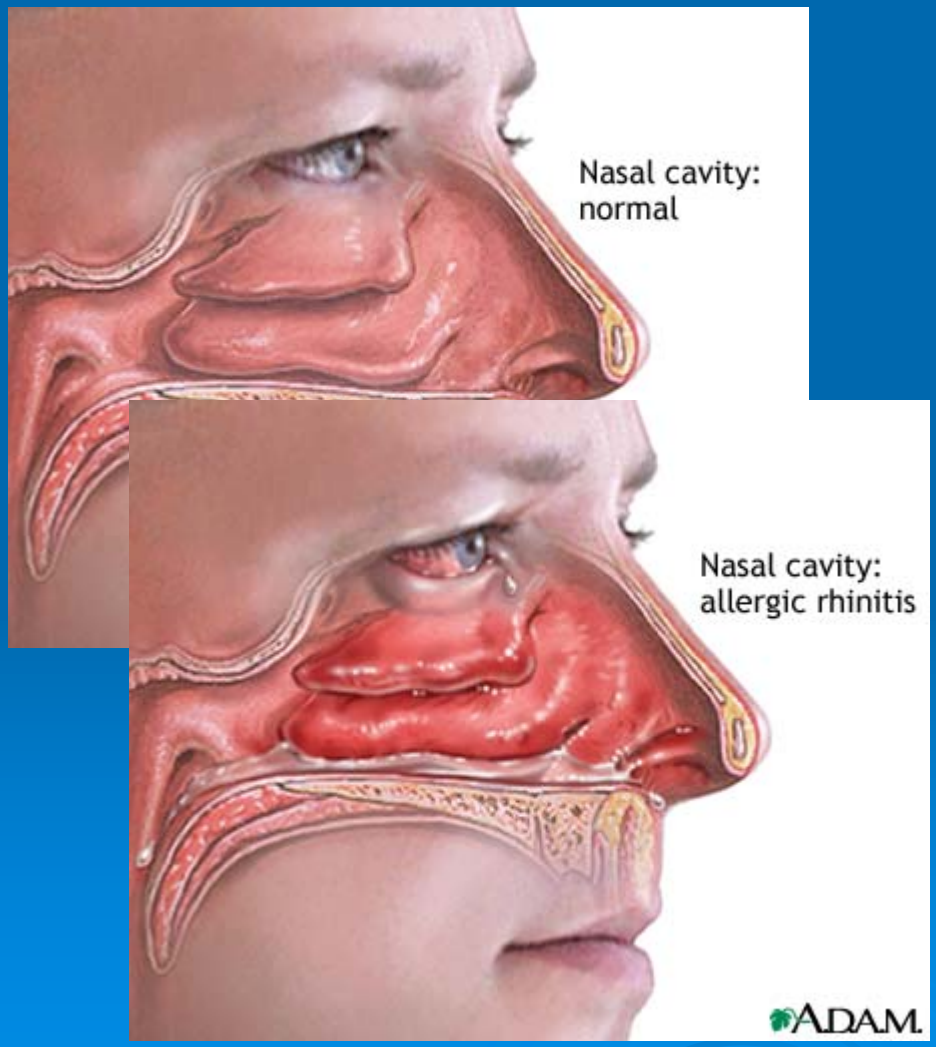
- ✓ *Worsening of symptoms on exposure to aeroallergens*
- ✓ *Seasonal variation in symptoms related to pollination of trees, grasses, and weeds*
- ✓ *A family history of atopic disease*
- ✓ *An environmental history assessing exposure to indoor and outdoor allegens and the presence of associated allergic conditions*

Family history

- Because allergic rhinitis has a significant genetic component, a positive family history for atopy makes the diagnosis more likely.
- A greater risk of allergic rhinitis exists if both parents are atopic than if one parent is atopic.
- However, the cause of allergic rhinitis appears to be multifactorial, and a person with no family history of allergic rhinitis can develop allergic rhinitis.

Diagnosis of Allergic Rhinitis

1. History & symptoms of recurrent or persistent rhinitis and/or associated health effects
2. Signs of atopy and recurrent or persistent rhinitis
3. Demonstration of IgE allergy
4. Exclusion of other causes of rhinitis

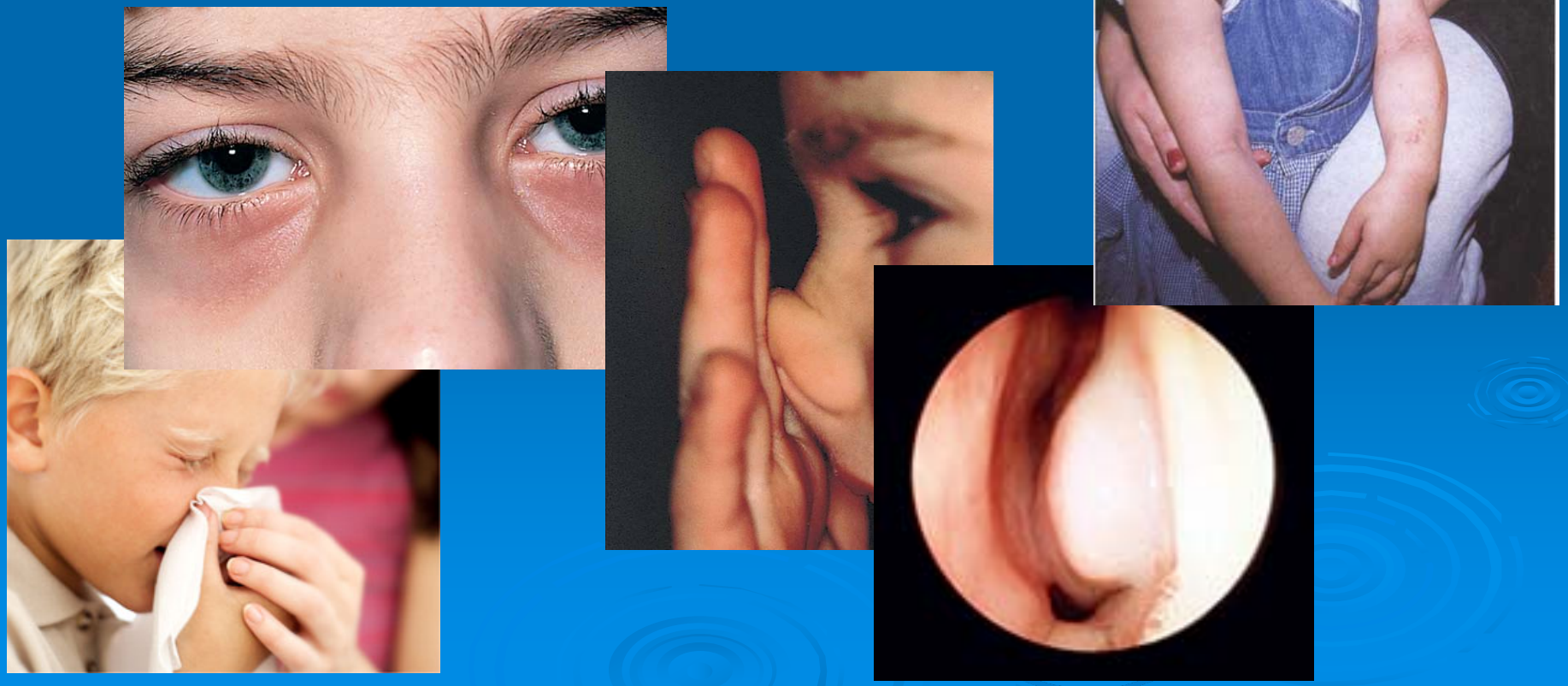


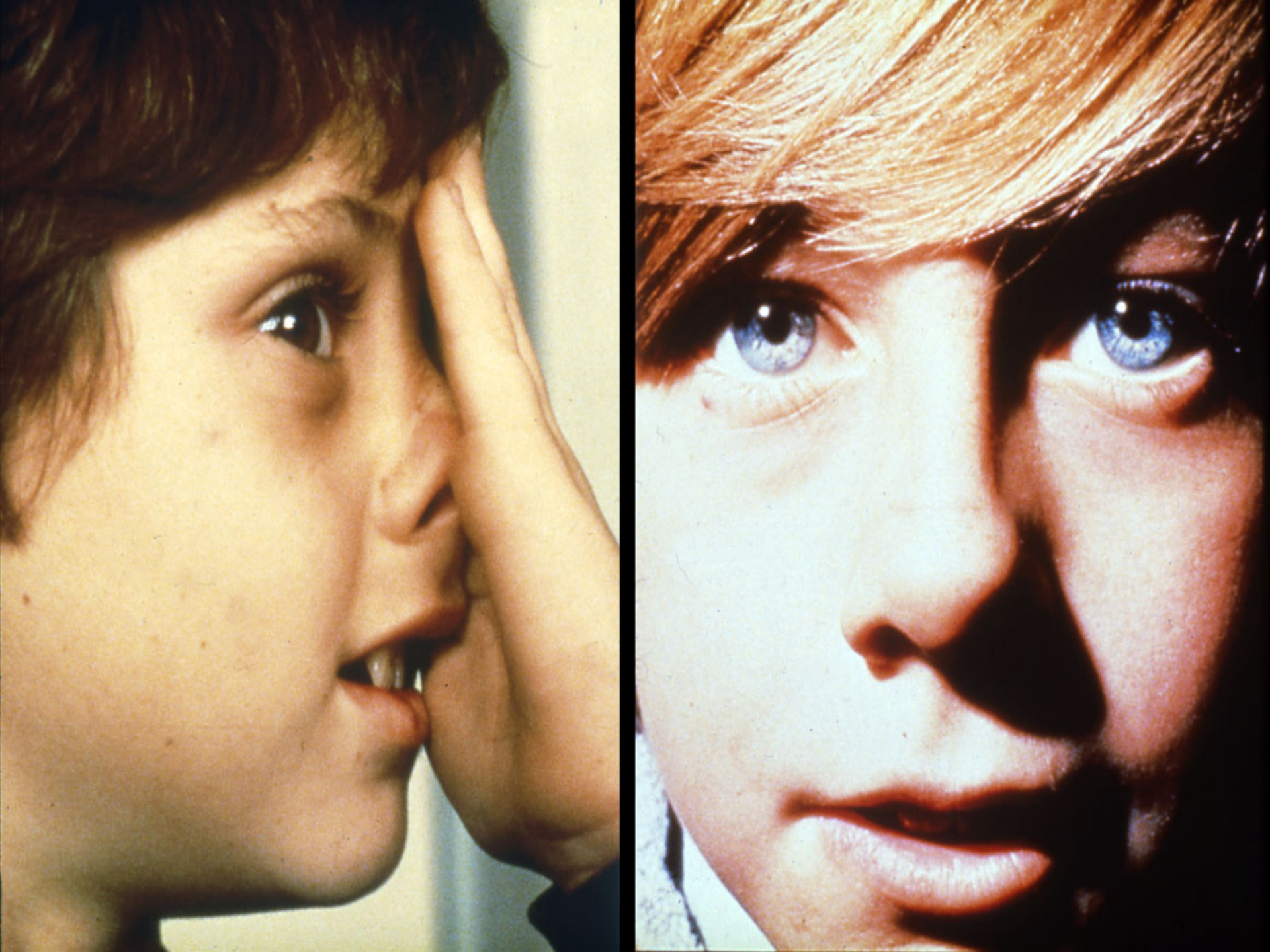
- Rhinorhoea
- Nasal blockage
- Postnasal drip
- Itchiness
- Sneezing
- Associated health effects

‼ **IgE mediated**

Diagnosis of Allergic Rhinitis

2. Signs of atopy and recurrent or persistent rhinitis





WORKUP OF PATIENTS WITH ALLERGIC RHINITIS CONT.

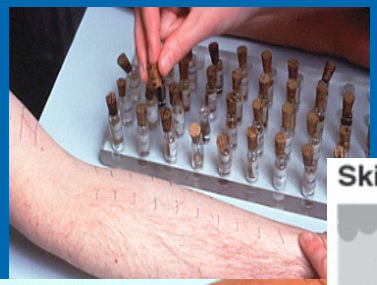
- BLOOD EOSINOPHILS 250-400 cell/mm3
- NASAL EOSINOPHILS>15/100 cells
- SPT
- NASAL PROVOCATION TEST
- RHINOMETRY
- IgE
- RAST

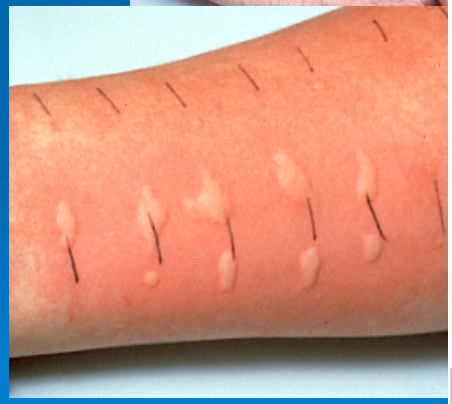
WORKUP OF PATIENTS WITH ALLERGIC RHINITIS

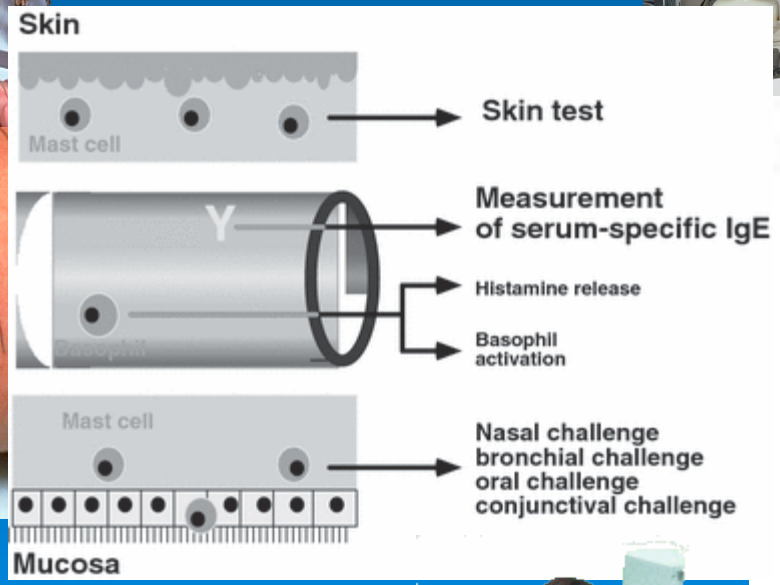
- PERIPHERAL BLOOD EOSINOPHILIA >400/ul IS COMMON BUT 50% OF PTS. HAVE NO EOSINOPHILIA ON ANY ONE OCCASION.
- NASAL EOSINOPHILS --> WRIGHTS STAIN >15/100 cells SIGNIFICANT

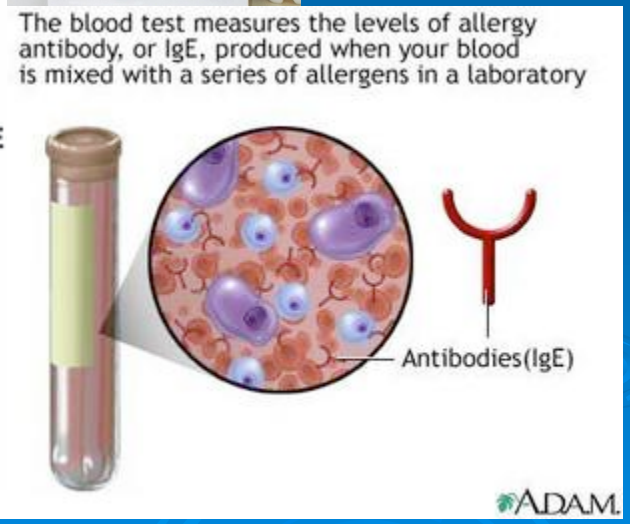
Diagnosis of Allergic Rhinitis

3. Demonstration of IgE allergy









SKIN PRICK TEST (SPT)

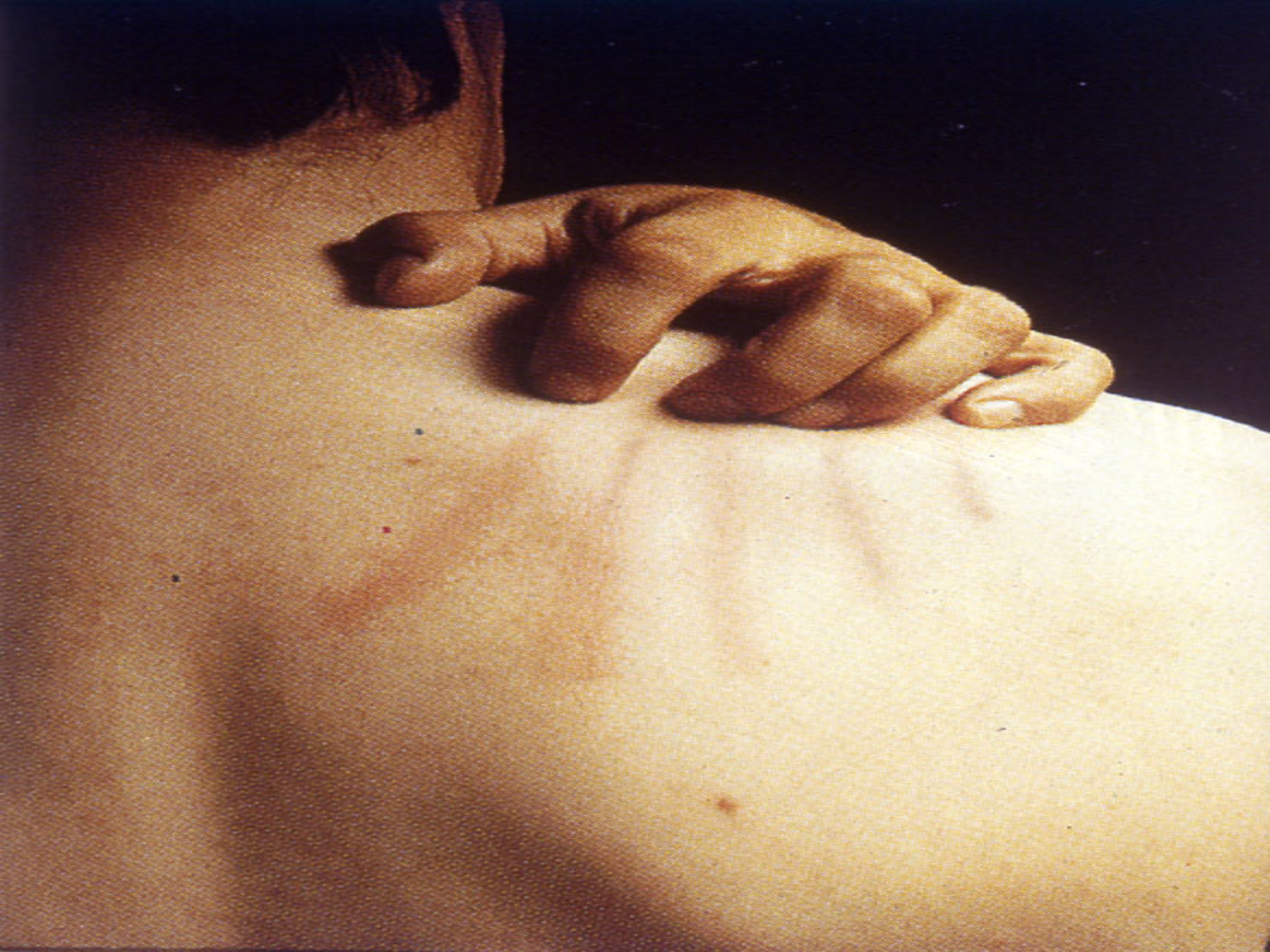
- POSITIVE RESULT WHEN WHEAL >3mm MORE THAN CONTROL
- 80% OF +VE SKIN TEST GIVE +VE RAST
- AND 50% GIVE+VE CHALLENGE
- PANEL OF TEST ANTIGENS APPROPRIATE TO THE LOCALITY AND SEASON AND HISTORY SHOULD BE USED.

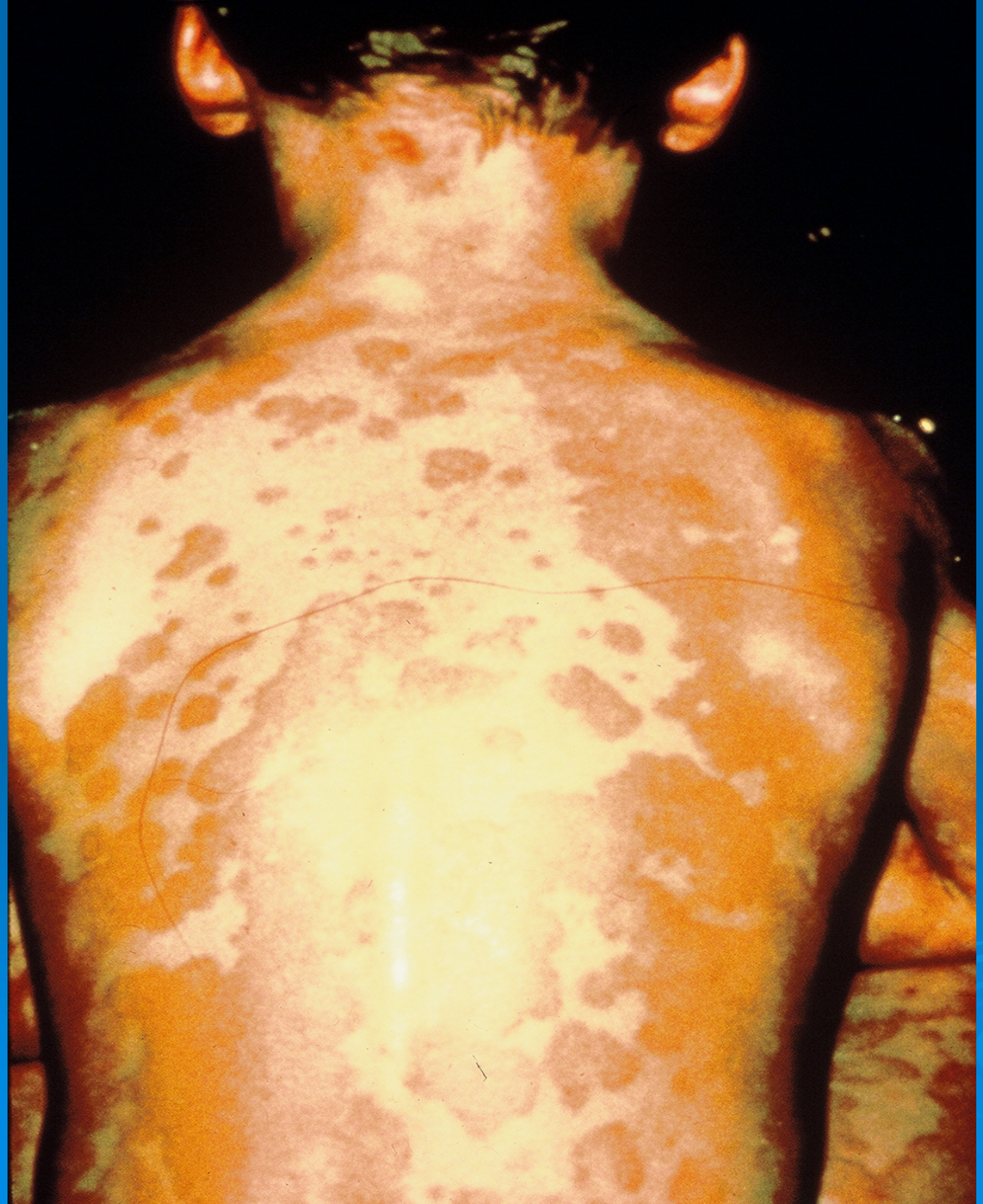
The most important ancillary test to confirm the diagnosis of allergy is the skin test, which is the gold standard in this regard. The skin test results must be interpreted in light of the history to determine the importance of a positive test.

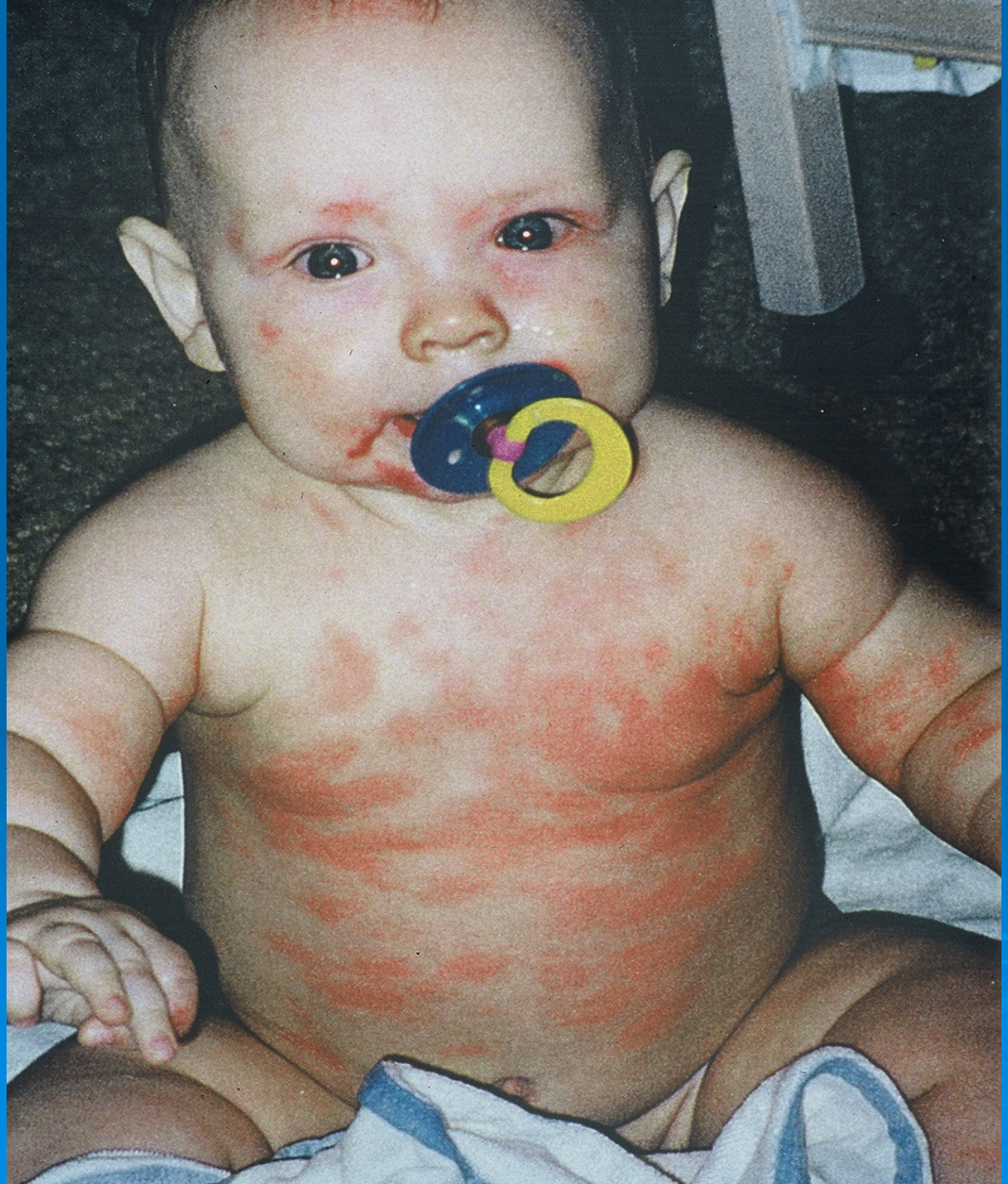
Recording and Scoring Skin-Test Results

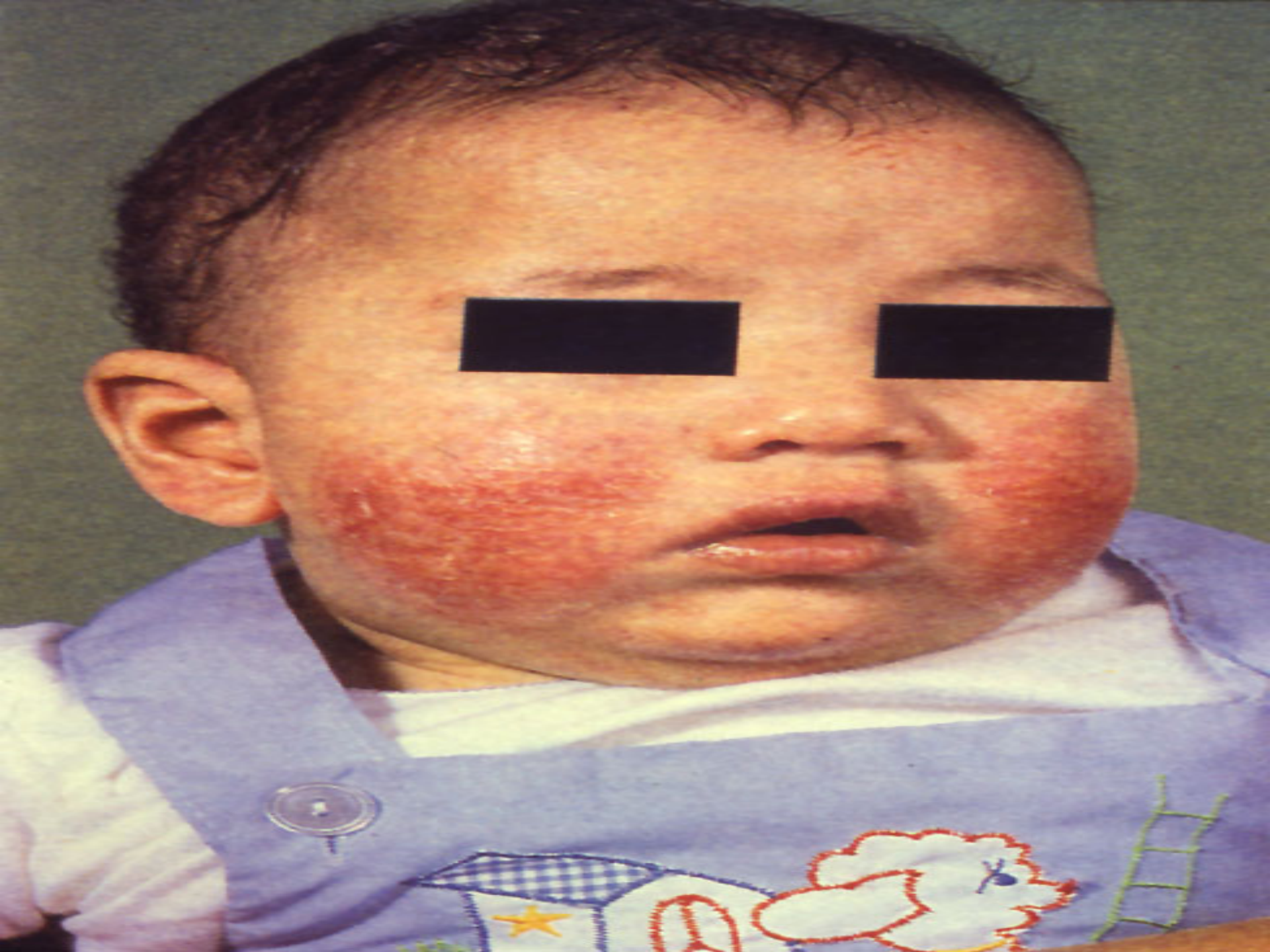
Skin-test reactions to allergens are normally evaluated 15-20 min after the tests have been placed, when the reactions are typically maximal. The best method to record the results of skin tests is to measure the greatest diameter of the wheal and flare in millimeters and record these results for all tests and for the positive and negative controls. After measurement, the result of a test can be easily recorded as, for example, 5/21, meaning that the wheal was 5 mm in greatest diameter and the flare was 21 mm in diameter. Any epicutaneous test that produces a wheal at least 3 mm larger than the wheal of the negative control with a larger surrounding flare is normally considered positive for the presence of allergen-specific IgE.

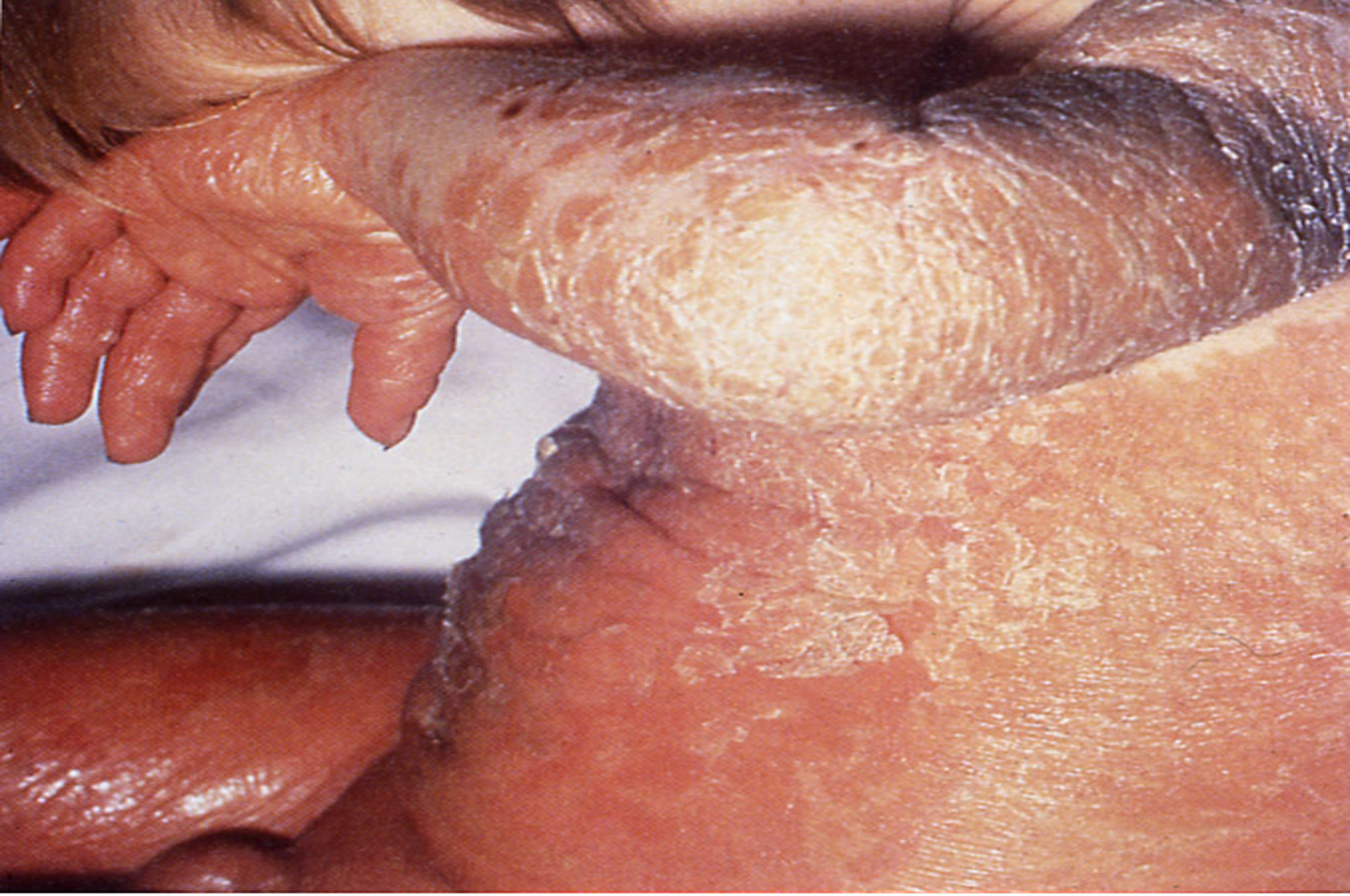
ALLERGIC DERMATITIS AND ATOPIC ECZEMA



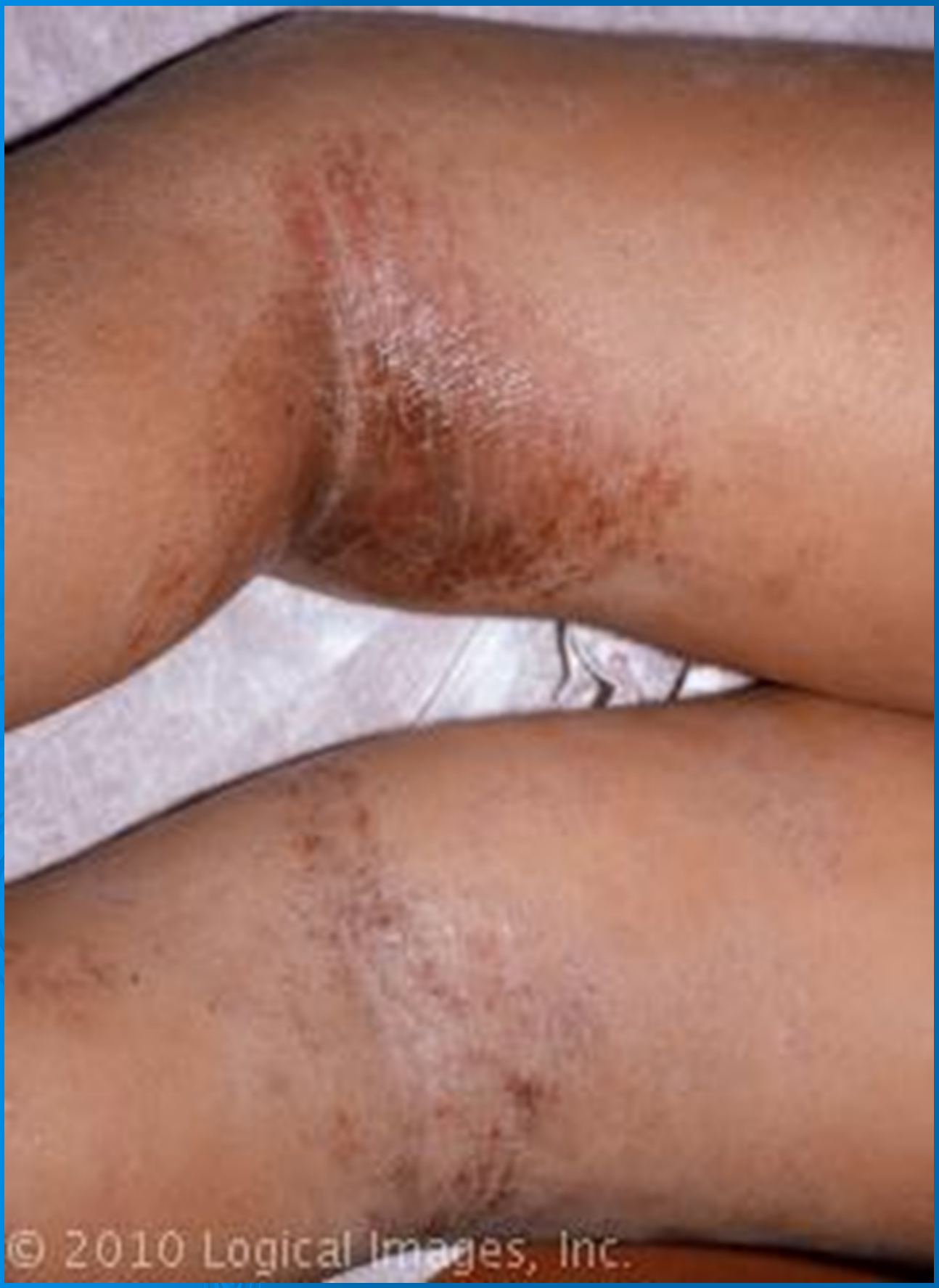








Atopic Eczema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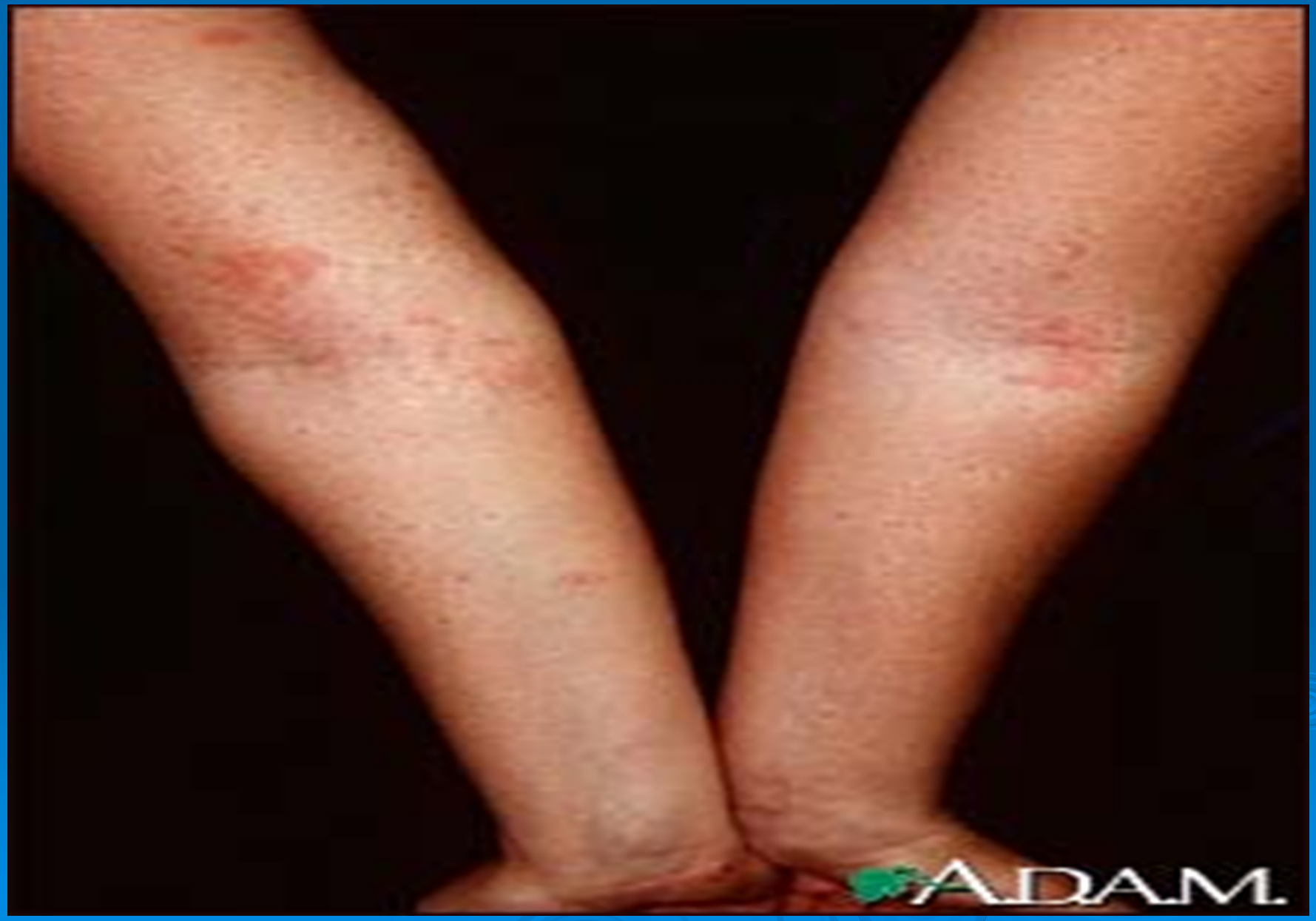
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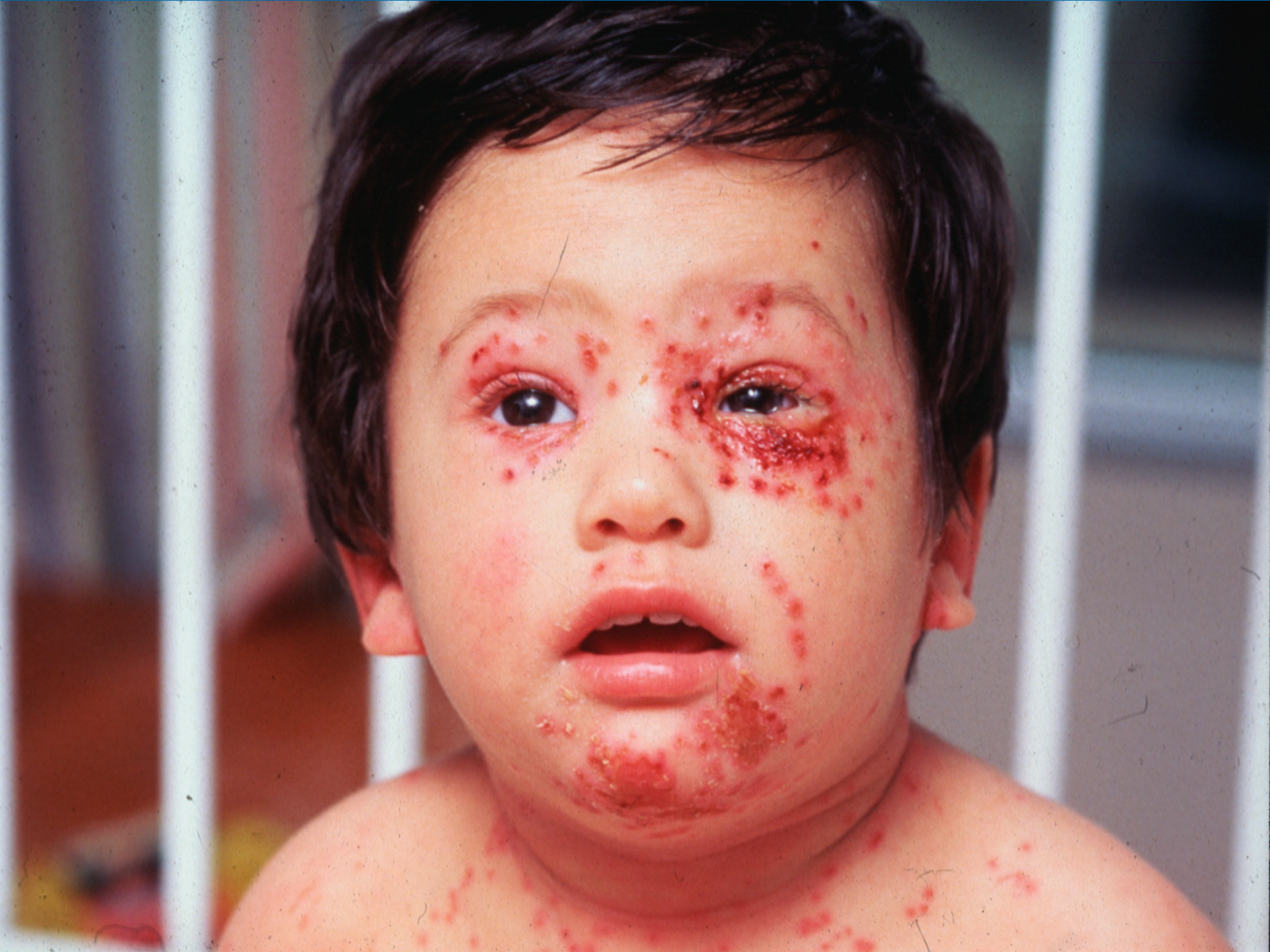
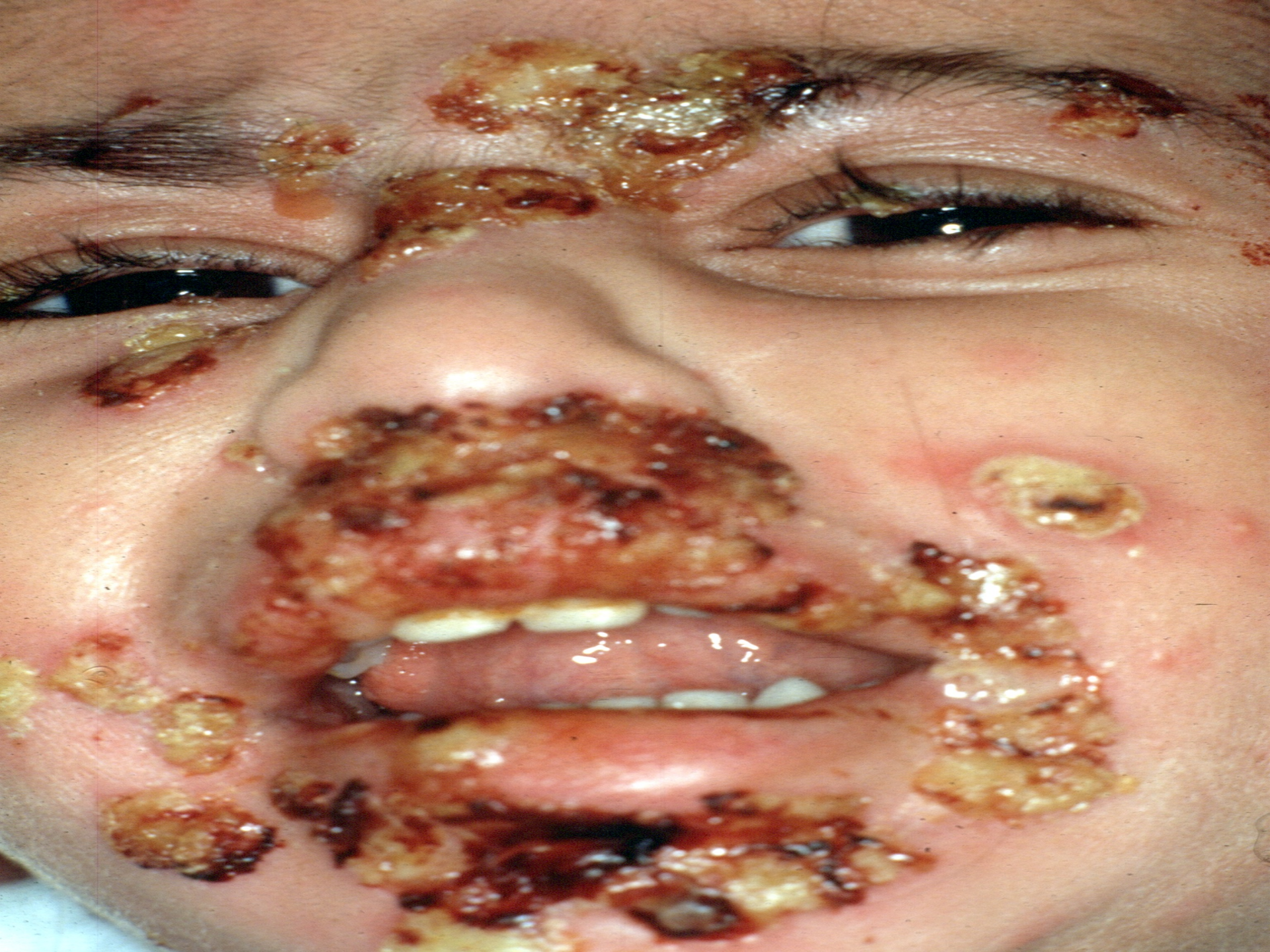
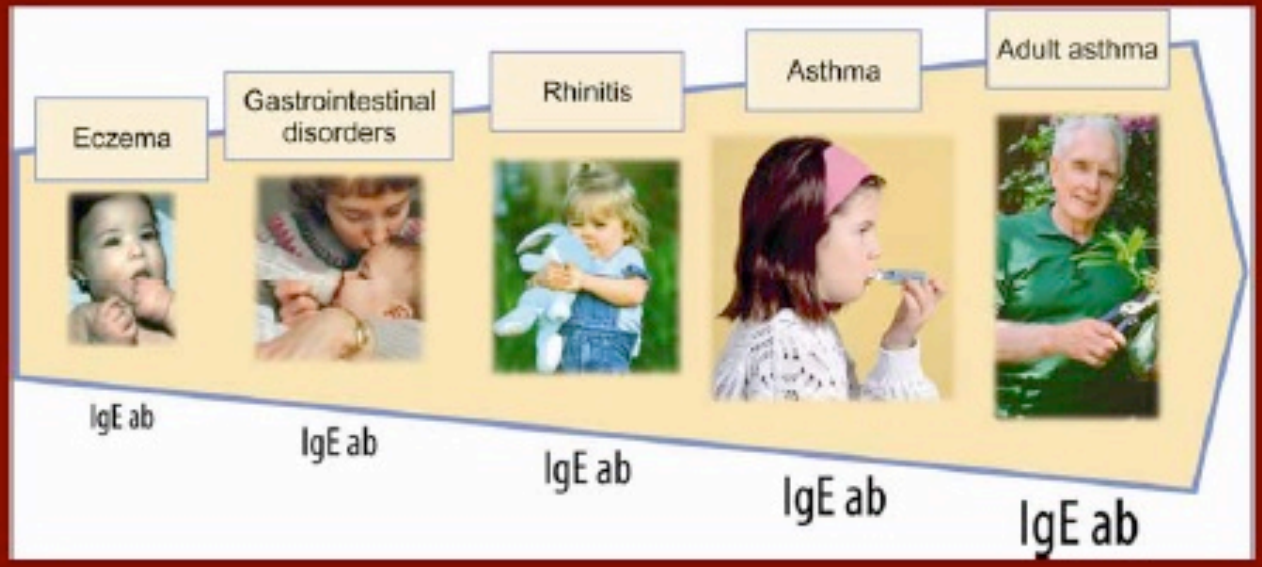
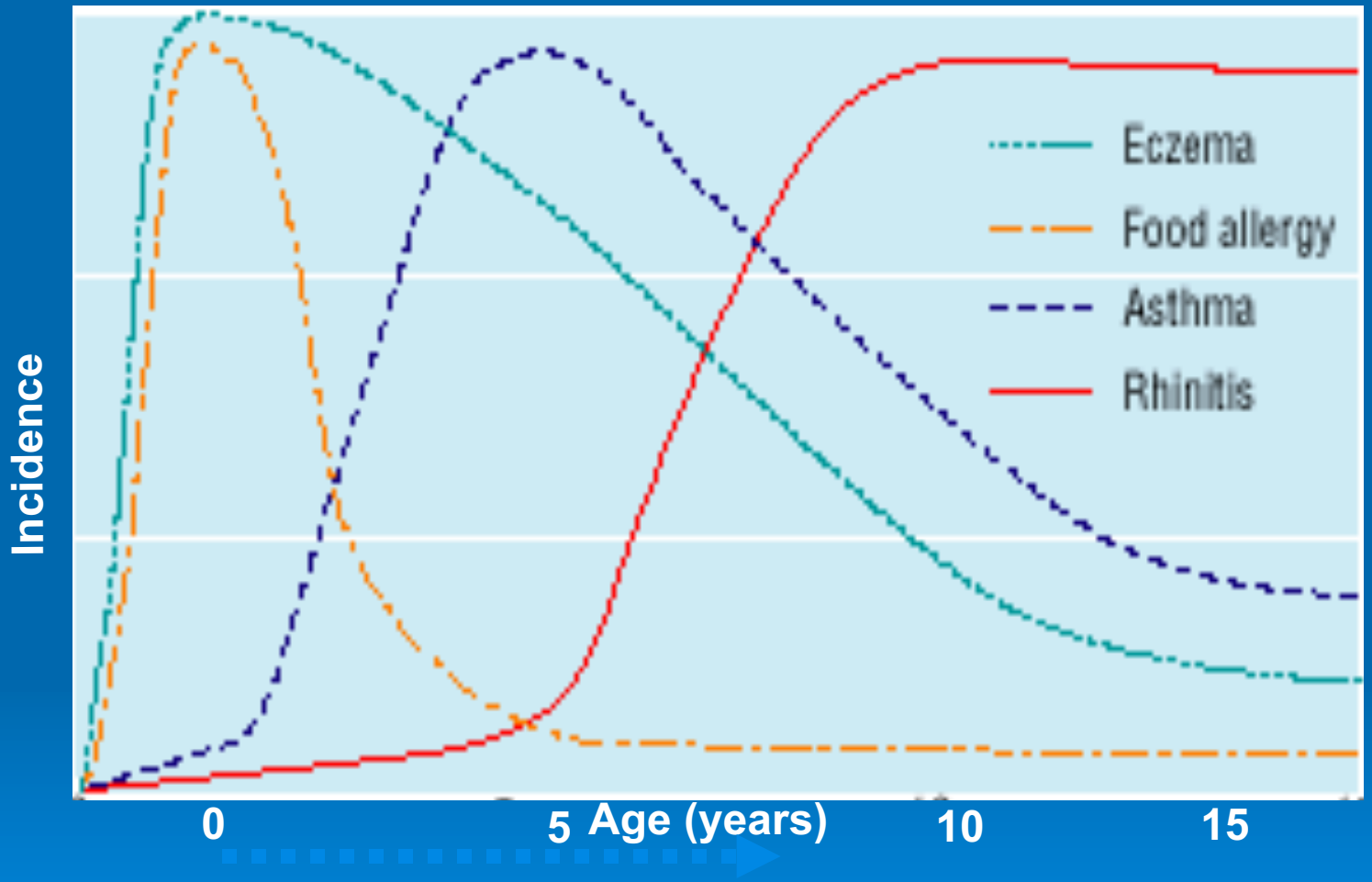




Allergy symptoms and progression



THE “ATOPIC MARCH”

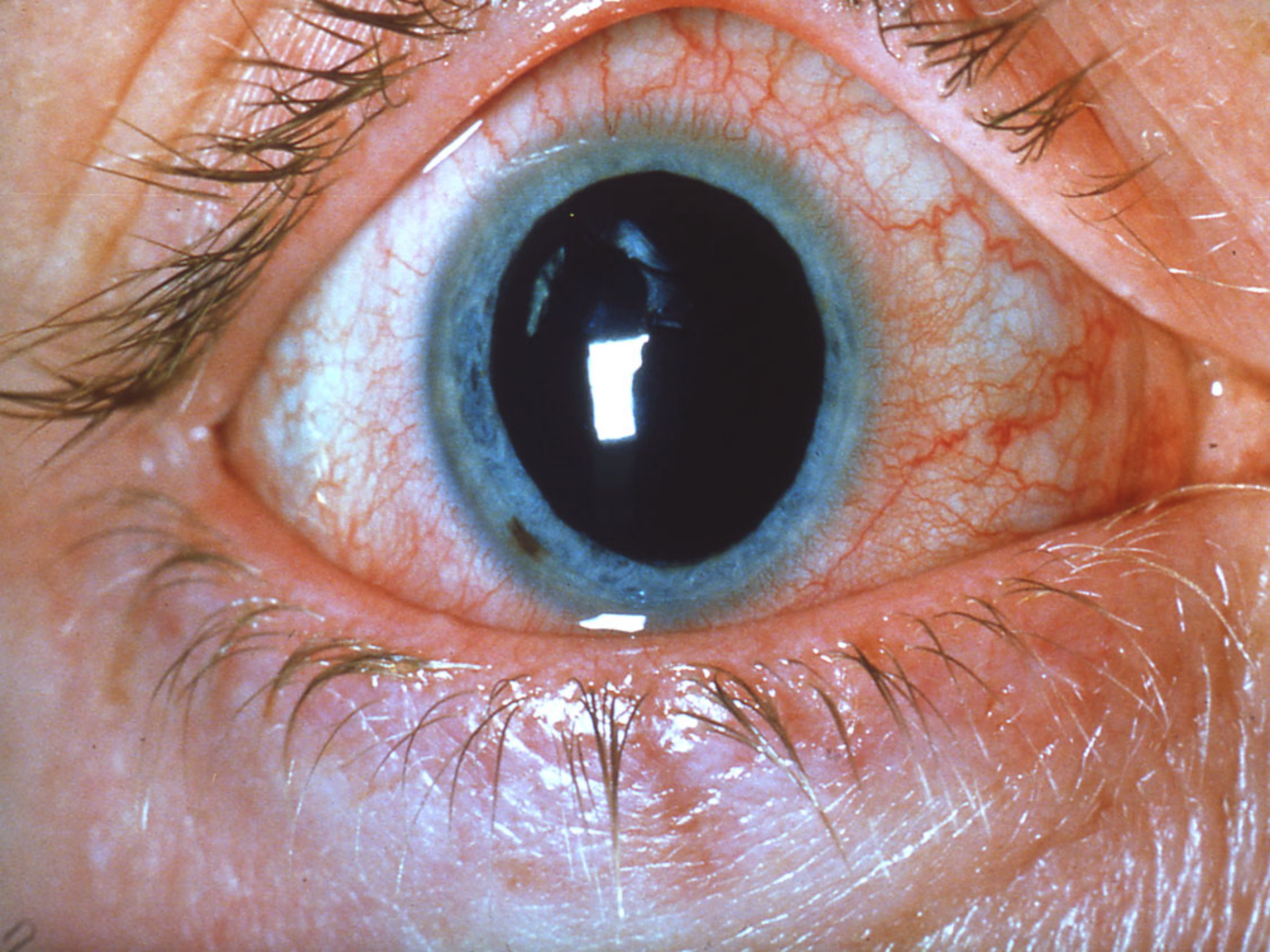


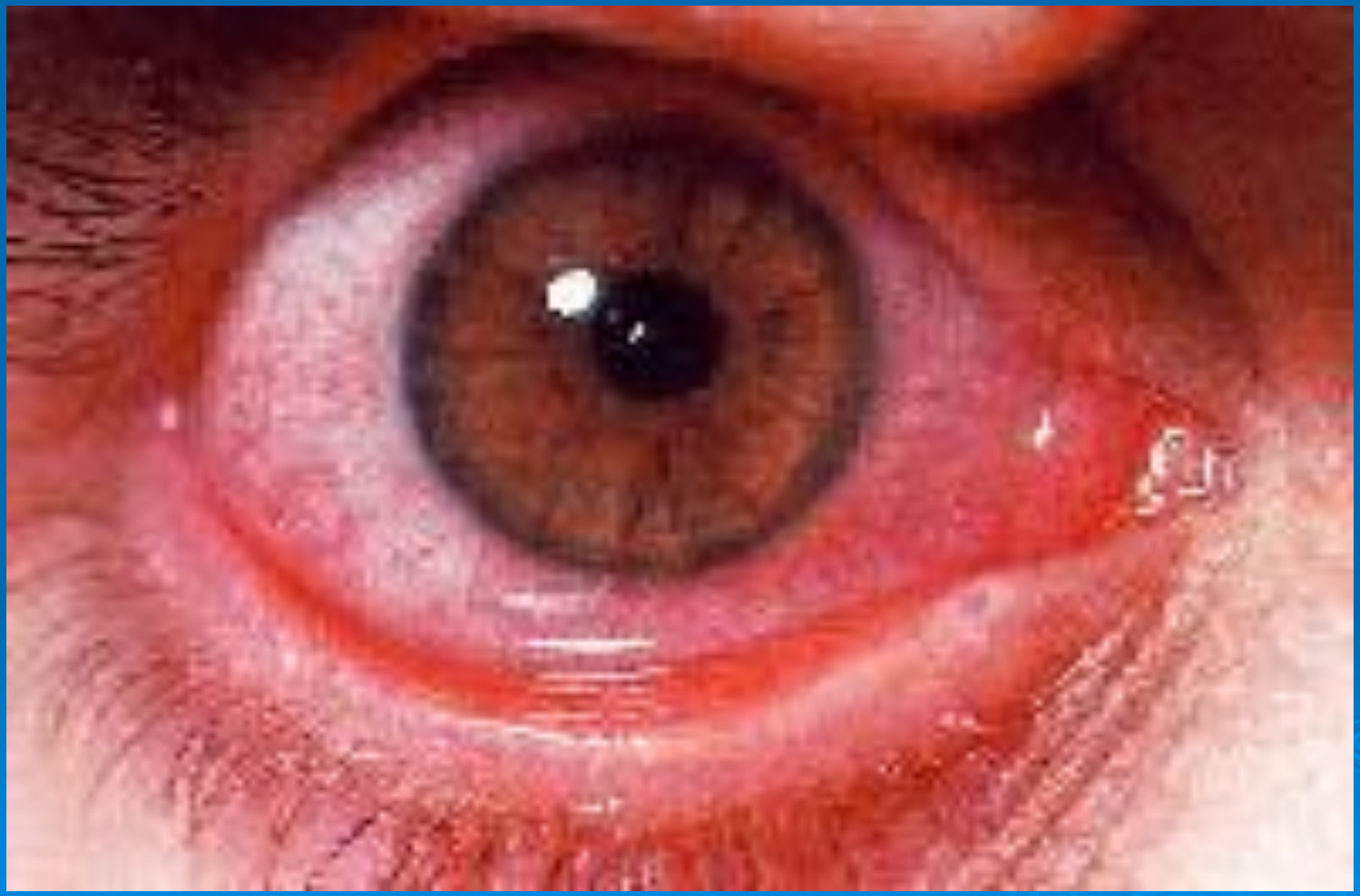
*IgE levels in **blood***

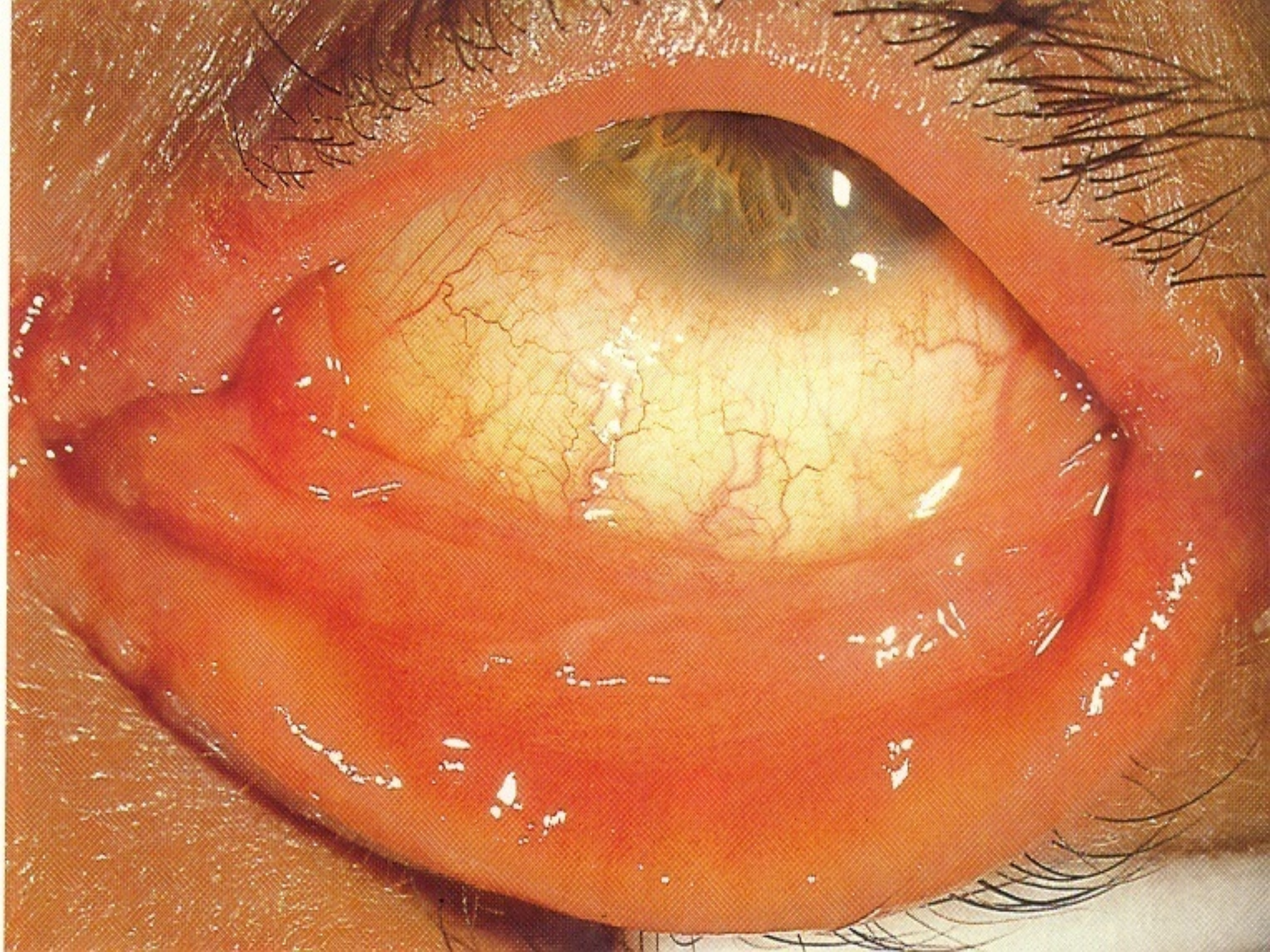
→ ***AD** is in most cases the first manifestation of the **atopic disposition***

Modified from Barnetson & Rogers. *BMJ* 2002, 324:1376–9

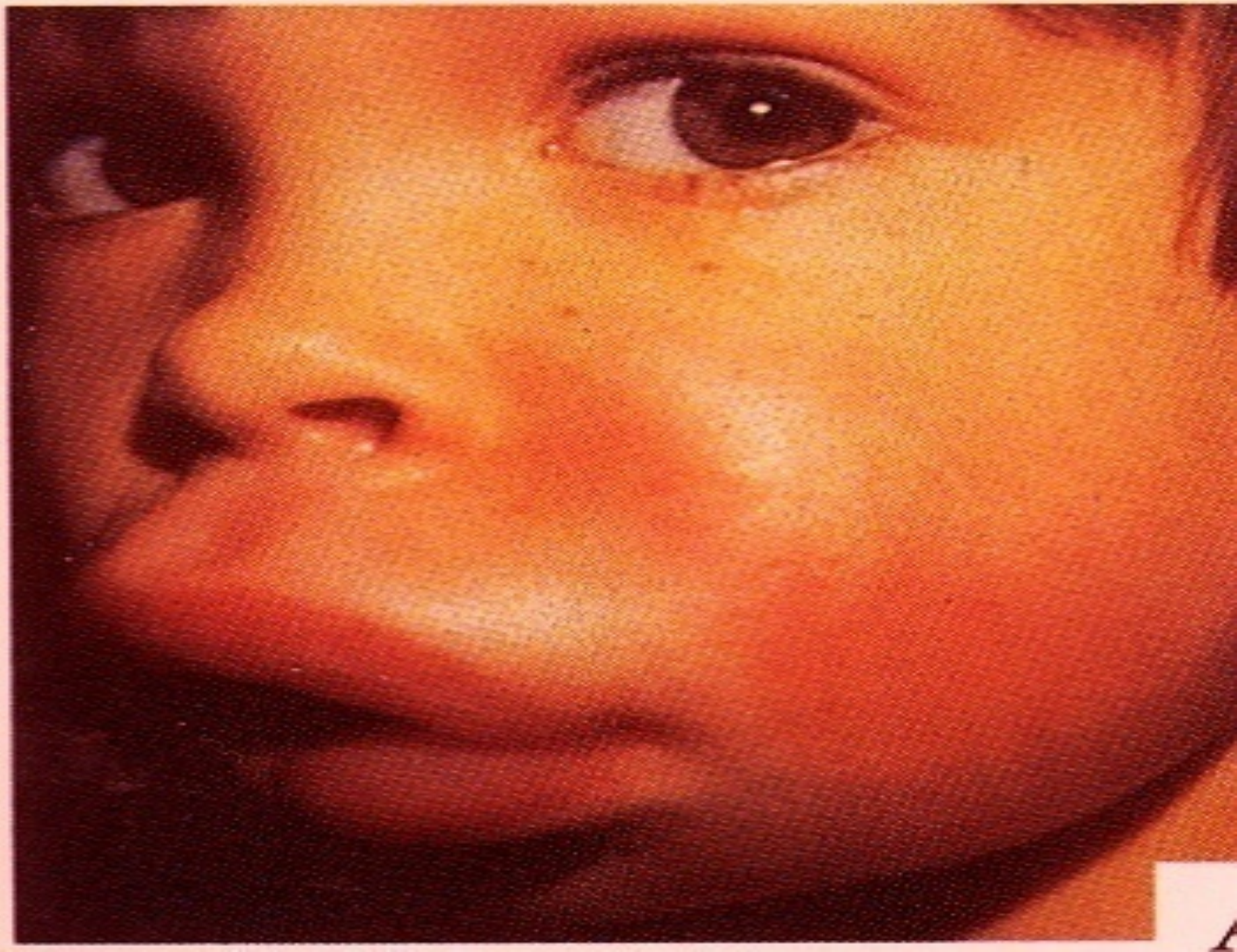
ALLERGIC CONJUCTIVITIS

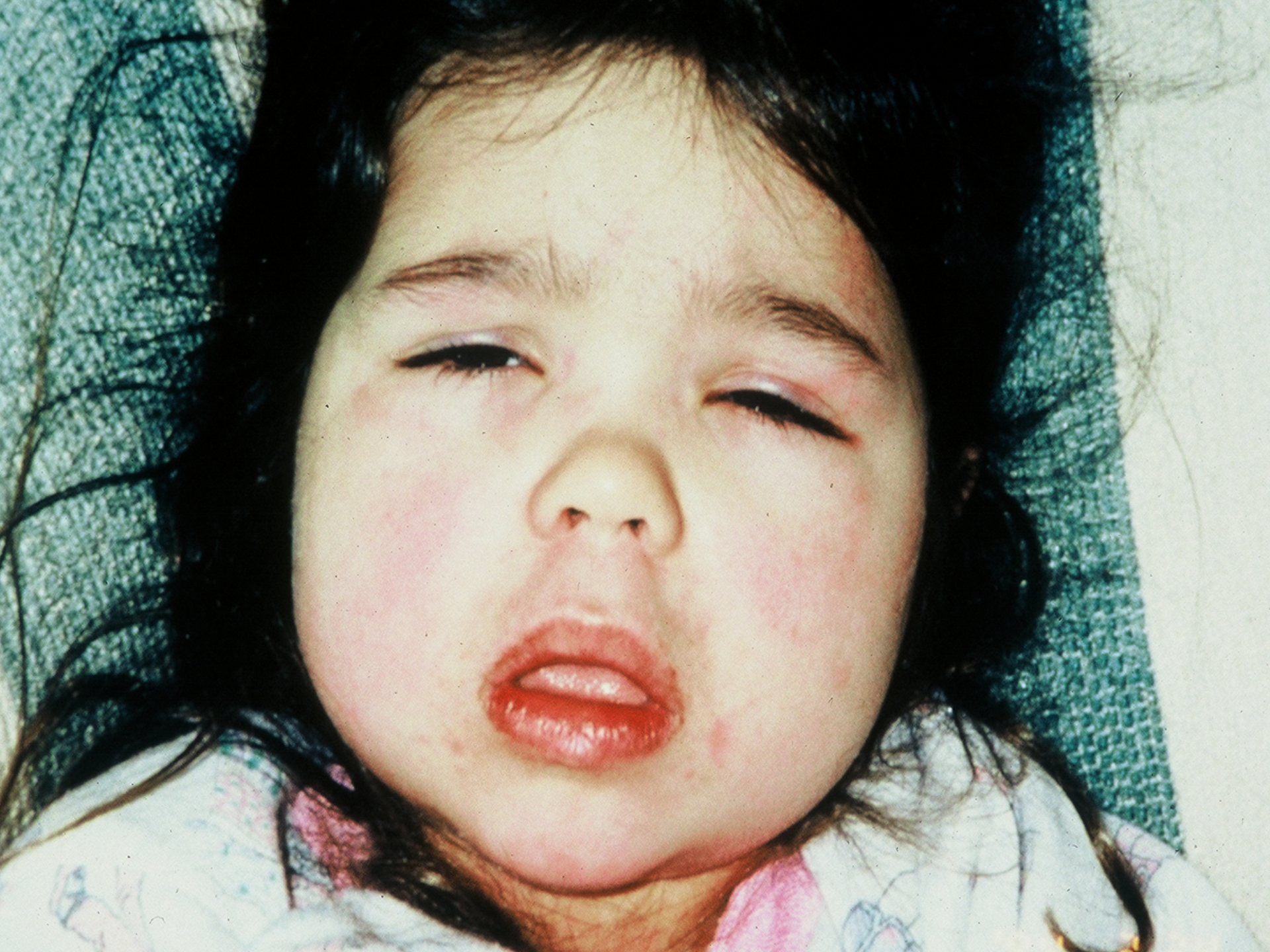


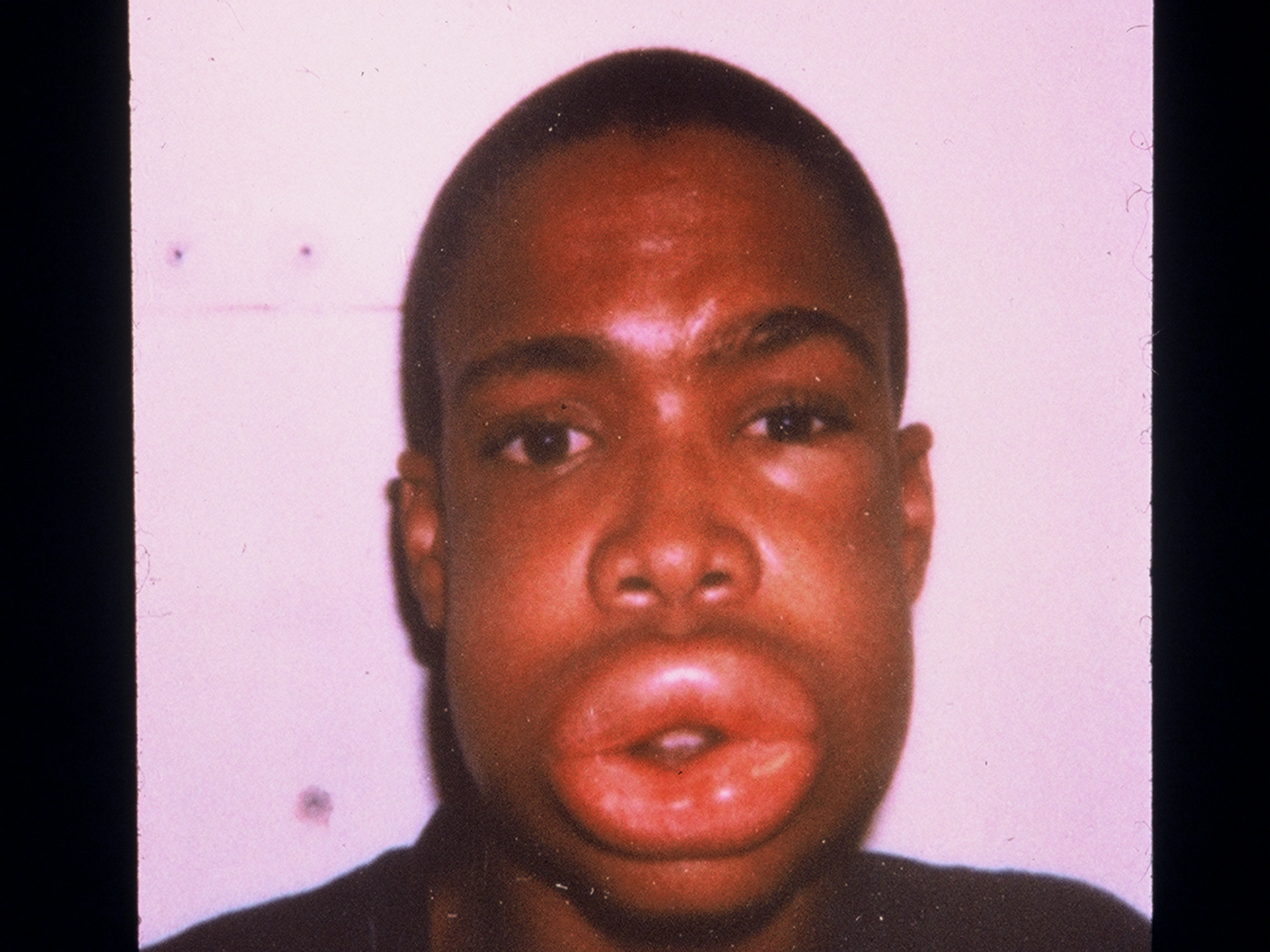


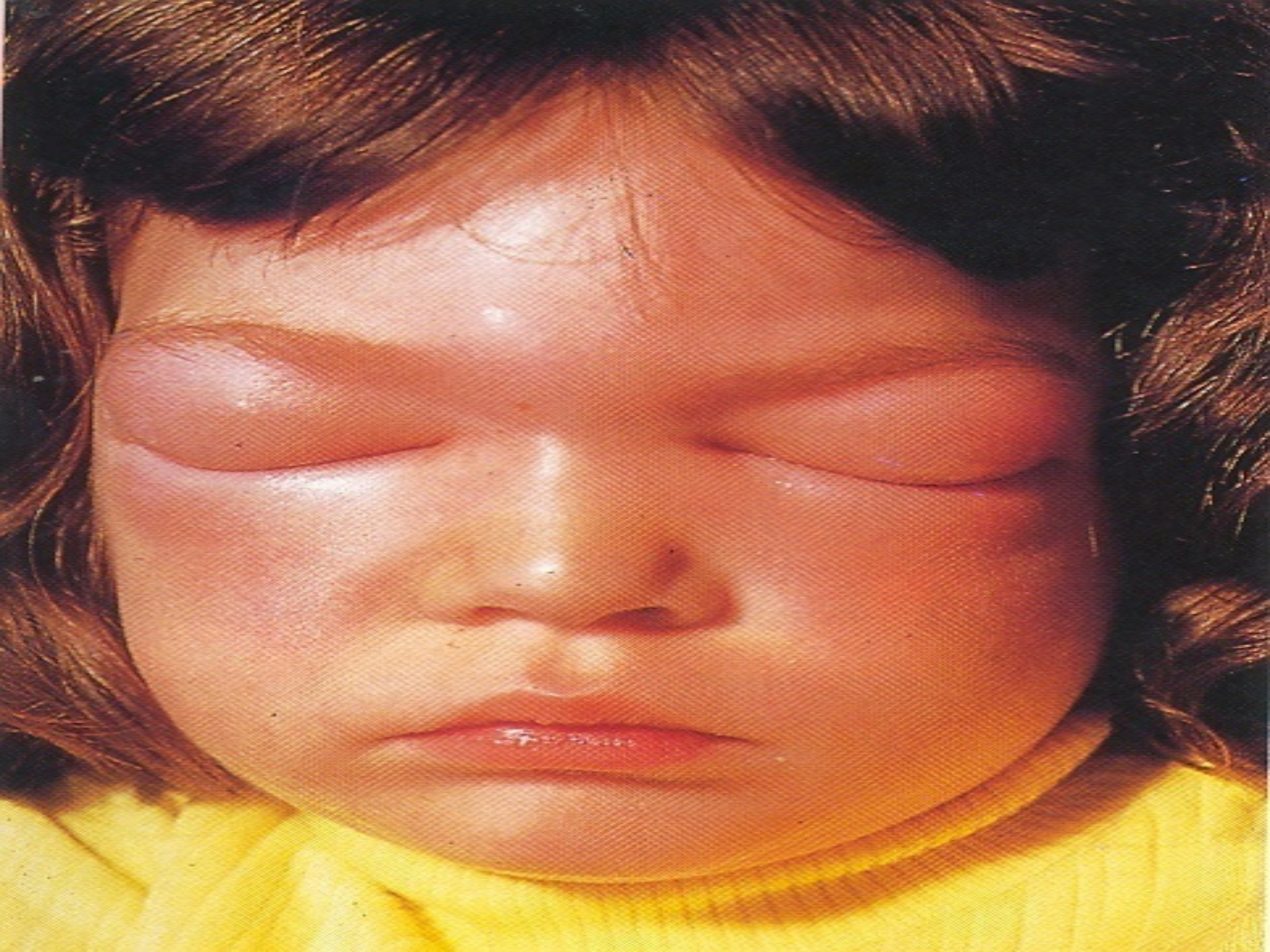


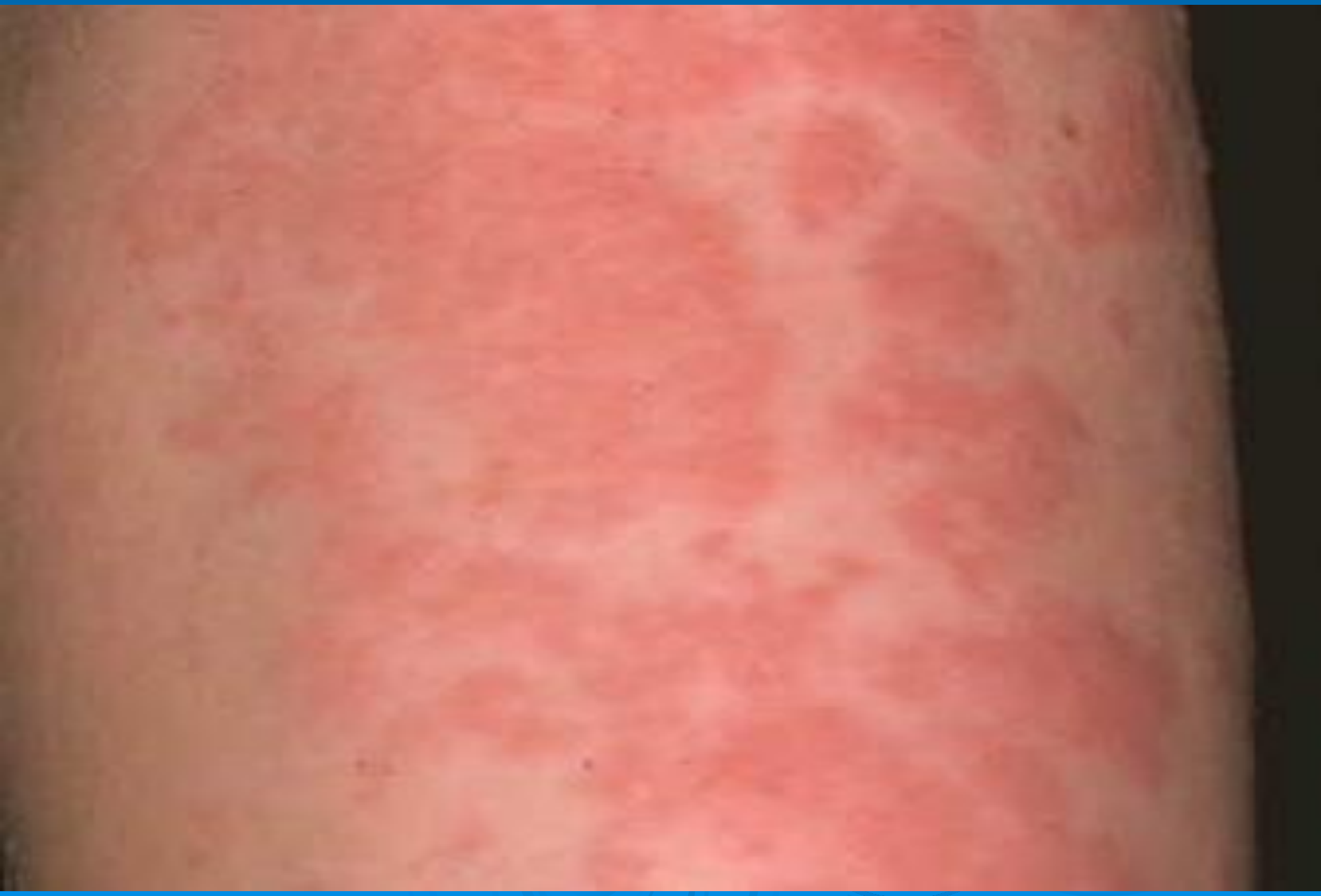
URTICARIA AND ANGIOEDEMA











Types of Urticaria/Angioedema

- Acute urticaria/angioedema – lasts less than 8 weeks
- Chronic urticaria/angioedema – lasts more than 8 weeks
  - Idiopathic , autoimmune
  - Urticarial vasculitis
- C1 inhibitor deficiency angioedema

FOOD ALLERGY

Classical (class 1) food allergens

Peanut	Ara h1, Ara h2, Ara h3	
Cow's milk	Caseins a, b, k	Bos d8
	B-Lactoglobulin	Bos d5
	A-Lactalbumin	Bos d4
	Bovine serum albumin	Bos d6
Eggs	Ovomucoid	Gal d1
	Ovalbumin	Gal d2
Shrimp	Tropomyosin	Pen a1
Codfish	Parvalbumin	Gad c1
Lipid transfer proteins		
	Apple	Mal d1, Mal d4
	Peach	Pru p1, Pru p2, Pru p3
	Hazelnut	Cor a1, Cor a2

Adverse Reactions to Food

IgE-Mediated → Non-IgE Mediated

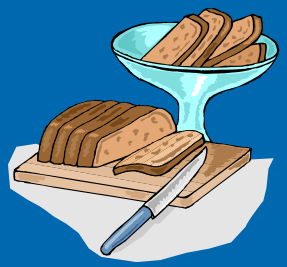
- Oral Allergy Syndrome
- Anaphylaxis
- Urticaria

- Eosinophilic esophagitis
- Eosinophilic gastritis
- Eosinophilic gastroenteritis
- Atopic dermatitis

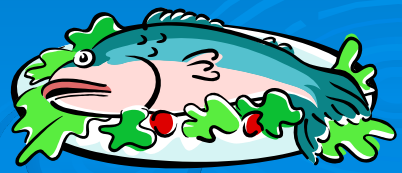
- Protein-Induced Enterocolitis
- Protein-Induced Enteropathy
- Eosinophilic proctitis
- Dermatitis herpetiformis

Incidence of Allergy to Specific Foods

- In young children: 90% of reactions caused by:
  - Milk - Soy
  - Egg - Wheat
  - Peanut

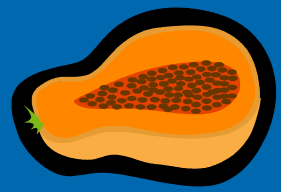


- In adults: 85% of reactions caused by:
  - Peanut - Tree nuts
  - Fish
  - Shellfish



Incidence of Allergy to Specific Foods

- Increasing incidence of allergy to “exotic foods” such as:
  - Kiwi
  - Papaya
  - Seeds: Sesame; Rape; Poppy
  - Grains: Psyllium



Frequently allergenic foods

- Most common food allergies in young children:
  - Milk (casein, whey)
  - Eggs
  - Wheat (gluten)
  - Soy
  - Peanuts
  - Tree nuts
  - Shellfish

- Most common food allergies in older children & adults
  - Fish
  - Shellfish
  - Peanuts

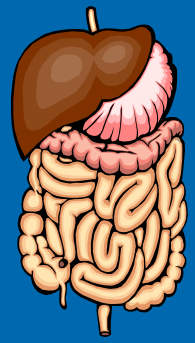
Food Allergy Prevalence in Specific Disorders

Disorder	Food Allergy Prevalence
Anaphylaxis	35-55%
Oral allergy syndrome	25-75% in pollen allergic
Atopic dermatitis	37% in children (rare in adults)
Urticaria	20% in acute (rare in chronic)
Asthma	5-6% in asthmatic or food allergic children
Chronic rhinitis	Rare

Prevalence of Clinical Cross Reactivity Among Food "Families"

Food Allergy	Prevalence of Allergy to > 1 Food in Family
Fish	30% -100%
Tree Nut	15% - 40%
Grain	25%
Legume	5%
Any	11%

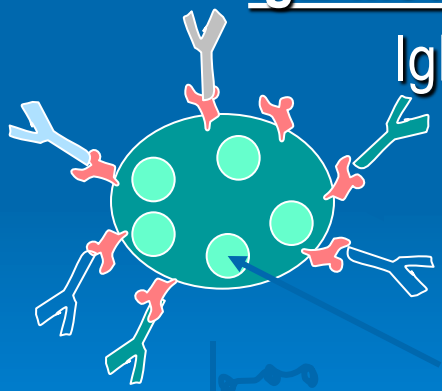
Pathophysiology: Immune Mechanisms



- Protein digestion
- Antigen processing
- Some Ag enters blood

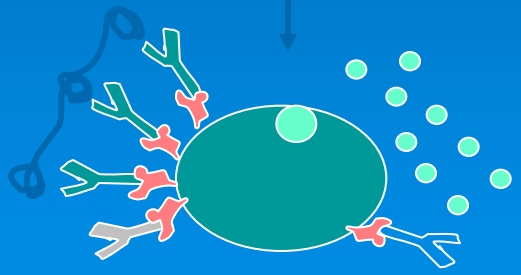
IgE-Mediated

IgE-receptor



Mast cell

Histamine



APC

Non-IgE Mediated

B cell

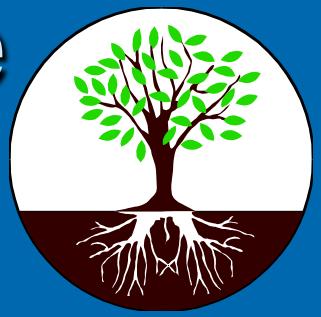
T cell

- TNF-α
- IL-5

Oral Allergy Syndrome (OAS)

- OAS refers to clinical symptoms in the mucosa of the mouth and throat that:
- Result from direct contact with a food allergen
- In an individual who also exhibits allergy to inhaled allergens.
- Usually pollens (pollinosis) are the primary allergens
- Pollens usually trigger rhinitis or asthma in these subjects

Oral Allergy Syndrome
Characteristics



- Inhaled pollen allergens sensitise tissues of the upper respiratory tract
- Tissues of the respiratory tract are adjacent to oral tissues, and the mucosa is continuous
- sensitisation of one leads to sensitisation of the other
- First described in 1942 in patients allergic to birch pollens who experience oral symptoms when eating apple and hazelnut
- OAS symptoms are mild in contrast to primary food allergens and occur only in oral tissues

Oral Allergy Syndrome
Allergens

- Pollens and foods that cause OAS are usually botanically unrelated
- Several types of plant proteins with specific functions have been identified as being responsible for OAS:
  - Profilins
  - Pathogenesis-related proteins
  - Lipid Transfer Proteins

Oral Allergy Syndrome
Allergens

- Profilins are associated with reproductive functions
- Pathogenesis-related proteins tend to be expressed when the tree is under “stress” (e.g. growing in a polluted area)
- Lipid Transfer Proteins induce IgE Antibodies,resistant to heat,gastric acid and digestive enzymes

Oral Allergy Syndrome
Cross-Reactivity

- Occurs most frequently in persons allergic to certain weeds and tree pollens
- eg. Ragweed pollen
  - Mugwort pollen
  - Grass pollens

Oral Allergy Syndrome
Associated foods

- Foods most frequently associated with OAS are mainly fruits, a few vegetables, and nuts
- The foods cause symptoms in the oral cavity and local tissues immediately on contact:
  - Swelling
  - Throat tightening
  - Tingling
  - Itching
  - “Blistering”

Oral Allergy Syndrome

Cross-reacting allergens

- Birch pollen (also: mugwort, and grass pollens) with:
  - Apple
  - Stone Fruits (Apricot, Peach, Nectarine, Plum, Cherry)
  - Kiwi Fruit
  - Orange - Peanut
  - Melon - Hazelnut
  - Watermelon - Carrot
  - Potato - Celery
  - Tomato - Fennel

Oral Allergy Syndrome

Cross-reacting allergens

- Ragweed pollen with:
  - Banana
  - Cantaloupe
  - Honeydew
  - Watermelon
  - Other Melons
  - Zucchini (Courgette)
  - Cucumber

Latex Allergy

- Allergy to latex is thought to start as a Type IV (contact) hypersensitivity reaction
- Contact is with a 30 kd protein, usually through:
  - Abraded (non-intact) skin
  - Mucous membrane
  - Exposed tissue (e.g. during surgery)

Latex Allergy
Related foods

- Foods that have been shown to contain a similar 30 kd antigen include:
  - Avocado - Tomato
  - Banana - Celery
  - Kiwi Fruit - Peanut
  - Fig - Tree Nuts
  - Passion Fruit - Chestnut
  - Citrus Fruits - Grapes
  - Pineapple - Papaya

THANK YOU !