بسم الله الرحمن الرحيم

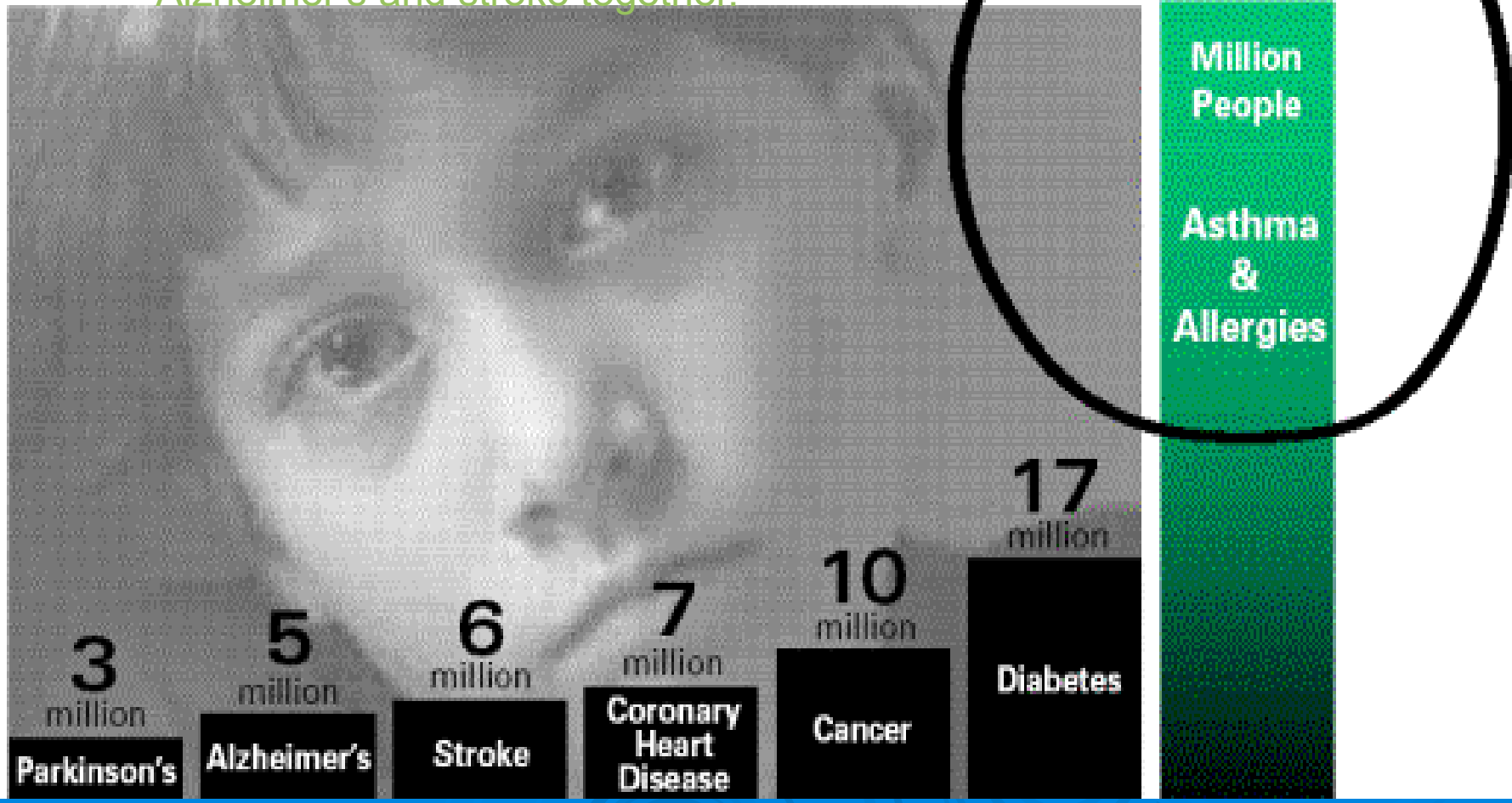
COMMON PEDIATRIC ALLERGIES

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

Notice that it is more common than Parkinson's, Alzheimer's and stroke together.



PREVALENCE OF ATOPY AND ASTHMA IN PRIMARY SCHOOL CHILDREN IN AUSTRALIA

Asthma diagnosed	31.0%
Hay Fever	38.4%
Eczema	24.8%









When we talk about allergic manifestations it could be due to:
weed, fungi, insects, animal, dust mites or food

- In 2013 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

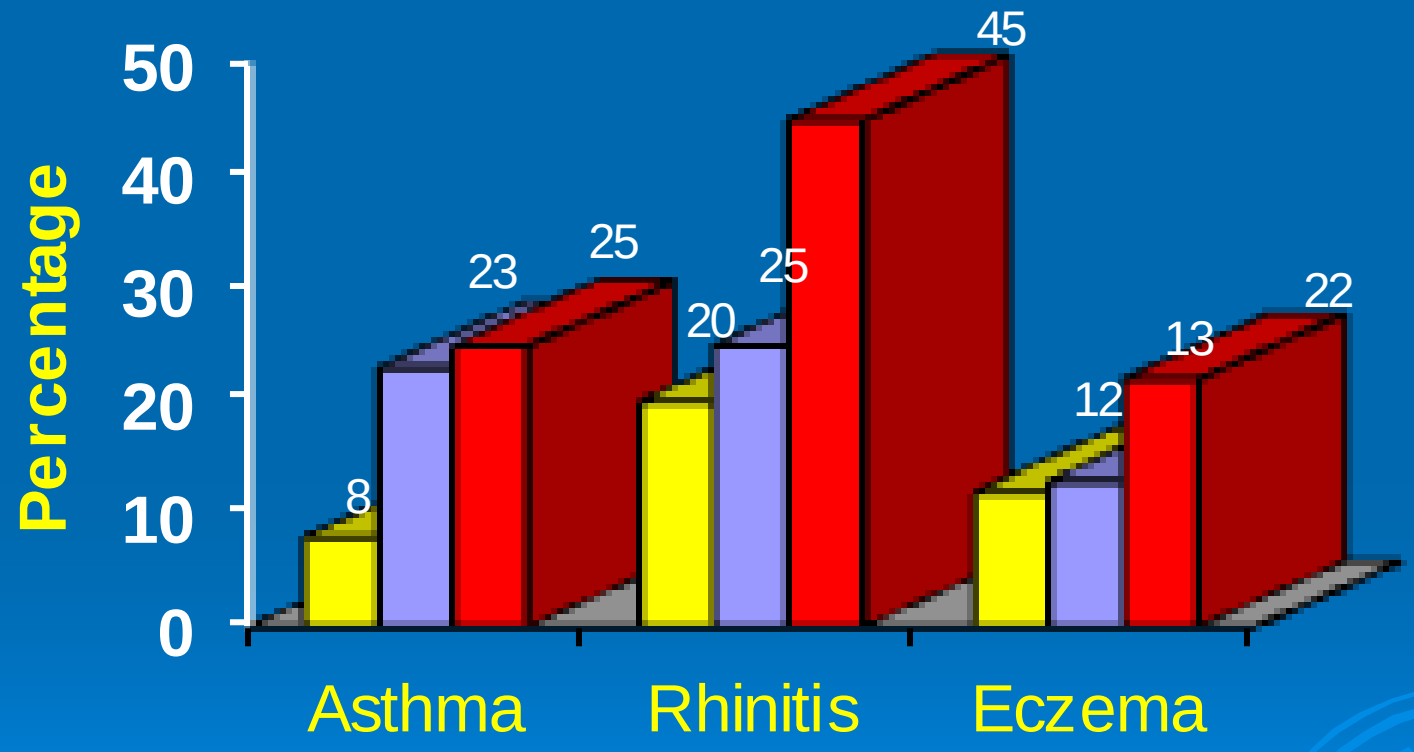
Syed Mohammad Moazzam Aarif, Ahmed Ali Al-Mohammed

International Journal of Students' Research

Volume 5 Issue 1 Year 2015 www.ijsronline.com

Prevalence of Asthma, Rhinitis and Eczema in Saudi Arabia

The numbers are increasing.



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

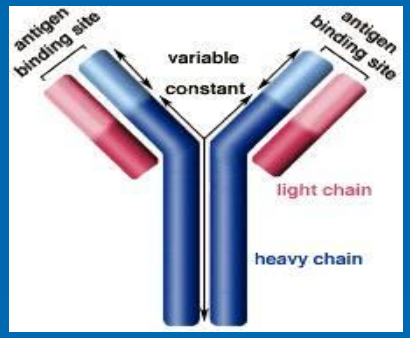
HYPERSENSITIVITY

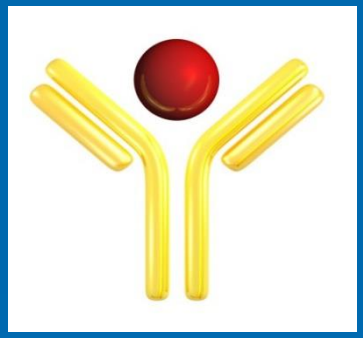
When we talk about hypersensitivity, we talk about possible manifestations of allergy which is usually discussed in lab environment. But when we talk about allergy we're talking about clinical manifestations. So, they are interchangeable, but allergy is used more by physicians and immunologists use hypersensitivity.

Wasn't presented

Humoral – Antibody (Extracellular Response)

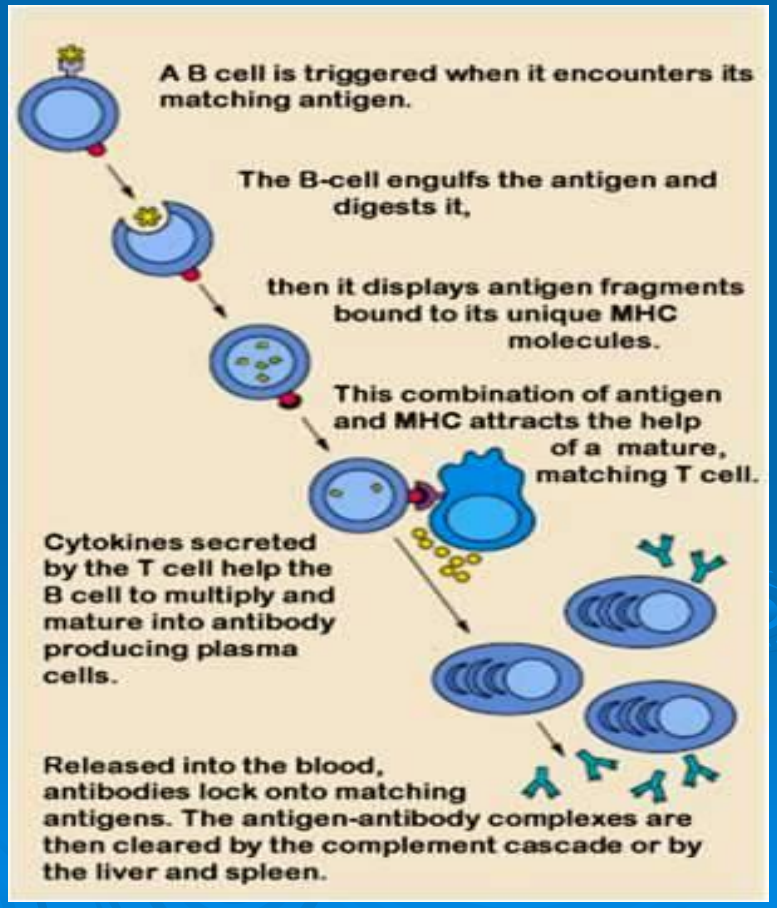
- **B cells**
- **Plasma Cells - produce antibodies**





Antibody-antigen Complex

- **Helper T Cells**
- **Memory Cells**



Allergens

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

What allergens exists in the environment?
Everything you can imagine can cause a reaction.

Allergens

The doctor read every word in the schedule

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

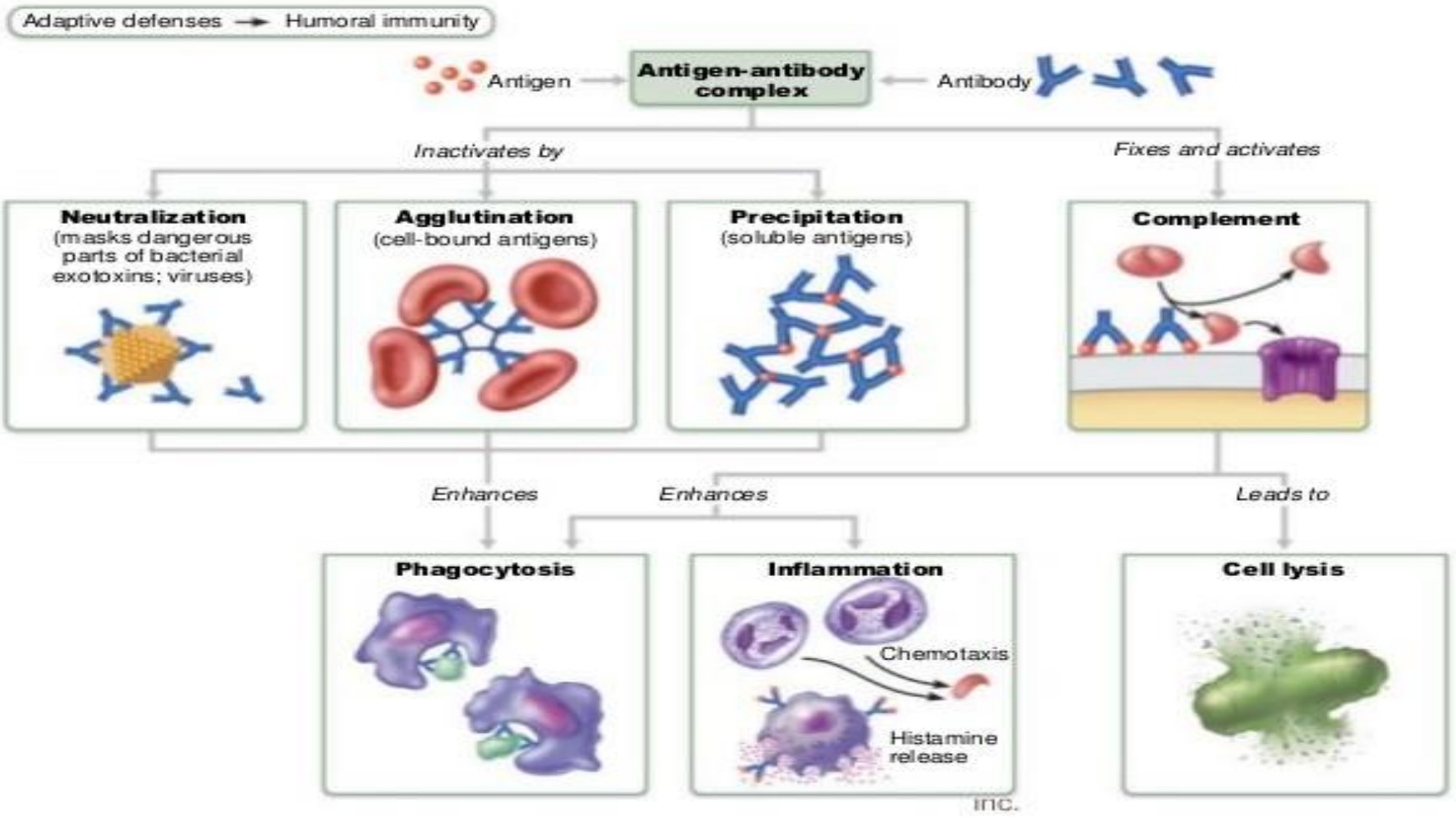
Insect products
- Bee venom
- Wasp venom
- Ant venom
- Cockroach calyx
- Dust mites

Mold spores

Animal hair and dander

Wasn't presented

Antigen-Antibody Complex Functions



These are the different types of allergic reaction which makes you more familiar with the interpretation of the results from the lab and explain it to the patients and colleagues.

Major difference: first 3 are humoral mediated, type 4 is cell mediated reaction.

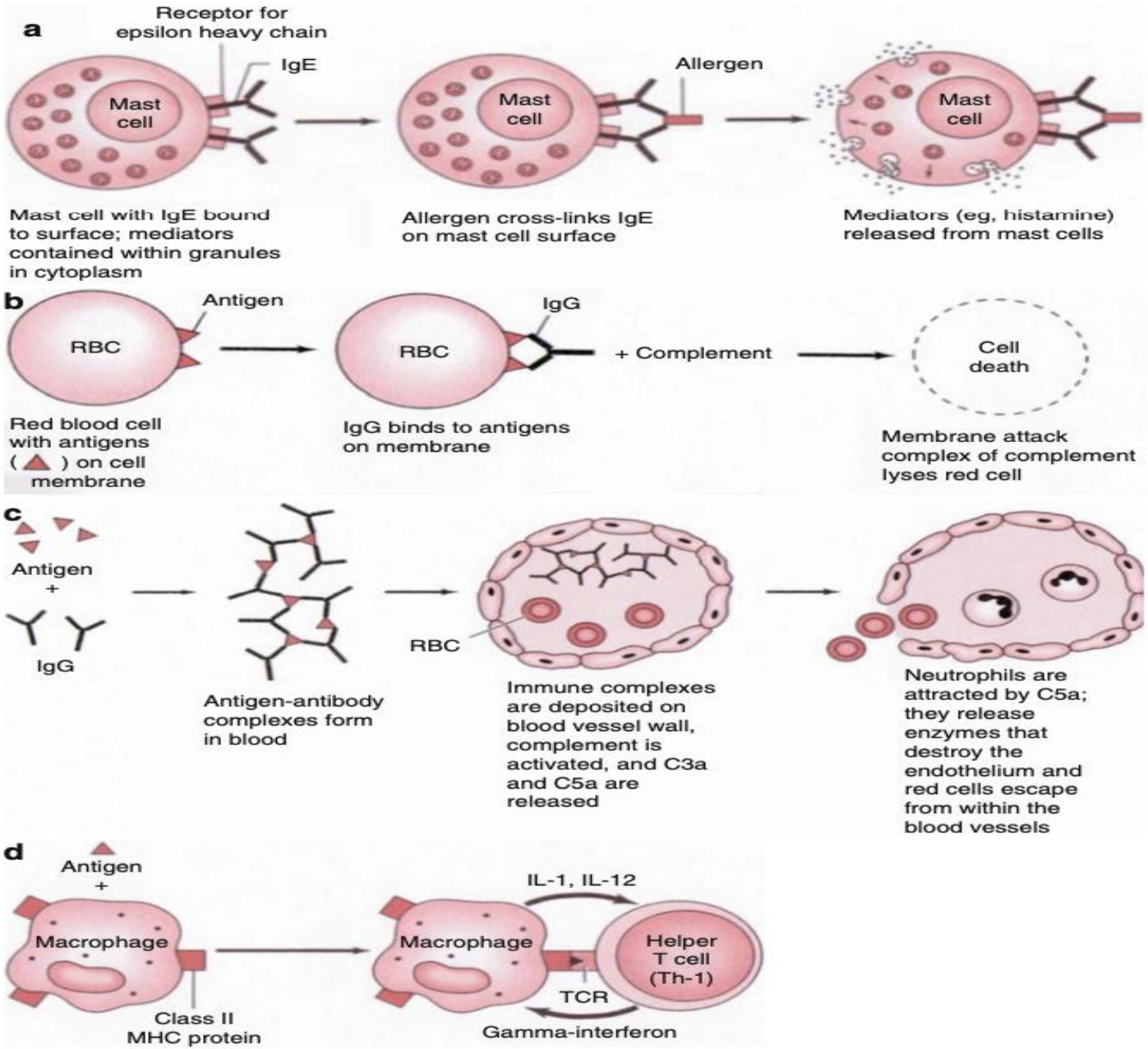
The doctor read every word in the schedule

Type	Reactions	Mechanism	Onset of action	Examples
Type I immediate hypersensitivity or anaphylactic Most common	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 Or both IgG and IgM	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) vascular reaction is more present
Type IV cell mediated 2nd most common	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 Most common reaction is BCG or PPD (TB reaction after taking vaccination)
		Direct killing of affected cells by CD8+ T cells		

Wasn't presented

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

Wasn't presented



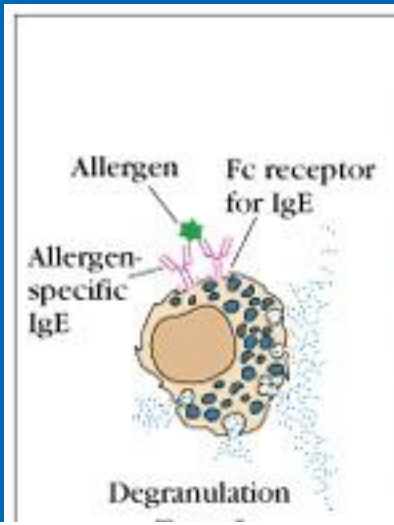
TYPE I Hypersensitivity Classic allergy

Wasn't presented

- 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.

GeLL and Coombs classification of hypersensitivities.



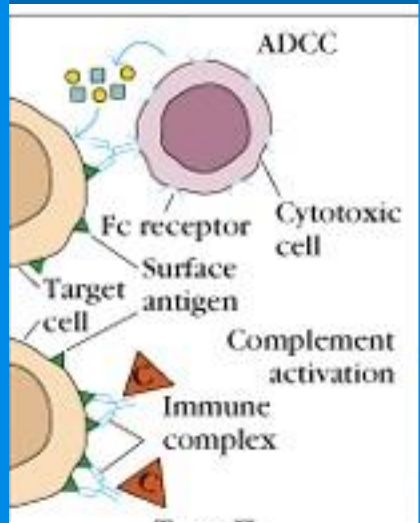
AllergyType I

IgE Mediated

Classic

Reaction in type 1 starts with 3 things:

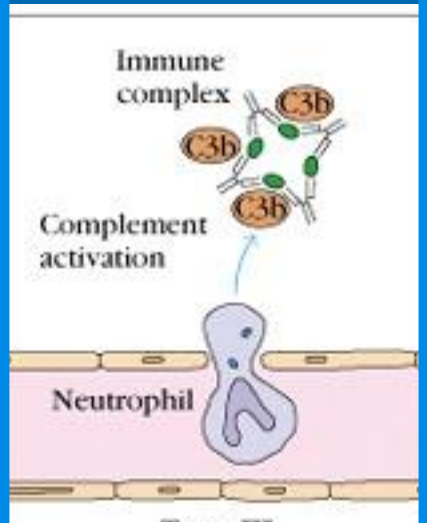
1) IgE
2) Allergen
3) Fc receptors



Type II

IgG/IgM Mediated

rbc lysis



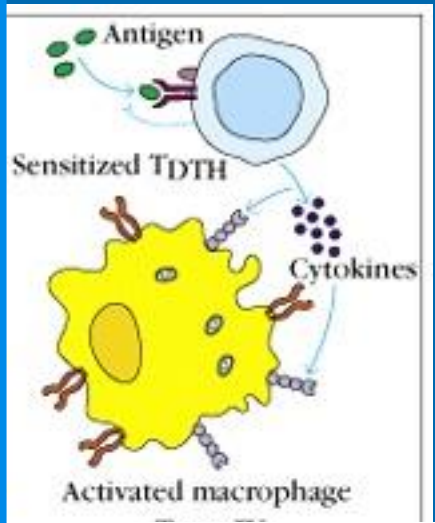
Rarely seen as a clinical allergic reaction

Type III

IgG Mediated

With immigration of inflammatory cells from the circulation into the tissue

Immune complex Disease



Type IV

T cell

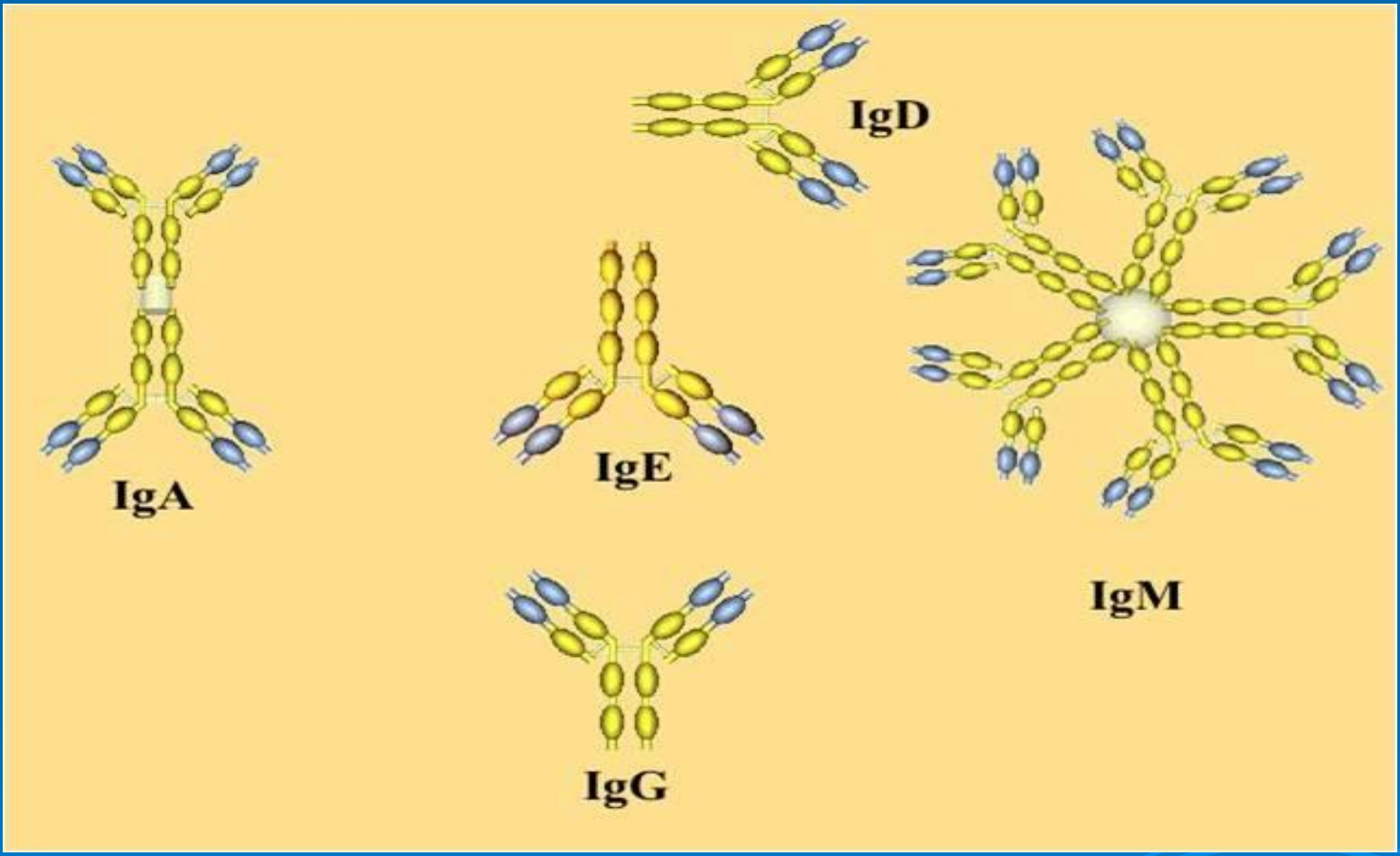
Delayed Type Hypersensitivity

Classes of Antibodies

Doctor went through it quickly

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.

Classes of Antibodies

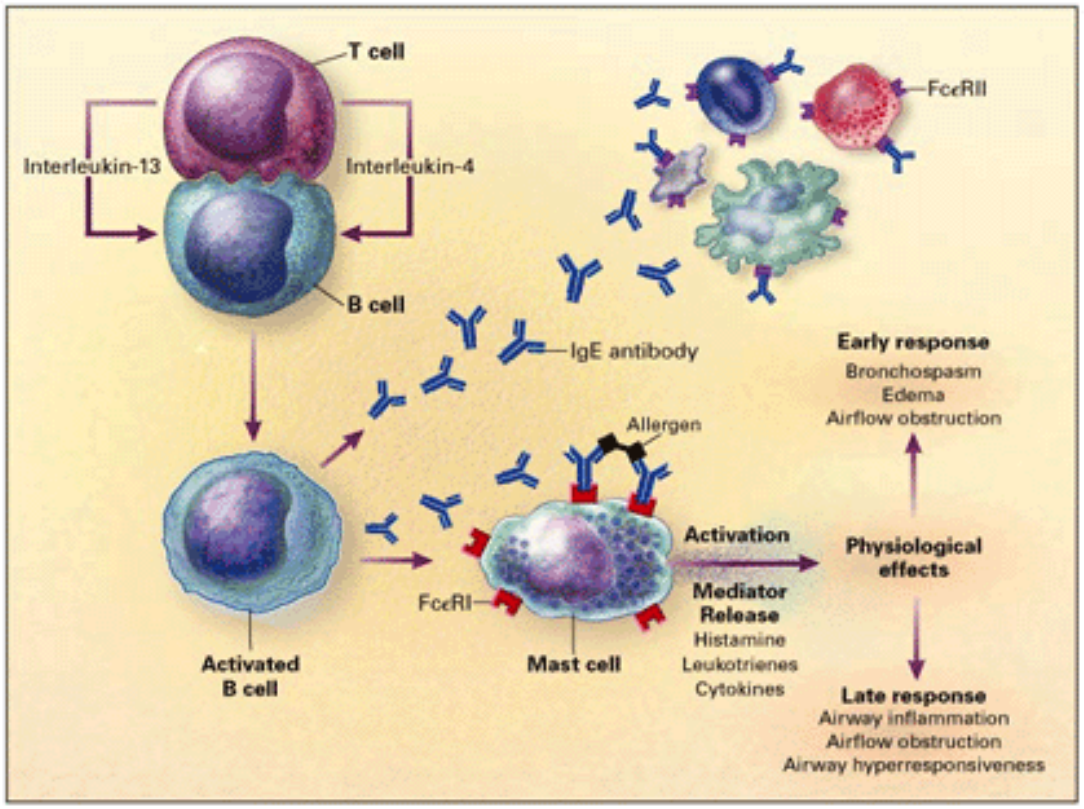


Another 2 types of antibodies:
IgA: local barrier in mucus membrane and skin.
IgD: paly a role in b cell and T cell ration.

Mechanisms of allergic response

Sensitization

Th2/B cell interaction



IL-4

IL-4R

CD40

Drive B cell Activation and IgE isotype switch.

T-cell is the most important which will activate IL that activates B-cell. B-cell then bound with Fc receptor. You must remember Fc receptor.

Fc receptor, IgE and mast cells will be connecting, and the allergen will connect to IgE and the result is activation and early response (degranulation) and late response which we will discuss later.

Mechanisms of allergic response

Wasn't presented

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)

The allergen fix on Fc receptor.

FcεR1

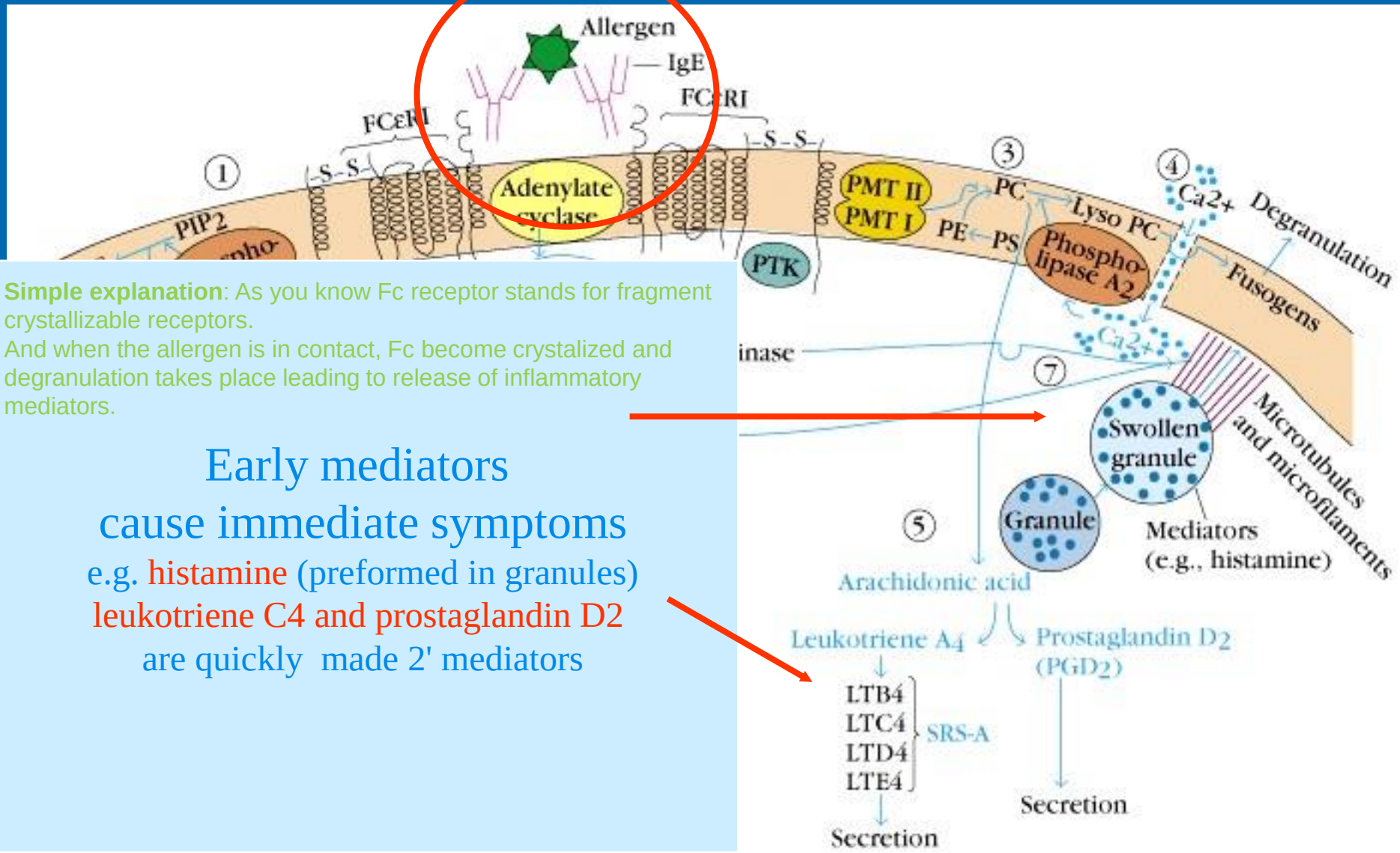
- high affinity IgE receptor found on
  - mast cells/basophils/activated eosinophils.

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

You can see now we're having more details and saying FcE, and going deeper we're saying FcER1.
Just know that Fc receptors are different receptors responsible for IgE, IgG or IgM. And FcER1 are specific receptors on the surface of eosinophils, mast cells or basophils.

This is just to explain why we're going into so much details.

FcεRI Triggers Release of Mediators



Simple explanation: As you know Fc receptor stands for fragment crystallizable receptors.
And when the allergen is in contact, Fc become crystalized and degranulation takes place leading to release of inflammatory 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 Type 1 hypersensitivity is leading to immediate effect by 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.

And leads to increase mediators of:

- Leukotrienes
- Prostaglandins

Mediators of Type I Hypersensitivity

Primary Mediators

Pre-formed mediators in granules

Will take place by activation of:

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

Wasn't presented

Type I Hypersensitivity Secondary mediators Mediators formed after activation

- Leukotrienes

Prostaglandines

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

Wasn't presented

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

Wasn't presented

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

Where the reaction of allergy can take place

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.

Patch test is a method that can tell us what the patient is allergic to as contact allergy. Ex: leather, nickel, hair dye.
We leave the patch 24-72 hours because it is cell mediated reaction NOT IgE mediated reaction!.

Stages of Type IV DTH

Sensitization stage

- Memory Th1 cells against DTH antigens are generated by dendritic (antigen presenting cells) 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.

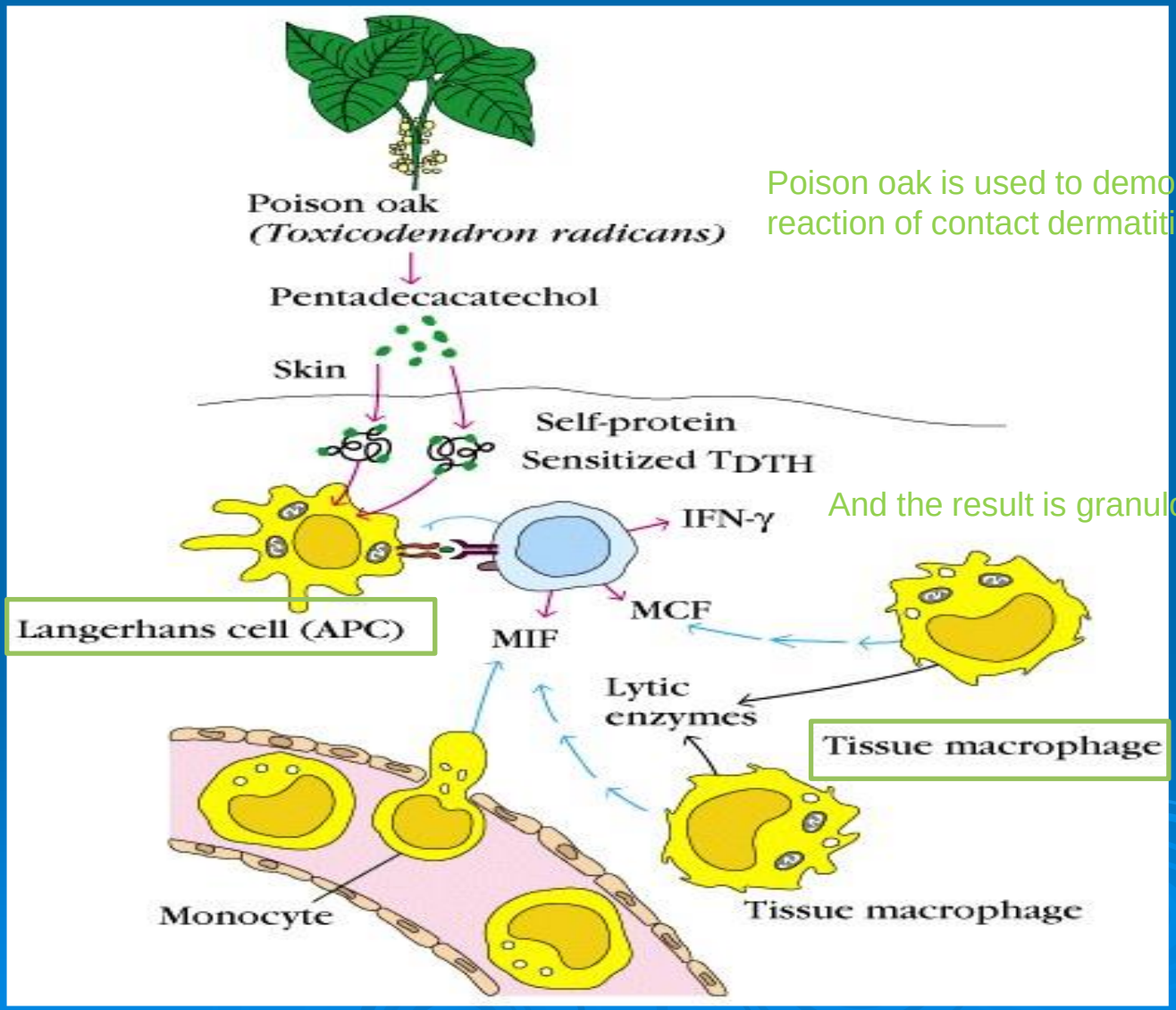
Ex: Keloid after surgery, BCG scar, lichenification.

Type IV DTH
Contact dermatitis

Contact dermatitis is the Most common presentation of delayed hypersensitivity reaction and remember it is cell mediated reaction (type 4). It is driven by Th1 memory cells, which will become activated after the next exposure.

- 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



Poison oak is used to demonstrate the reaction of contact dermatitis

And the result is granuloma formation

Delayed type hypersensitivity (DTH)

The doctor went through them as they can cause DTH

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

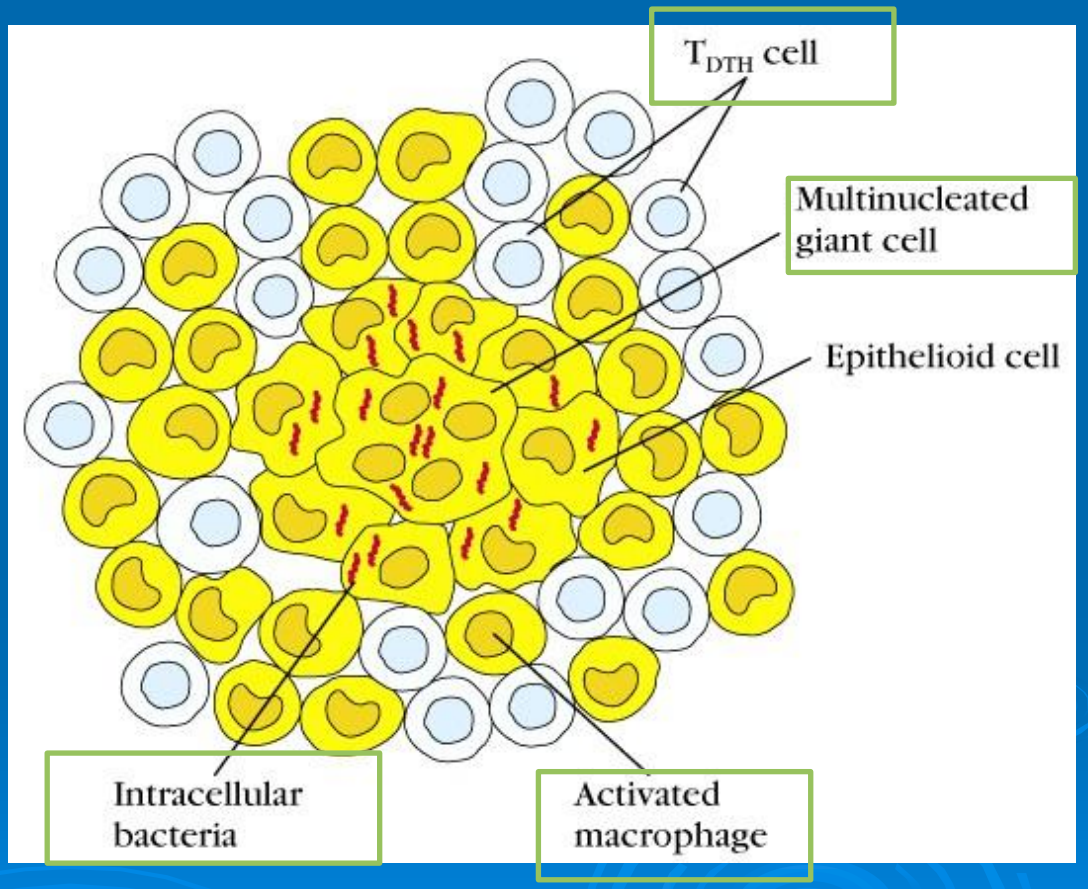
Intracellular bacteria	Intracellular viruses
Mycobacterium tuberculosis	Herpes simplex virus
Mycobacterium leprae	Variola (smallpox)
Listeria monocytogenes	Measles virus
Brucella abortus	Contact antigens
Intracellular fungi	Picrylchloride
Pneumocystis carinii	Hair dyes
Candida albicans	Nickel salts
Histoplasma 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

This is what we see in chronic eczema and lichenification after chronic inflammation.



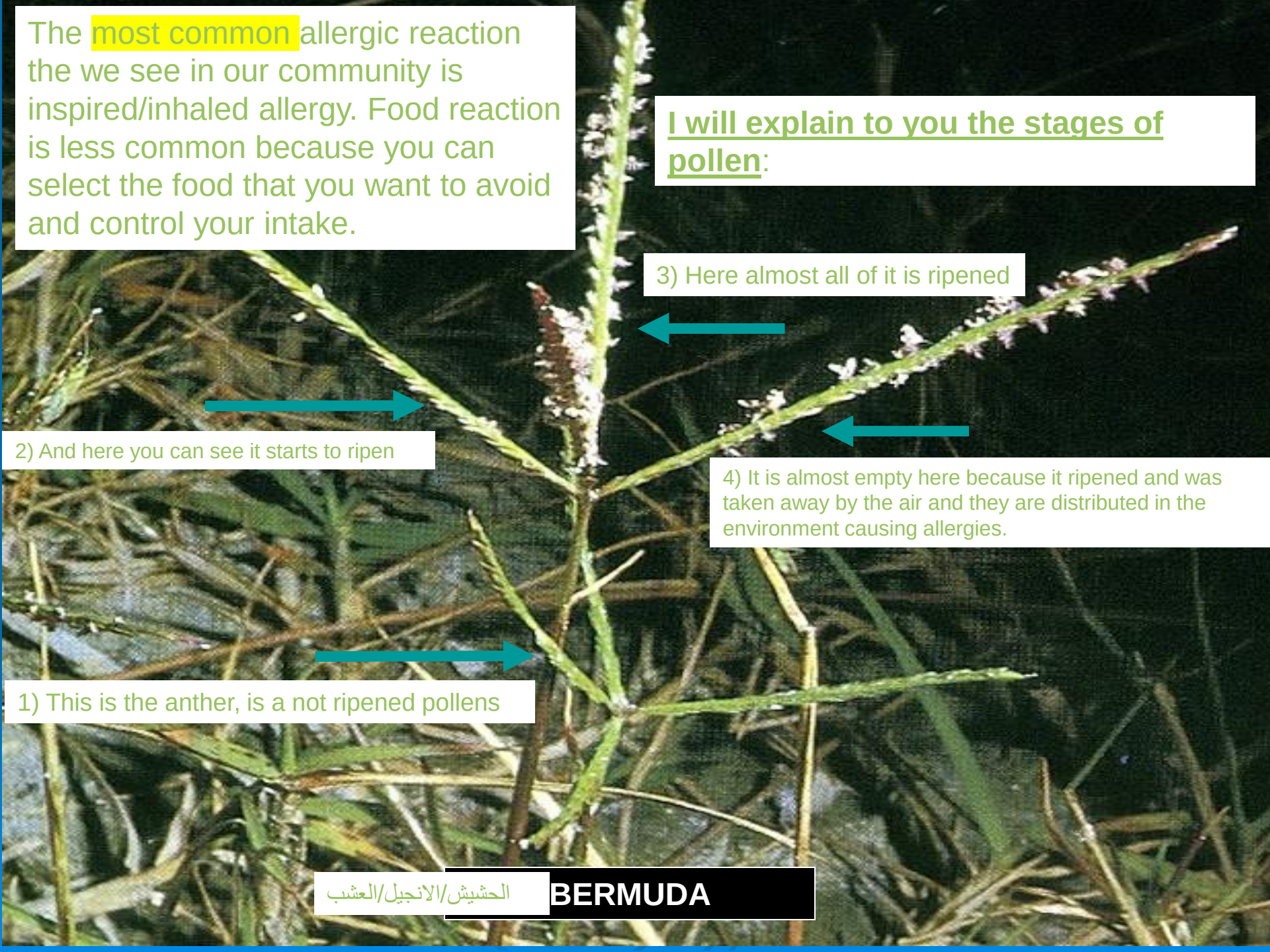
Drug reactions can be any Type of Hypersensitivity

One of the common scenarios that you are going to face is drug reaction, in this case you can see that penicillin can be IgG, IgM, IgE or cell mediated reaction depending on the route

TABLE 16-5 Penicillin-induced hypersensitive reactions

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

We conclude that drug reaction is mediated by all mediators of allergic manifestations/reaction


The most common allergic reaction the we see in our community is inspired/inhaled allergy. Food reaction is less common because you can select the food that you want to avoid and control your intake.
I will explain to you the stages of pollen:
3) Here almost all of it is ripened
2) And here you can see it starts to ripen
4) It is almost empty here because it ripened and was taken away by the air and they are distributed in the environment causing allergies.
1) This is the anther, is a not ripened pollens
الحشيش/الانجيل/العشب
BERMUDA

RYE

We see it in farms
mostly and maybe parks

Desert weed

اسماء مختلفة حسب المنطقة:
القصيم يسمونه رِغل
سكاك والجوف يسمونه رَغِل
طريف وحايل اسم ثاني

ATRIPLEX (RUGHL)

Amaranthus SP

سندار ، عرف الديك ، قطيفة

هذي مستزرعة, المزارعين اخذوا اللي على اليسار وحطوها في سماد وسقوها فتغيرت من
Wild plant نبات صحراوي
الى
Ornamental plant نبات زينة

لاحظوا ان النبتة المستأنسة (الحمراء) زهرتها اكبر واوراقها او المجموعة الخضرية اقل والثانية العكس
meaning less pollen in the red plant

Amaranthus SP

سندار عرف الديك ، قطيفة

Desert plant, we see a lot in our gardens والاستراحات


هذي نفس الشجيرات اللي قبل لكن هذي وهي بالصحراء,
لاحظوا ان تقريبا ما فيه ازهار فقط مجموعات خضرية
Anther
ما تتفتح الزهرة بس تطلع حبوب اللقلاح وتنتشر بالارض
Amaranthus Viridis (Orf Al-Deek, Cendar)

هذه ايضاً من النباتات الصحراوية واذكرها لكم لسببين:

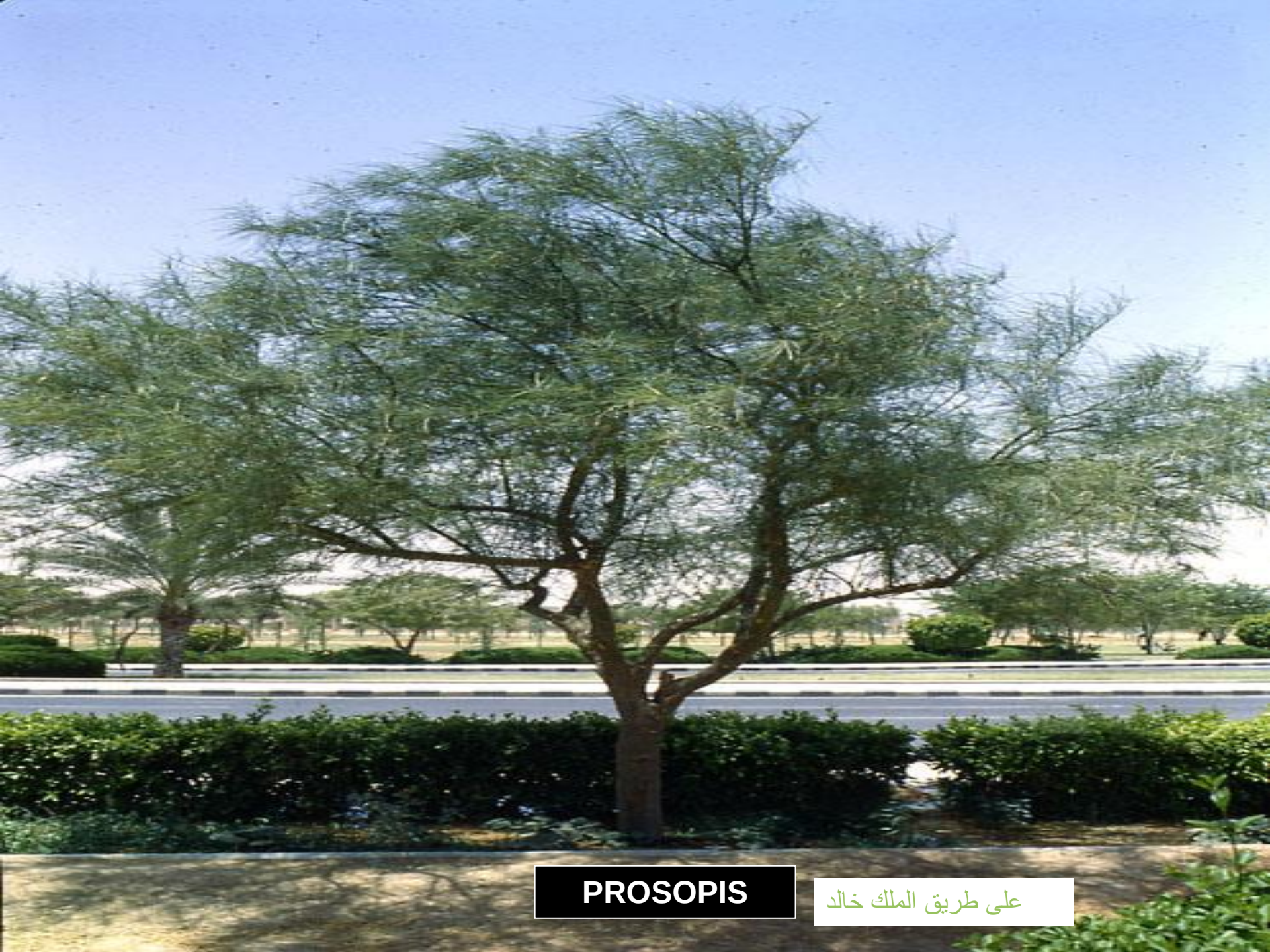
1- to make you familiar of the common plants and weeds that can cause allergy

2- when we make skin prick test for the patient (we will come to that later) we will be selecting plants and weeds that clinically relevant to our environment.

Salsola SPP. (Herm)

الهرن, القطيفة


نبتة صحراوية ولكن تنمو عندنا وهذه الصور
عند دوار الكتاب بالجامعة يعني منطقة محيطة
بالبشر وممكن يتحسسون
Chenopodium Album (Etra) العطرة


PROSOPIS
على طريق الملك خالد


The anther of prosopis
مازال يحتفظ بحبوب اللقاح
حبوب اللقاح انتثرت من عليه
مازال يحتفظ بحبوب اللقاح

حبة لقاح مكبرة خمس مئة الف مرة

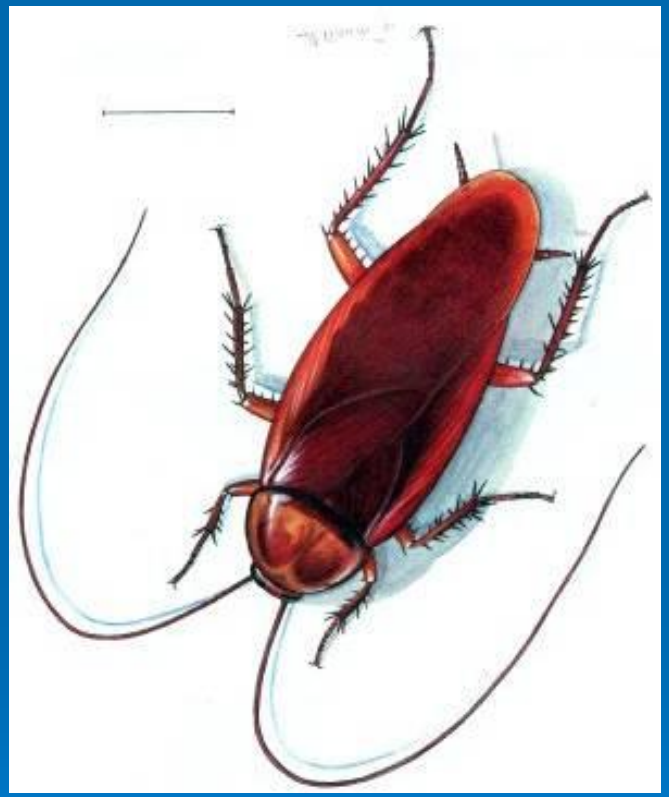
They are 1-2 microns, compared to RBCs with are 7 microns.


Animal dander antigen:
Cat-dander antigen
Dog-dander antigen
Cat

DOGS

Cockroach antigen

COCKROACH



AMERICAN COCKROACH

- Found indoors: mattresses air condition, indoor plants
- They are humidity dependent allergen (living in temperature of 20-25 and humidity 50-70), if they go outside under the sun they will die and if you go to the desert you won't find them.

ALLERGIC RHINITIS

Now we will come to clinical presentations of allergy:

1- Allergic rhinitis is the MC presentation. (remember suspected AR in SA is 45%)

Health Effects of Allergic Rhinitis

It is not just simple sneezing and blocked nose

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

For the diagnosis of AR, the most important key is history

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*

اذا دخلت حديقة او رحت استراحة او طلعت مخيم او اذا جا غبار او رحت اشتري غنم او اذا رحت جدة

- ✓ *Seasonal variation in symptoms related to pollination of trees, grasses, and weeds*

والله في الشتاء ما عندي مشكلة بس اذا جا اخر الصيف سبتمبر اوكتوبر ونوفمبر وتغير الجو وجانا الغبارتبدا الاعراض عندي لان الغباريحمل الكثير من حبوب اللقاح

- ✓ *A family history of atopic disease*

Both parents have allergy: 50% one of the kids will have allergy
Both parents and one sibling: up to 75%.

- ✓ *An environmental history assessing exposure to indoor and outdoor allegens*

انا كويس بالنهار بس اقل ما ادخل سريري ابدا احك جسمي وابدا افرك عيوني واعطس هنا نفكران فيه دست مايت بالمرتبة او المخدة

and the presence of associated allergic conditions

Asthma or conjunctivitis or whatever

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

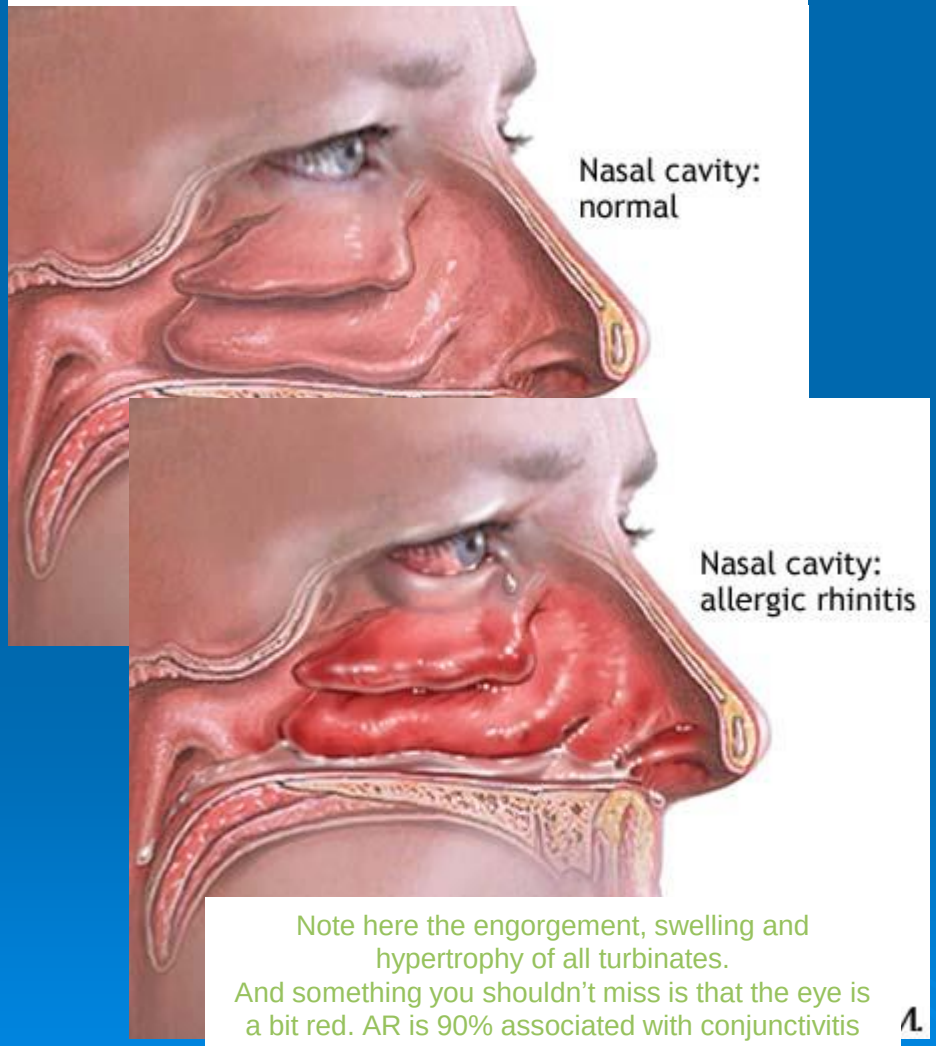
1. History & symptoms of recurrent or persistent rhinitis and/or associated health effects
2. Signs of atopy and recurrent or persistent rhinitis

   Atopy: dry skin, eczema.
3. Demonstration of IgE allergy

   Check if it's IgG, IgE, IgM or cell mediated reaction
4. Exclusion of other causes of rhinitis

   Other causes: vasomotor rhinitis, foreign body

When you're looking at the nose, the most important part of the nasal cavity is middle/ anterior turbinate to because it is visible.



Note here the engorgement, swelling and hypertrophy of all turbinates.
And something you shouldn't miss is that the eye is a bit red. AR is 90% associated with conjunctivitis

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

!! IgE mediated

If it's it is IgE mediated is there any: nasal drip, postnasal drip, nosal blockage, sneezing or asthma association.

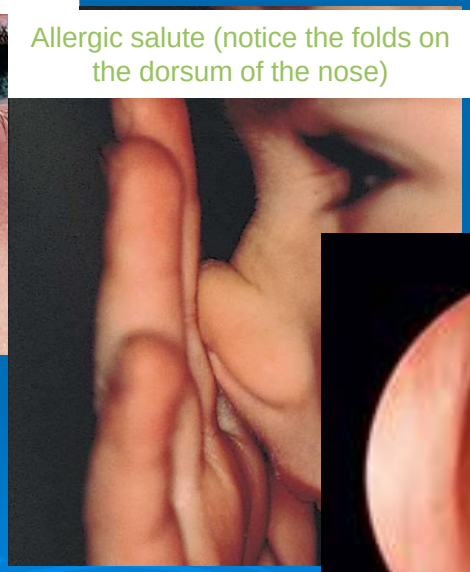
Diagnosis of Allergic Rhinitis

2. Signs of atopy and recurrent or persistent rhinitis

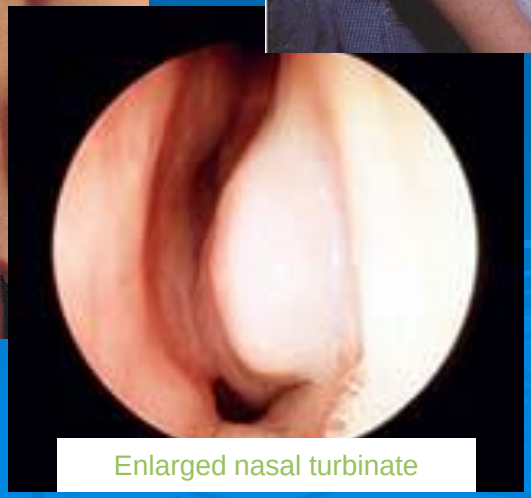
Child presents with eczema

Allergic shiner (allergy is one of the causes not the only cause)

Allergic salute (notice the folds on the dorsum of the nose)



Nasal septum problem from itching the nose and moving it right and left



Enlarged nasal turbinate

Fold on the dorsum of the nose caused by allergic slate (permanent fold)


Allergic shiner

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.

Other causes of peripheral eosinophilia:
- Helminthic infestation
- Eczema
- Food allergy

So we do nasal eosinophils, because nasal eosinophils are not cause by anything other than respiratory allergy.

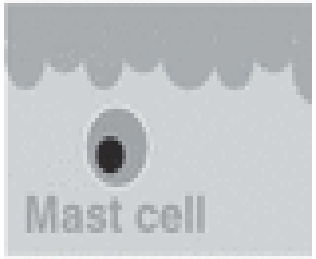
- NASAL EOSINOPHILS --> WRIGHTS STAIN >15/100 cells SIGNIFICANT

Diagnosis of Allergic Rhinitis

3. Demonstration of IgE allergy

Summary of laboratory diagnostic which we do in allergic rhinitis

Skin

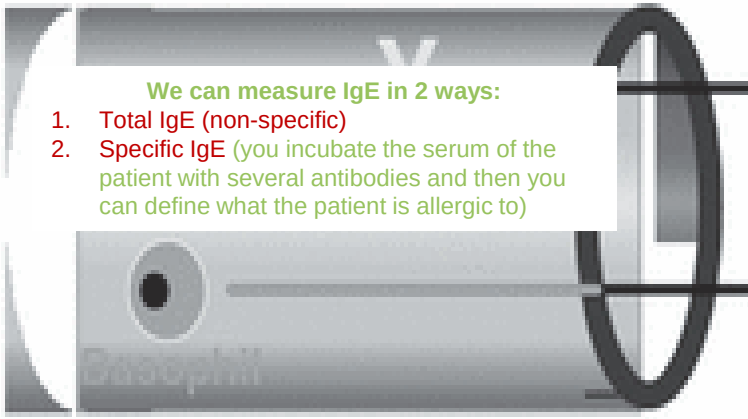


Skin prick test:

- Gold standard of making dx of allergy
- You can use any part of the body but most common is volar aspect of arm or the back and in children we preferer doing it on volar aspect arm because doing it on the back scares them.
- We use our environmental allergens or food allergens.
- You drop the solution on the skin then you prick the skin with a needle.
- Results: wheels, and erythema.

→ Skin test

The blood test measures the levels of allergy antibody, or IgE, produced when your blood is mixed with a series of allergens in a laboratory



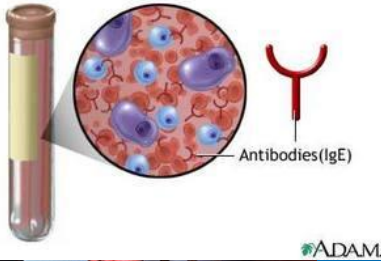
We can measure IgE in 2 ways:

1. Total IgE (non-specific)
2. Specific IgE (you incubate the serum of the patient with several antibodies and then you can define what the patient is allergic to)

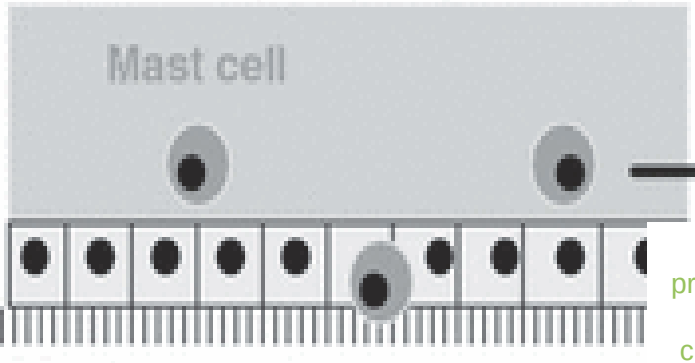
→ Measurement of serum-specific IgE

→ Histamine release

→ Basophil activati



BAT: you incubate basophils with an allergen and if there's release of histamine this means that basophils are activated and patient has allergy



→ Nasal challenge
bronchial challenge
oral challenge
nctival cha

Starting with nasal provocation/ challenge which we don't do frequently in children, because you need cooperation.

SKIN PRICK TEST (SPT)

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

اختبر المريض بالمحسسات اللي تتواجد في منطقته وبيئته
مثلا بالجوف فكروا بالزيتون اكثر من النباتات الصحراوية
Jeddah or eastern region think of humidity dependent allergens: dust mites, fungi.

Why is skin prick the gold standard?

1- you can select the allergens.
2- you do it on the patient's skin and you can know what is the patient's reaction at this point in time.
3- you can read the reaction immediately in 20 minutes
4- less expensive

Skin test Is important for 2 reasons:

1- to diagnose

2- to plan for appropriate management (eliminating/decreasing exposure to allergen or immunotherapy)

Management:

A- if you can get rid of the allergen, advise that to decrease the environmental exposure. Ex: pet, tree near the house

B- if patient can't get rid of it, we plan for immunotherapy (injection or solution under the tongue)

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.

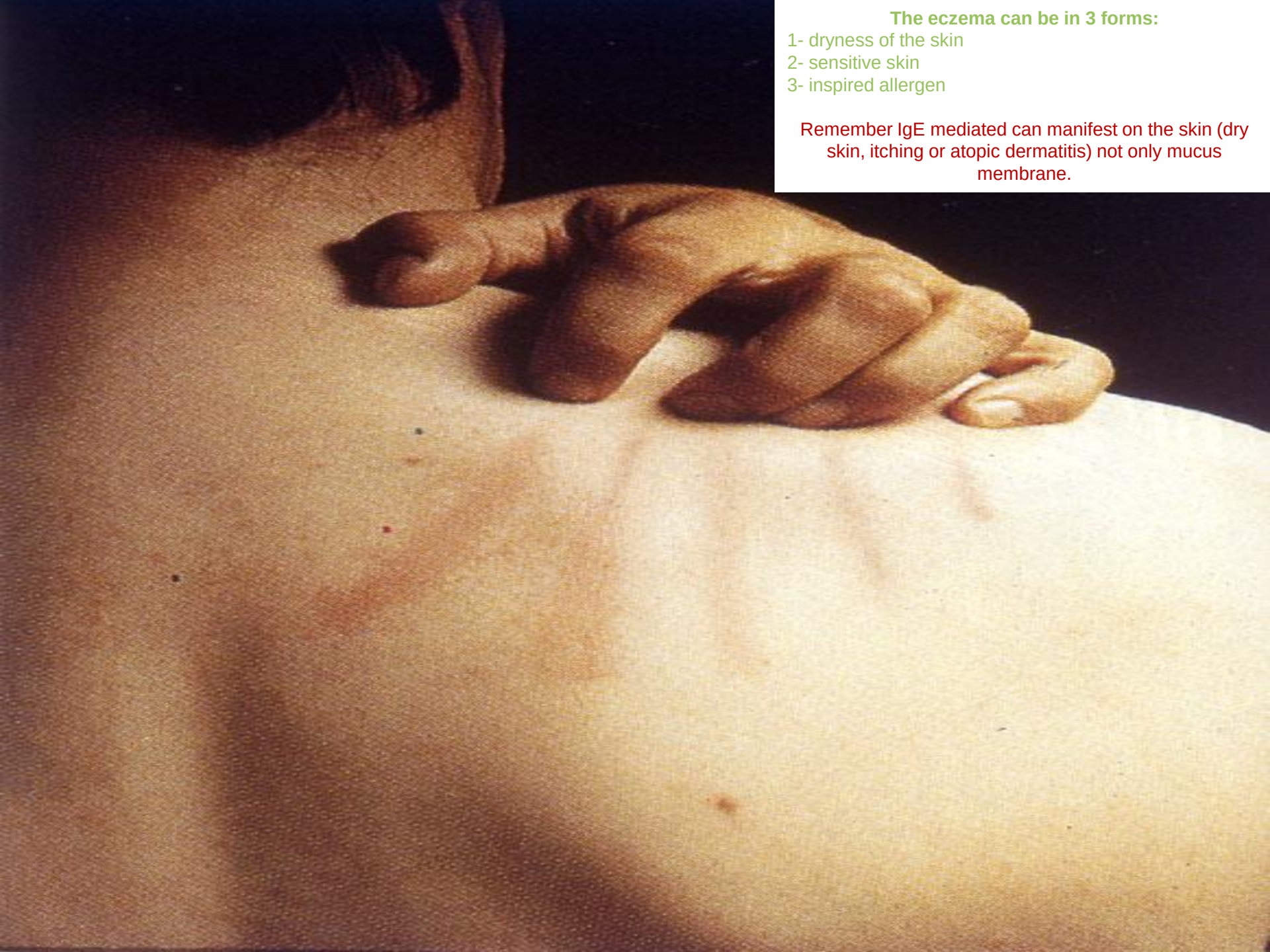
Recording and Scoring Skin-Test Results

Any wheel above 3mm we consider it positive

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

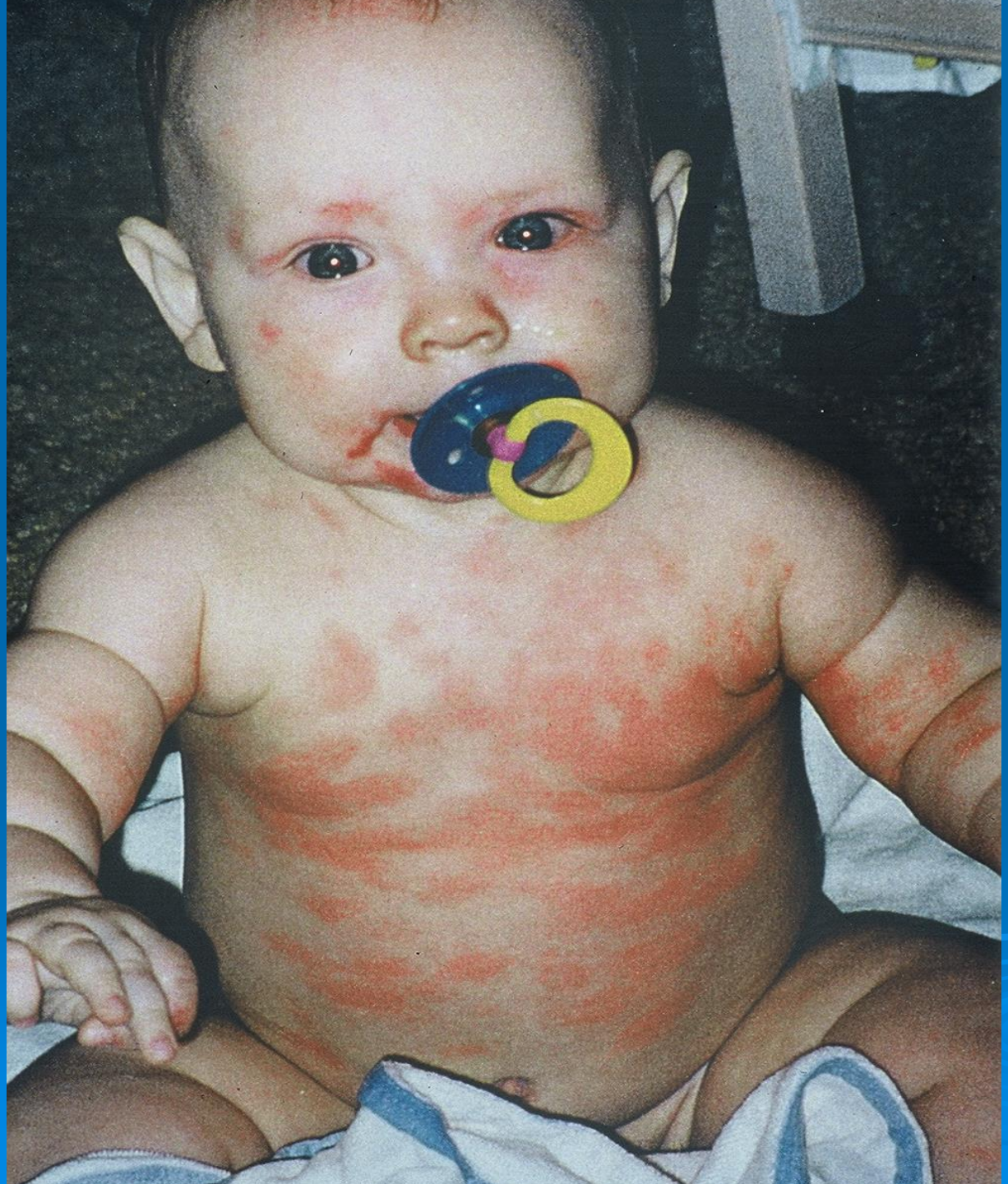
We will not discuss asthma because you have a whole lecture about it



The eczema can be in 3 forms:

1- dryness of the skin
2- sensitive skin
3- inspired allergen

Remember IgE mediated can manifest on the skin (dry skin, itching or atopic dermatitis) not only mucus membrane.




This is common in children of atopic families; they have atopic dermatitis manifested mainly on cheeks and in particularly in those who may have allergy to cow milk protein

Eczema can be so nasty affecting large portion of the skin and peeling/scaling ,may occur. As well as it could affect the fold (popliteal region, antecubital area).
Those are important signs of atopy because when you take history, and you see the patient is itching and you notice dorsal nasal fold then you can associate it with the history.

Atopic Eczema


© 2010 Logical Images, Inc.

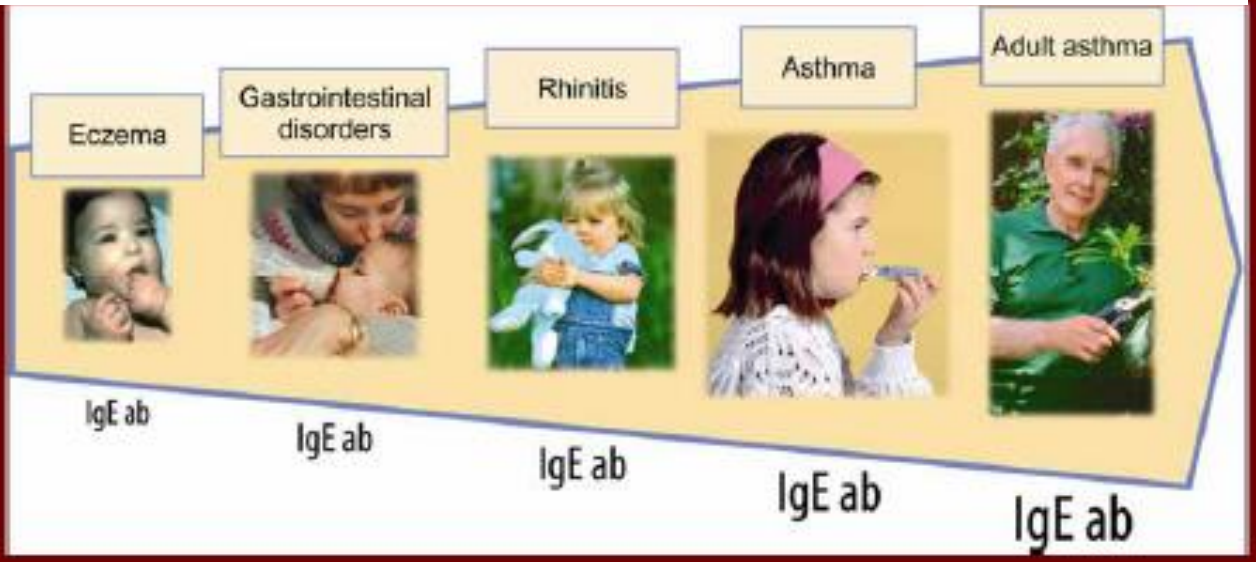

A.D.A.M.

- Patients can present only with atopic dermatitis (shown in previous picture)
- But if there is any complications, they may have also superimposed infection.
- This child has viral infection (herpetic) of the eczema. Notice that the child is having eczema without AR and you can see there's no redness of conjunctiva it white.


Bacterial infection
with pustule.

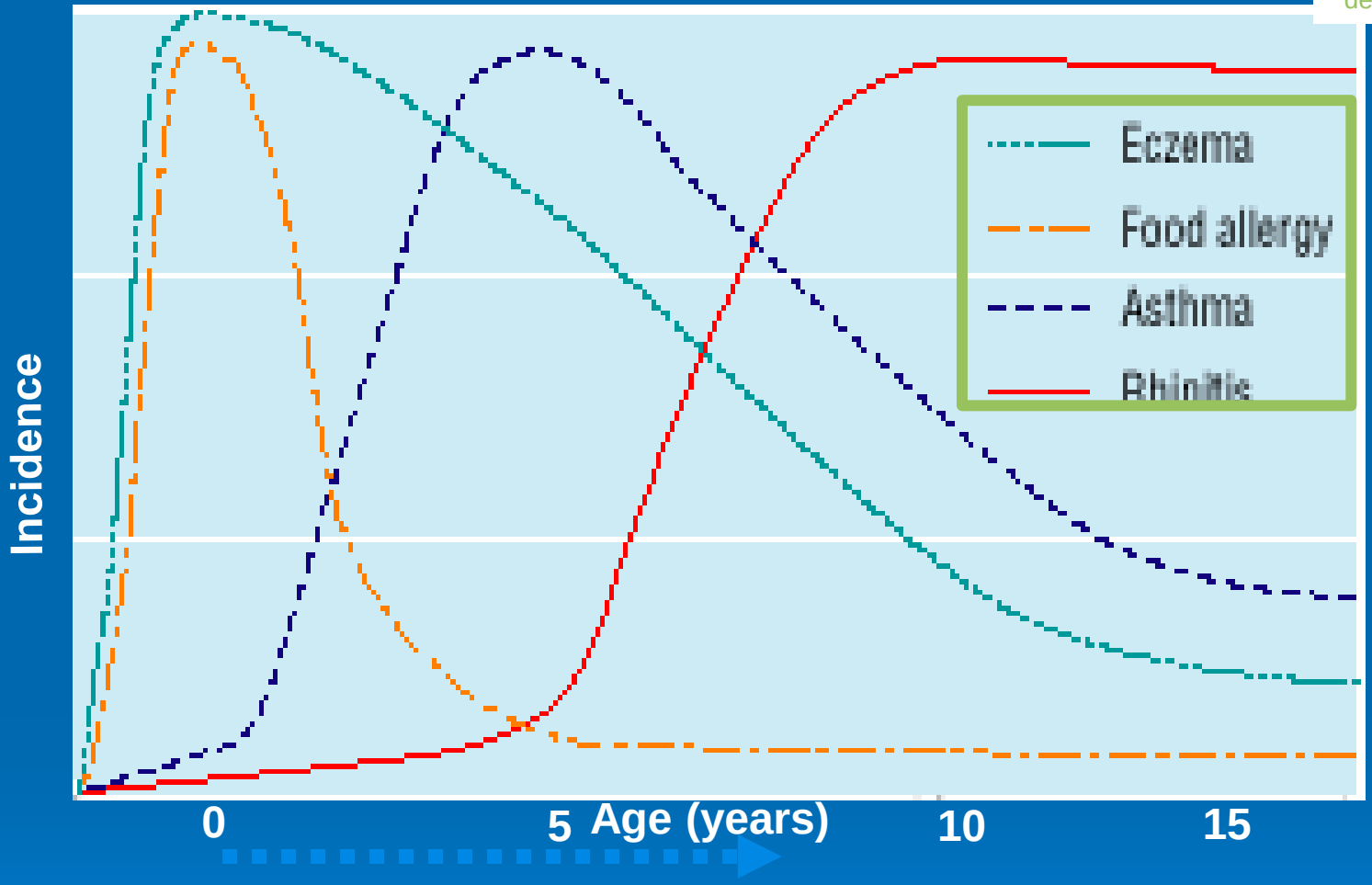
Allergy symptoms and progression

In summary: the IgE mediated allergy progresses from eczema to food allergy in infancy or rhinitis in toddlers or asthma in preschool child or even adults. We call this the atopic march



THE “ATOPIC MARCH”

Means that there’s atopy presenting in different stages of development of age.



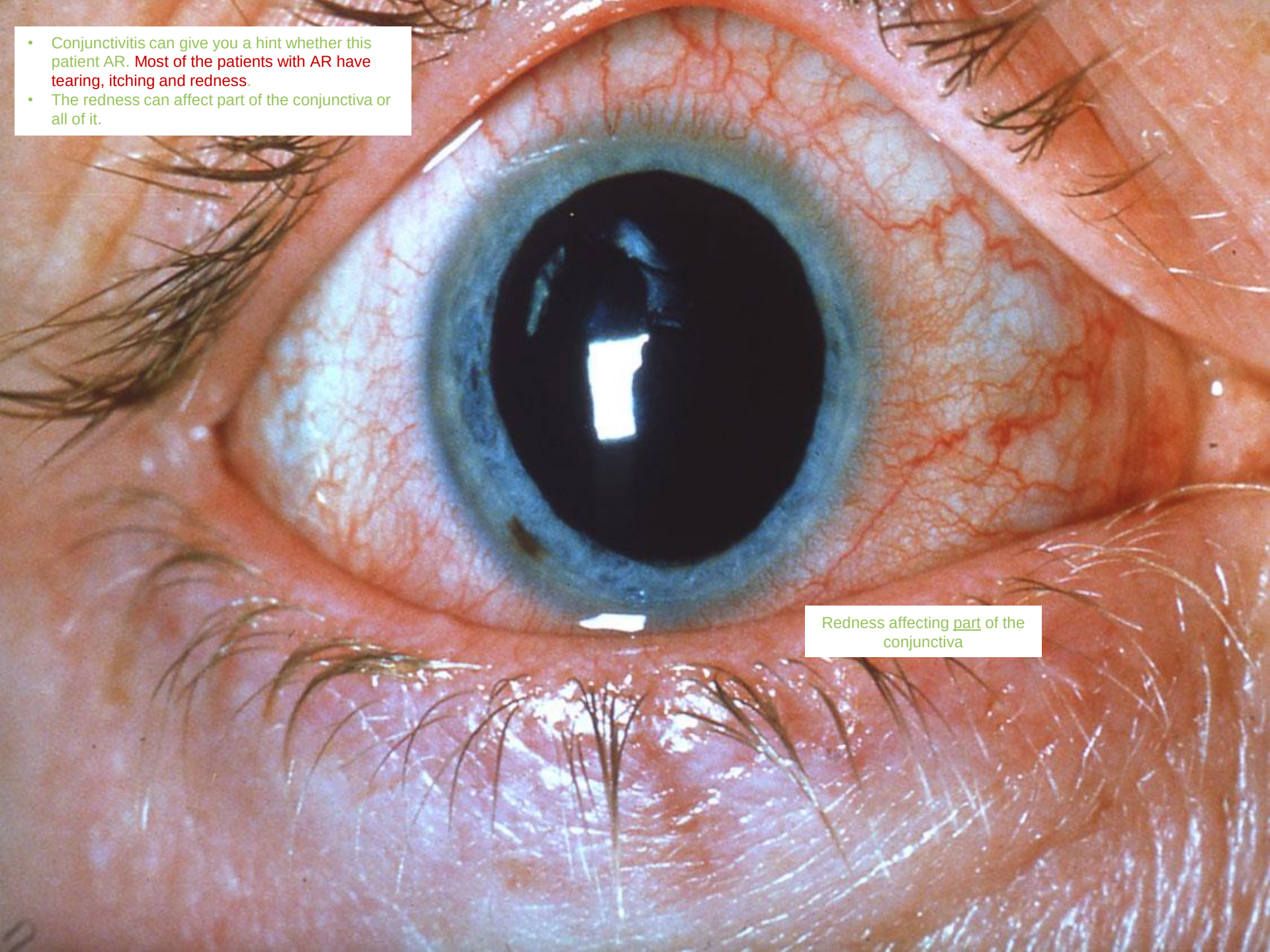
*IgE levels in **blood***

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

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

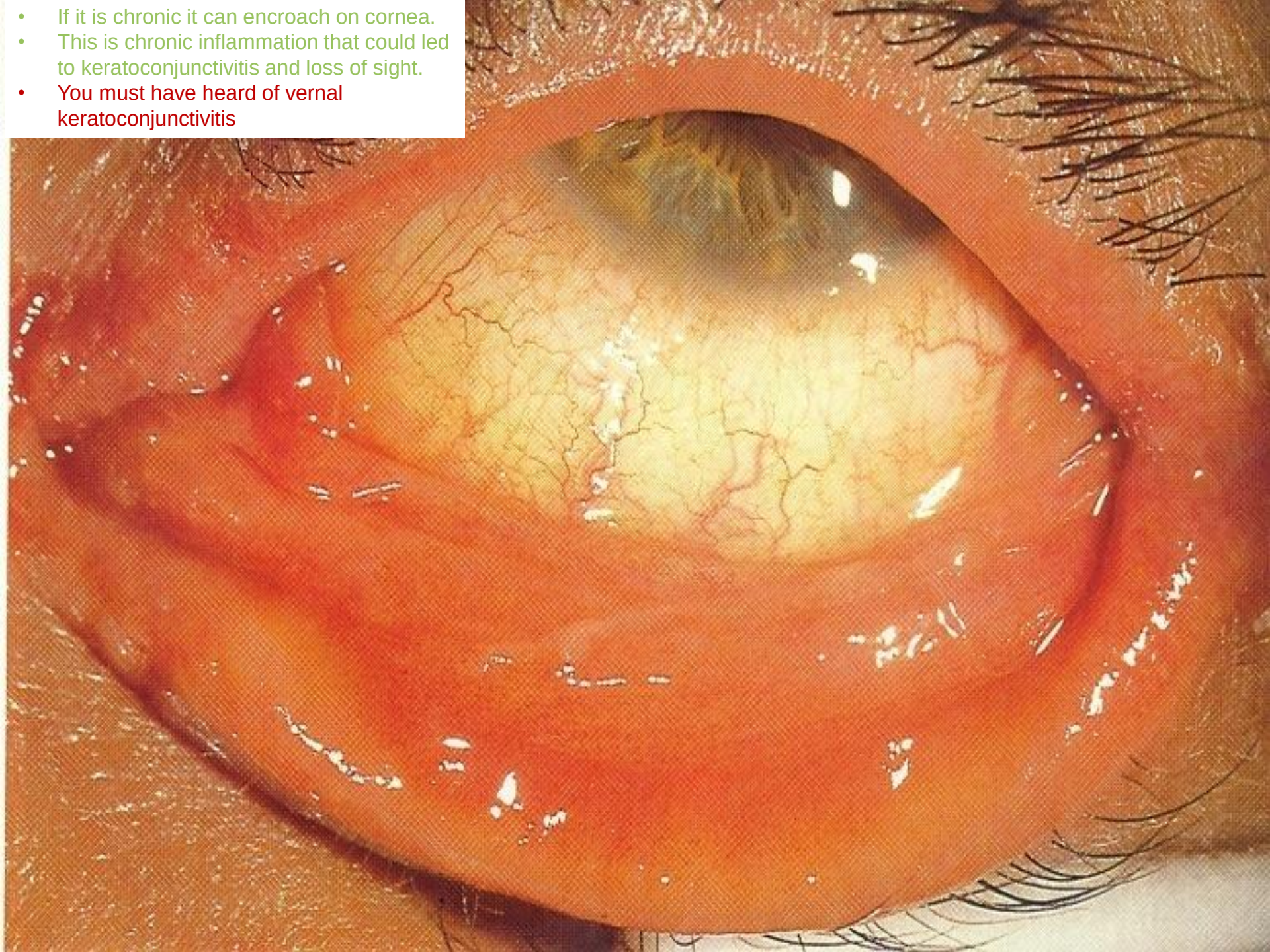
One of the most manifestations of allergy

ALLERGIC CONJUCTIVITIS


• Conjunctivitis can give you a hint whether this patient AR. Most of the patients with AR have tearing, itching and redness.
• The redness can affect part of the conjunctiva or all of it.
Redness affecting part of the conjunctiva


Diffuse Redness and
engorgement of the conjunctiva

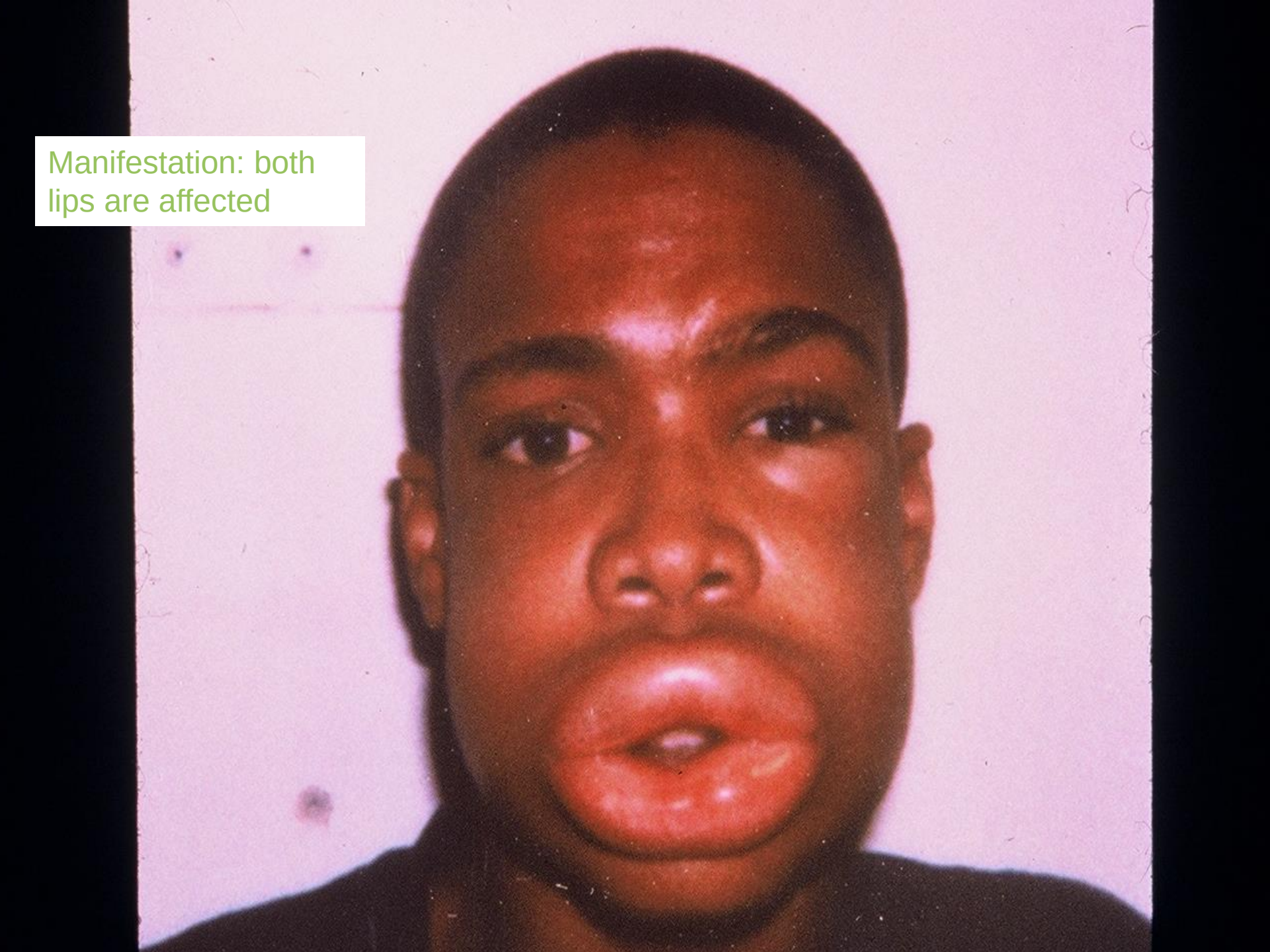
- If it is chronic it can encroach on cornea.
- This is chronic inflammation that could led to keratoconjunctivitis and loss of sight.
- You must have heard of vernal keratoconjunctivitis



URTICARIA AND ANGIOEDEMA

- Main presentation of urticaria /angioedema is IgE mediated however there's a vascular component in it.
- This is important because the manifestation of urticaria/angioedema of vascular reaction present as swelling is in the soft tissue (lips, eyes, ear) and you must be very cautious as those patient maybe develop threatening/fatal acute upper airway obstruction.


she can’t open
use of


Manifestation: both lips are affected


Manifestations: eye
affected more than lips

Can be on skin only

So it is IgE mediated however it is vascular driven in clinical manifestations

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

We must consider it as DDx when we see urticaria/angioedema which has nothing to do with the classical allergic manifestations

FOOD ALLERGY

Classical (class 1) food allergens

- The complex part of this that the patient might have allergy to something that isn't present in your RAST test. And sometime something I present in RAST but doesn't cause clinical manifestations

- Those are the allergens in peanuts that we have discovered (much more we haven't discovered yet)
- And each allergen has its own specific FC receptor.
- FcE is for IgE mediated, so FcER1 we will be referring to Ara h1 for example.

Peanut	Ara h1, Ara h2, Ara h3	
Cow's milk	(MC) 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

- The same for cow milk, the allergic reaction is not caused by one protein only.
- We have more than 6 caseins fractions.
- That's why in patient with cow milk allergy you may be able to diagnose by RAST test.
- Casein is the part of the milk that freeze, and the liquid part of the yoghurt is lactoglobulin.

we say ADRs to food not allergy to food because some are NOT IgE mediated.

Adverse Reactions to Food

- Based on the fact of different proteins in the food, the ADRs to food goes from IgE mediated to non IgE mediated. Remember the penicillin table, the same is valid for food allergy.

IgE-Mediated → Non-IgE Mediated

- **Oral Allergy Syndrome**
- **Anaphylaxis**
- **Urticaria**

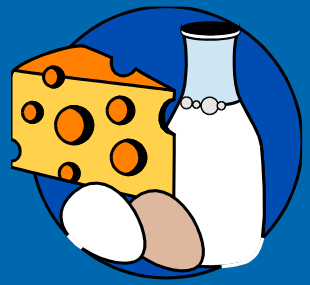
- MC IgE mediated is oral allergy syndrome

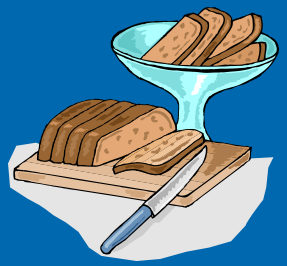
- **Eosinophilic esophagitis**
- **Eosinophilic gastritis**
- **Eosinophilic gastroenteritis**
- **Atopic dermatitis**

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

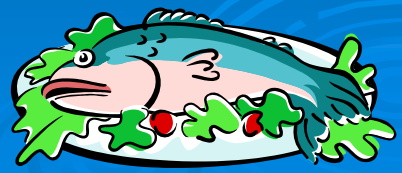
Incidence of Allergy to Specific Foods

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





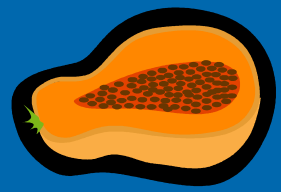
- In adults: 85% of reactions caused by:
  - Peanut - Tree nuts
  - Fish
  - Shellfish



Incidence of Allergy to Specific Foods

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

- We are encountering due to civilization, frequent traveling and frequent food transfer from continent to continent .



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
  - Tree nuts

- Usually, the first manifestation is exposure to cow milk because many kids take cow milk instead of breastmilk. But even breastmilk can carry with it something that the child can't tolerate, Ex: 100% breastfed infant and his mother ate peanuts/tree nuts/soya/sesame and the infant has strong background of atopy in family can have allergic manifested reaction.

البيتنس ينتمي للبقوليات اما التري نتس ينتمي للمكسرات

Why is this important?

- Because they have cross reactivity
- People who have allergy to peanut could have allergy to anything in Legumes family.

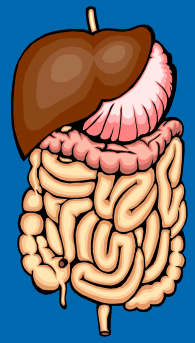
Food Allergy Prevalence in Specific Disorders

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%

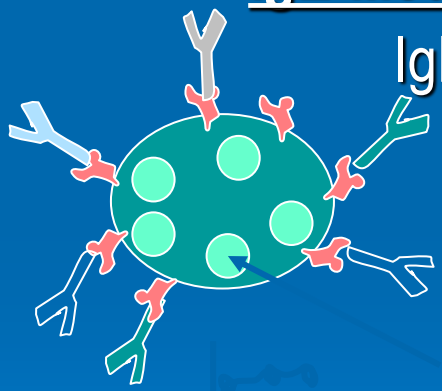
Pathophysiology: Immune Mechanisms



- Protein digestion
- Antigen processing
- Some Ag enters blood

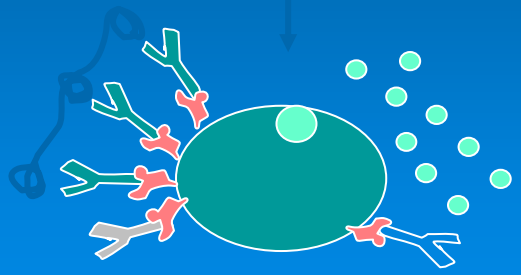
IgE-Mediated

IgE-receptor



Mast cell

Histamine



APC

Non-IgE Mediated

B cell

T cell

- TNF-α
- IL-5

Oral Allergy Syndrome (OAS)

OAS has 3 properties:
1. Acquired
2. Transient
3. Mot of OAS patient has inhalant/respiratory allergy

- 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.

Cross reactivity between inhaled allergens and food 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 Found in pollens and fruits
  - Pathogenesis-related proteins
  - Lipid Transfer Proteins

- **Scenario**: someone eats shrimp salad and feels numbness or itching of the lips and throat, so he stops and eats something else and the symptoms disappear. This is OSA.
- OSA has developed nowadays thanks to profilins and others, and now they discovered tropomyosin which Is present in dust mites and shrimp.

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

Similar to amaranthus

  - Mugwort pollen
  - Grass pollens

Popole who has allergy form these two have allergy to a lot of food that cause OSA

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"

- Genuine allergy usually starts early at age (7 months). But in someone who ate strawberries for his whole life (age of 10) and started having symptoms think of acquired allergy/OSA that has reactivity with other inhaled allergens.

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)

We see this more nowadays because medicine has developed and we can perform surgeries (latex gloives) for neonates at very early age, urinary catheter or peritoneal dialysis.

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 !