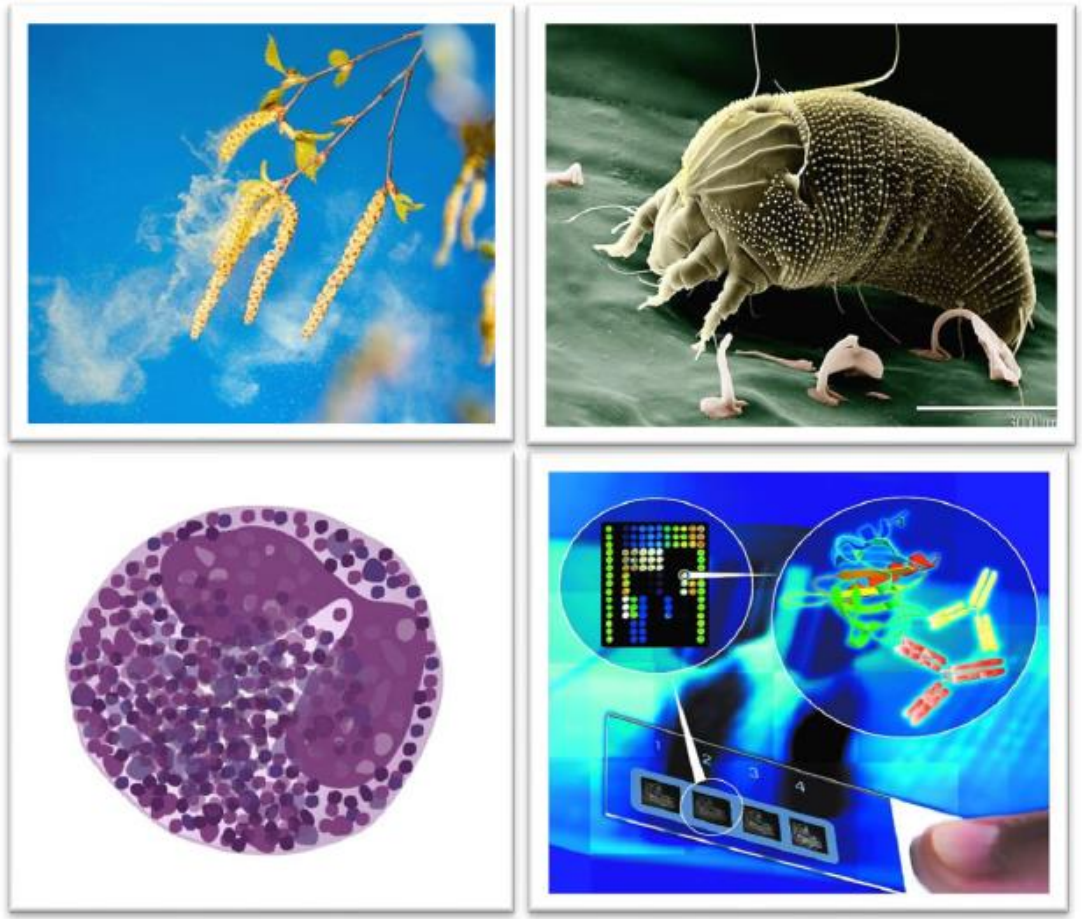
Type I hypersensitivities

Master D2HP
2024-2025

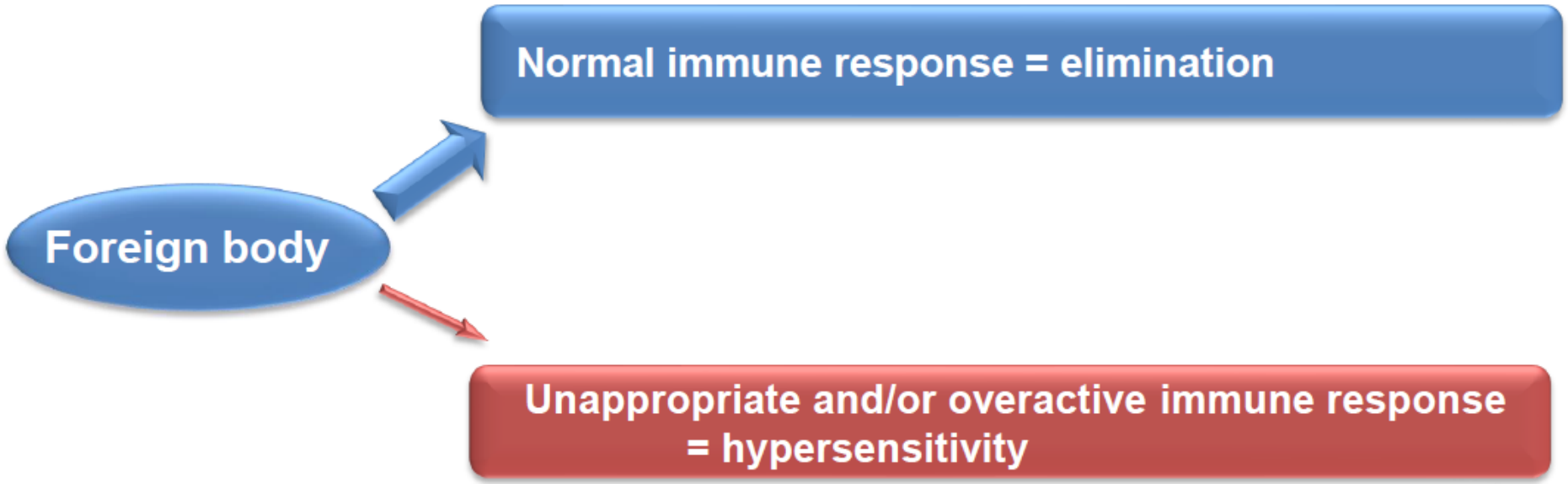
By Viviana Marin-Esteban

Allergy



Definition, epidemiology, mechanisms, treatments

Hypersensitivity



Gell and Coombs Classification :

Type I = immediate hypersensitivity

Type II = cytotoxic hypersensitivity

Type III = Immune complexes-mediated hypersensitivity

Type IV = delayed hypersensitivity

Type I or immediate hypersensitivity

- Clinical manifestations within a few minutes (max one or two hours)
- Linked to a genetic predisposition called atopy
- Needs a first asymptomatic exposure to the allergen
- IgE-mediated

History

- Charles Richet (Nobel 1913) described anaphylaxis while studying sea anemonea venom

•Reactions from second exposure

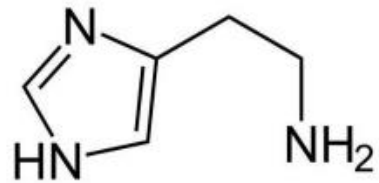
•Generalized reactions that can be lethal

•Long-lasting sensitization

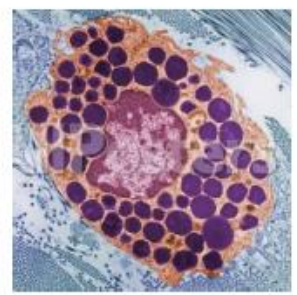
Jelly fish, see anemones

History

- **Anaphylaxis**: Portier and Richet (1902)
- Role of **histamine** (1929)



- Role of **mast cells** (1953)

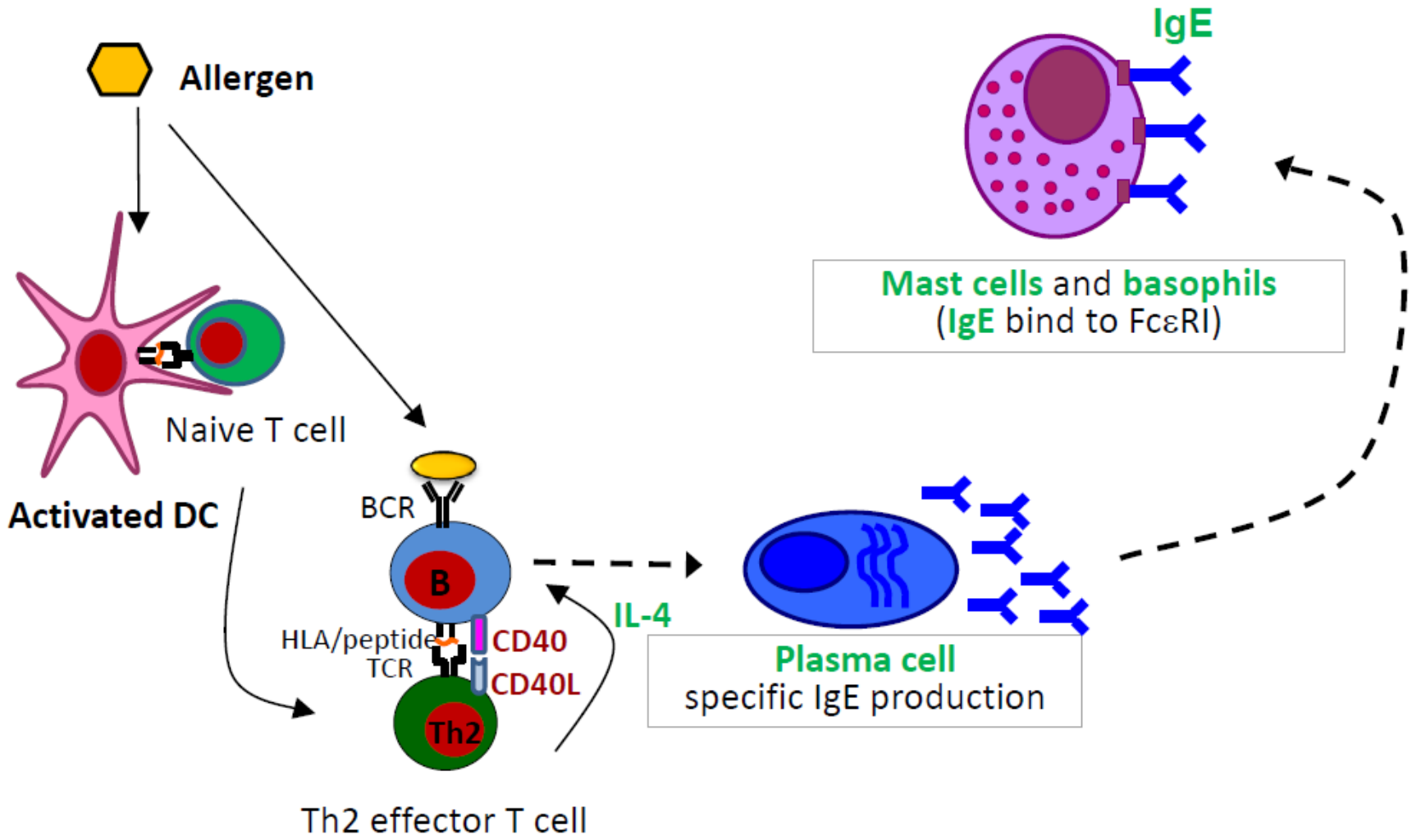


- Role of **IgE** (1968)

Type I hypersensitivity mechanism

To learn

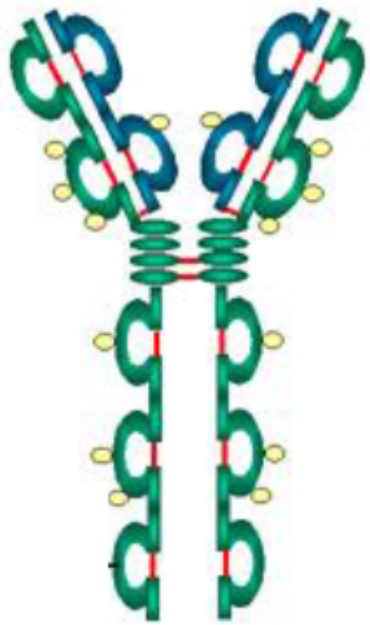
1st contact with allergen = sensitization



IgE and their receptors

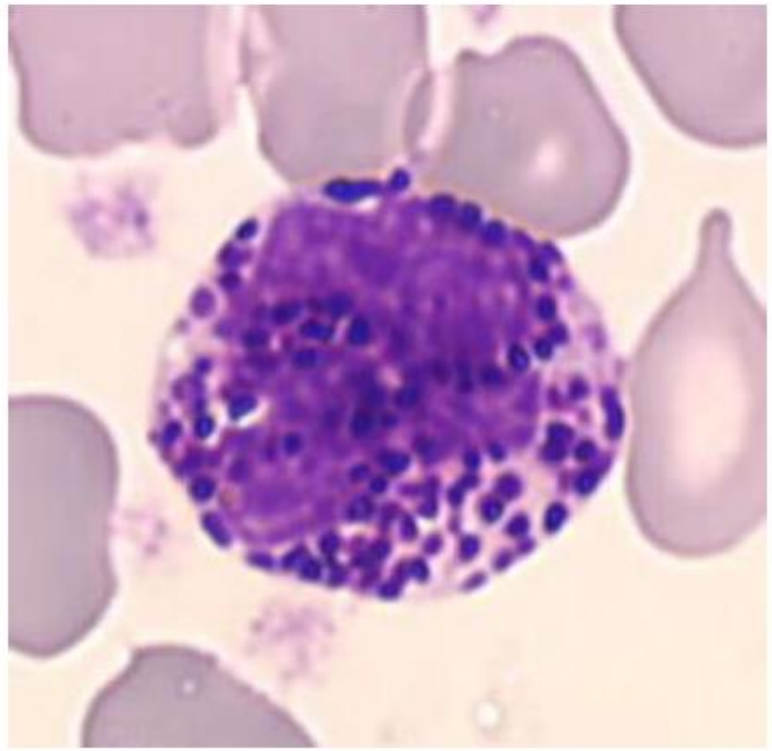
- Production enhanced by :
  - Genetics
  - Environnement

  (allergen-dependant)
- Unique Ig structure
- High affinity receptor :
  - Mast cells
  - Basophils



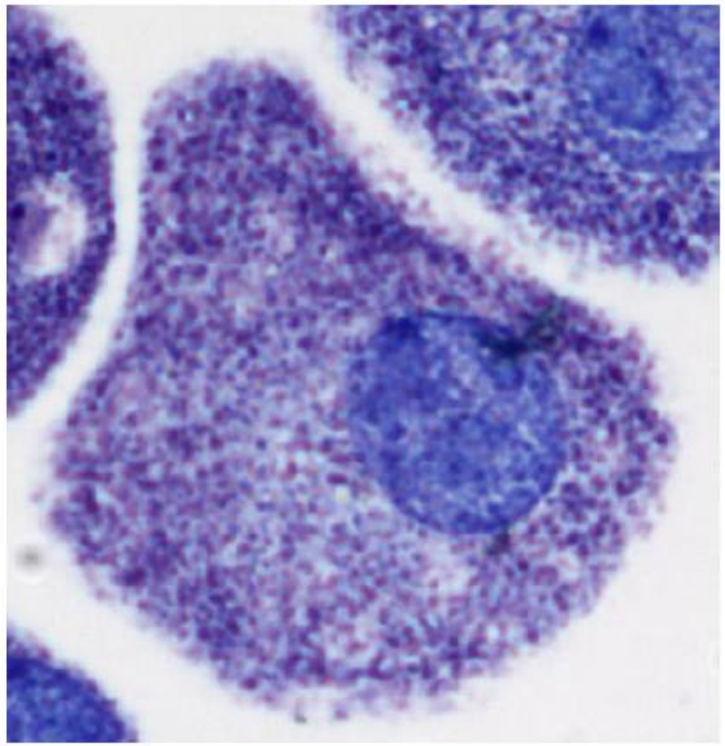
IgE

Basophils and Mast cells



Basophil

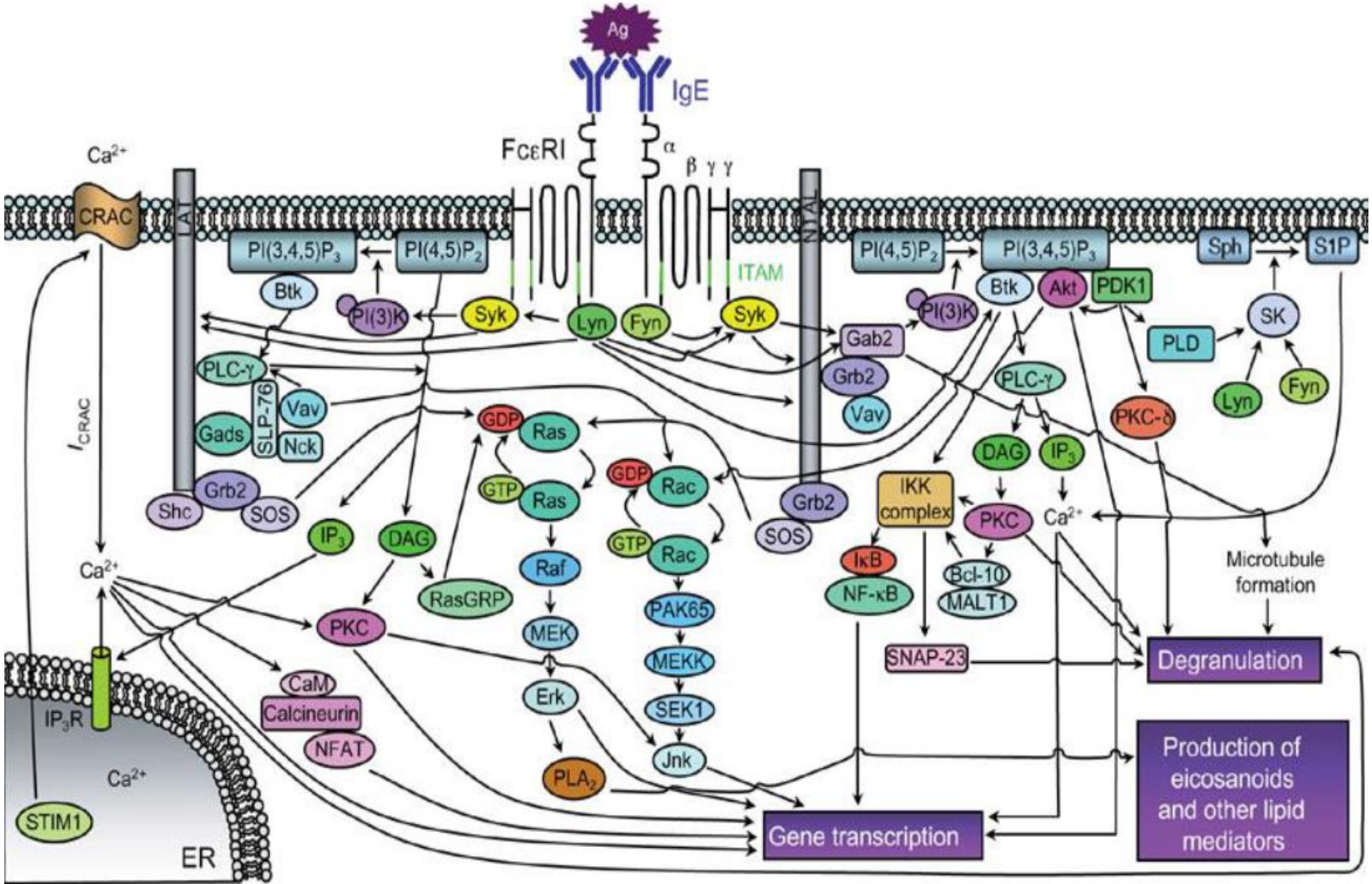
Blood
Histamine++
FcεRI



Mast cell

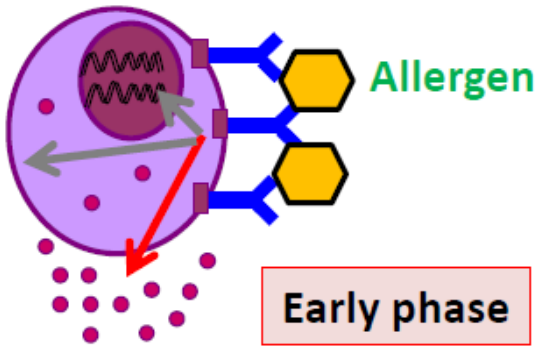
Tissues
Histamine++
Tryptase++
FcεRI

Signalling pathways



Type I hypersensitivity mechanism

Second contact with the allergen= Allergic reaction



Early phase

Degranulation of mast cells and/or basophils

Histamine

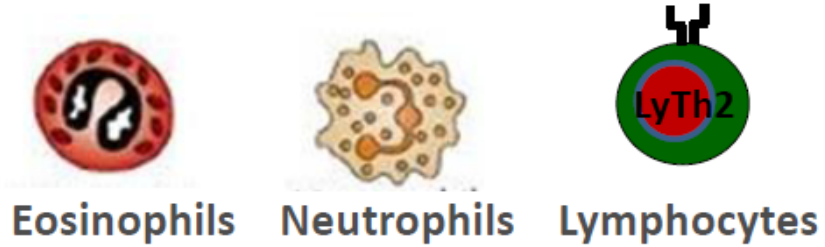
↓

Itching
↑ mucus secretion
Vasodilation
↑ vascular permeability
Smooth muscle fibers contraction

Late phase

Neo-synthesis of PG, LT, PAF
Cytokine production and cell recruitment

IL-3, IL-5, LT	IL-8, TNF, LT	IL-3, IL-4, IL-5



Eosinophils **Neutrophils** **Lymphocytes**

Clinical manifestations

Dermatologic:

Urticaria / Angiodema / Atopic dermatitis

Respiratory:

Rhinitis, conjonctivitis / Asthma

Digestive:

Vomitting, diarrhea, abdominal pain

Cardiovascular:

Anaphylaxis

Three emergencies : throat angiodema
acute severe asthma
anaphylaxis

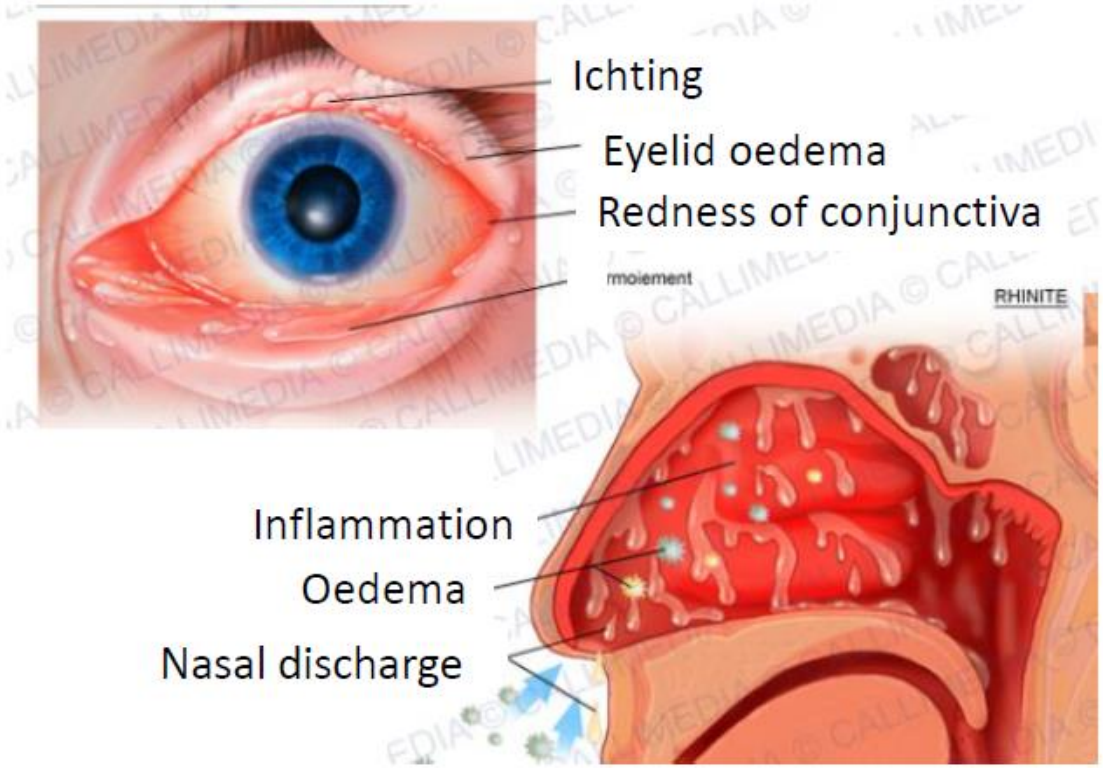
Urticaria (superficial cutaneous oedema)

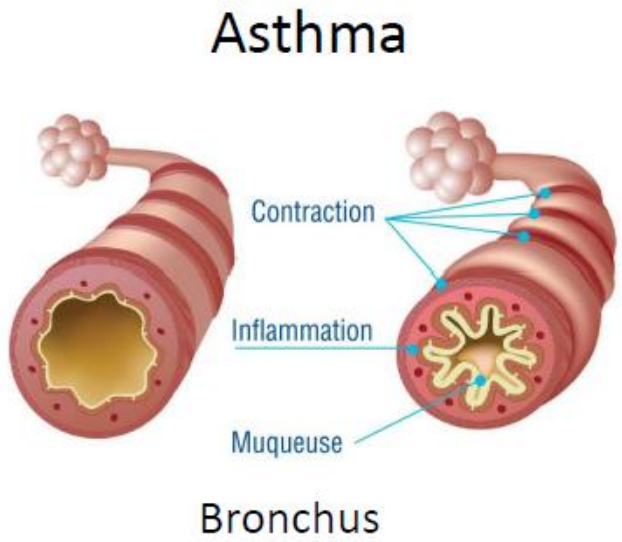
Many causes!
-Red Papules
-Itchy
-Fleeting

Angiodema

Deep (hypodermic) swelling of skin and/or mucosa

Rhinoconjunctivitis and asthma





Anaphylaxis

Systemic manifestation of immediate hypersensitivity. Can be lethal in a few minutes.

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Severity: Ring and Messmer classification

- **Grade I**: mucocutaneous manifestations
- **Grade II**: mild cardiovascular manifestations: low blood pressure, tachycardia, shortness of breath
- **Grade III**: severe cardiovascular and respiratory manifestations: collapsus, bronchospasm
- **Grade IV**: cardiac arrest

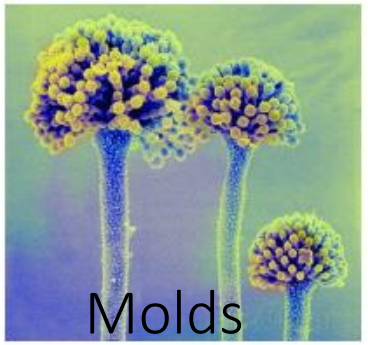
Triggers: the allergens

Airborne allergens


Pollens


Dust mites


Animal dander


Molds

Food allergens

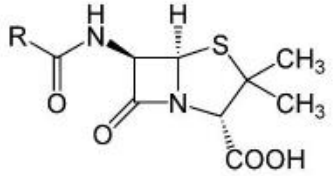

Nuts


Shellfish

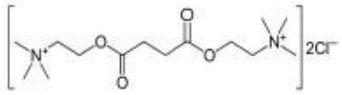

milk proteins


egg proteins

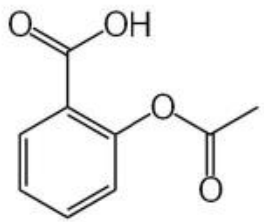
Drug allergens



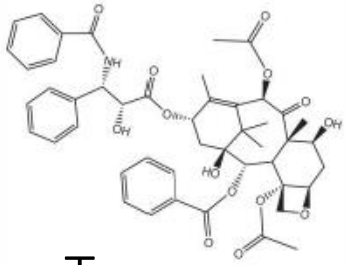
Penicillins



Curares



Aspirin


Taxanes

Importance of age

Frequency and type of allergy vary with age

Food allergy

- **Newborns: cow milk**
- **Infants : egg**
- **Children : peanut**
- **Adults : shellfish**

Cutaneous allergies

- **Infants and young children**

Respiratory allergies

- **Asthma: children**
- **Rhinite allergique : teenager and yound adult**

Drug and insect bites allergies: adults++

Diagnostic approach

1. Medical examination- Interview

Personnal and family medical background : *atopy*?

Disease history : *Suspected allergens?*

2. Immediate skin tests

→ *sensitization* to suspected allergens

3. Blood testing

Specific IgE measurment

→ *confirmation of sensitization*

Basophil activation test

Soluble mediators (anaphylaxis diagnosis)

4. *In vivo* provocation test

At a last resort, under surveillance in a hospital setting

→Only real evidence of allergy

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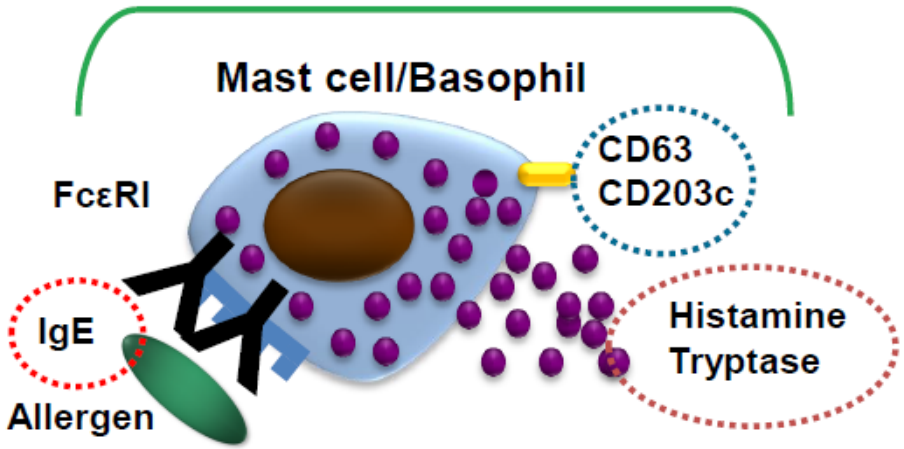
Biological diagnostic approaches

Skin tests (prick-test)



Basophil activation test
Flow cytometry

Degranulated mediators :
Histamine and **tryptase**

Specific IgE

Immediate skin tests :
Skin prick-test and Intradermic reaction

Prick- test

-Principle: a small quantity of allergen is introduced into epidermis with a lancet

-Lenght: 15 minutes

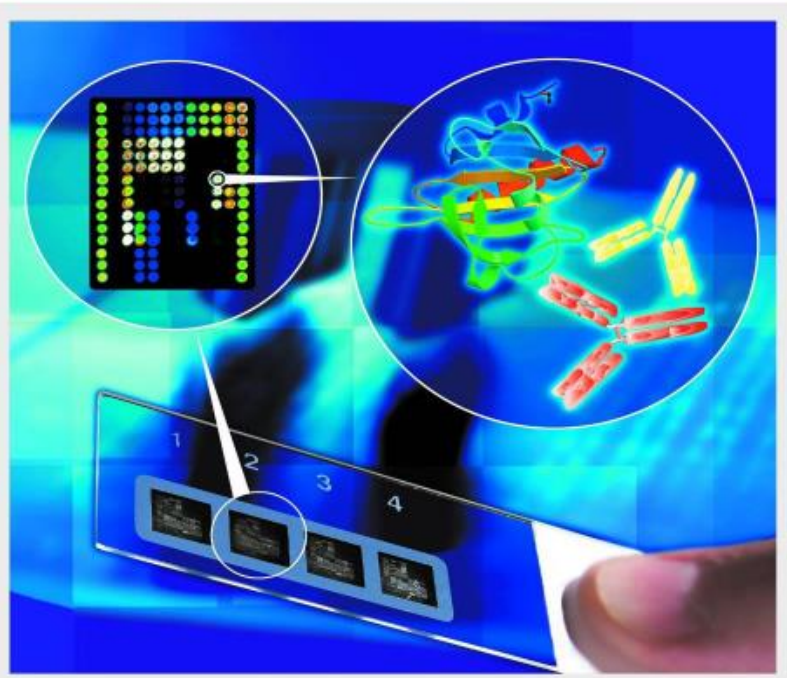
- Result: papule and redness at prick point
- Controls: positive (histamine), negative (buffer)
- Contraindications : severe skin disease, antihistamine medication in the last week.

Intradermal test

- Principle: injection of allergen into the dermis with a syringe
- Lenght: 15 min
- Result: papule and redness at injection point
- Indications : Mostly venom and drug allergies.
- Often used for delayed allergies.

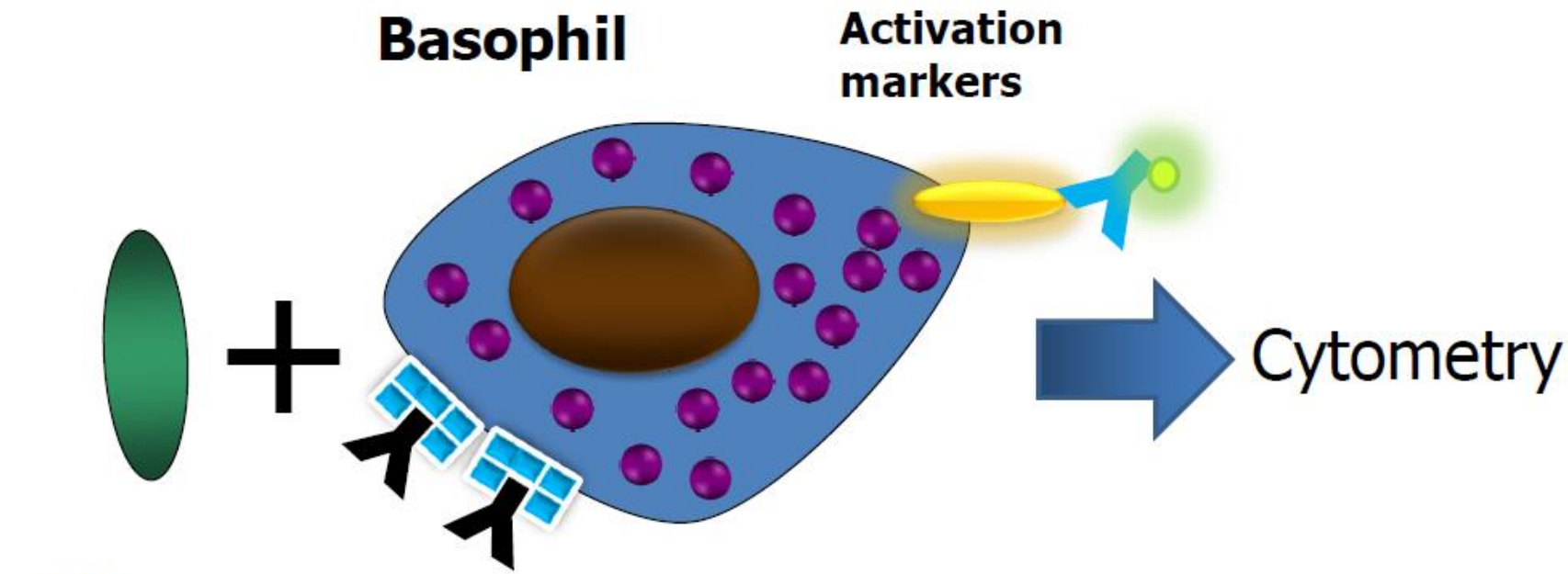
Specific IgE detection

- Special methods:
  - RIA
  - ImmunoCAP®
  - ISAC biochip

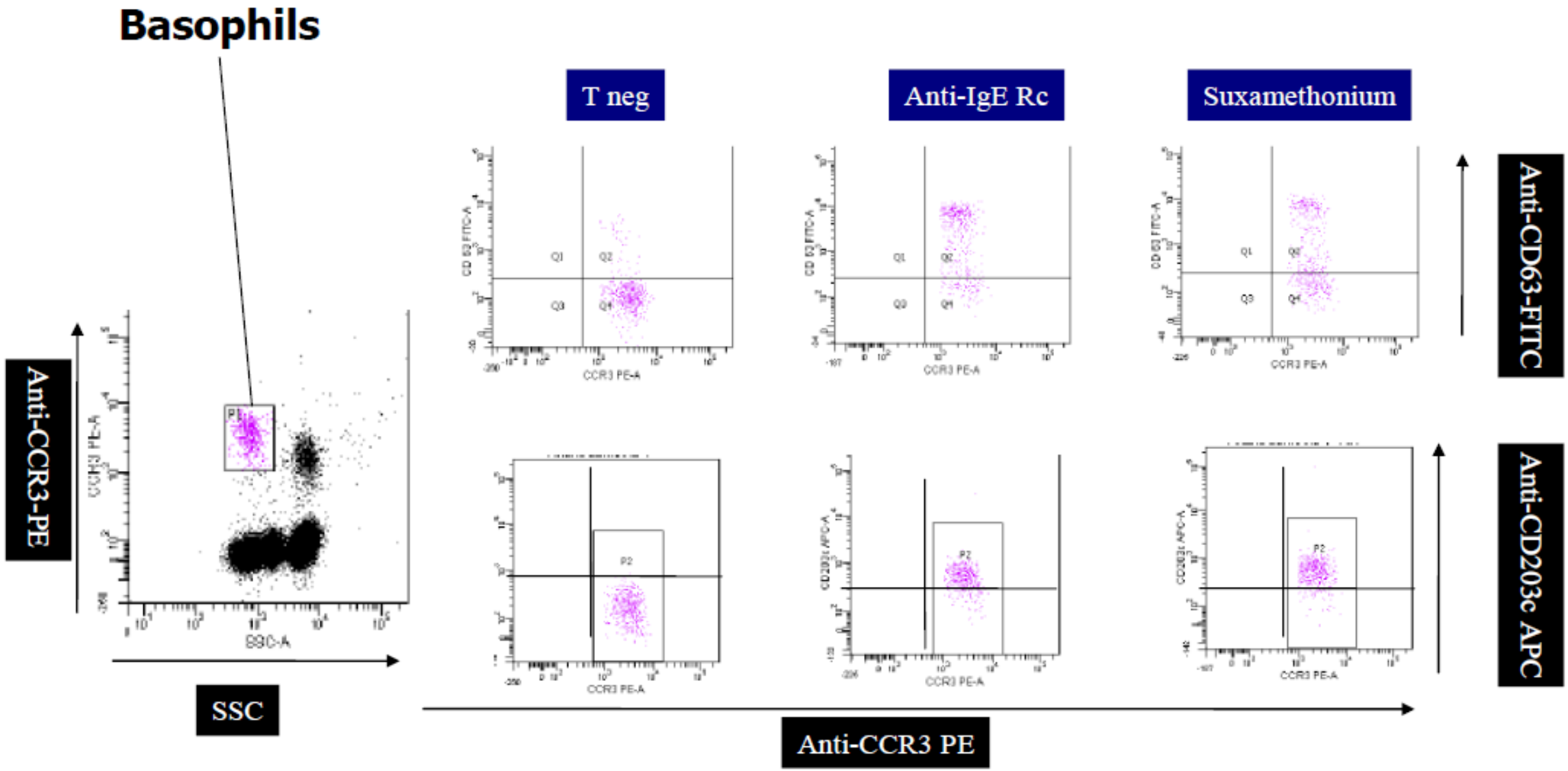


ISAC (Immuno Solid-phase Allergen Chip)

Anaphylaxis *in vitro*: Basophil activation test



Basophil activation test



Anti-allegy medications

Symptomatic treatment

Anti-histamines+++

Corticosteroids

Anti-leukotrienes } Asthma

B2-agonists } Asthma

Adrenalin } Anaphylaxis

Causal treatment

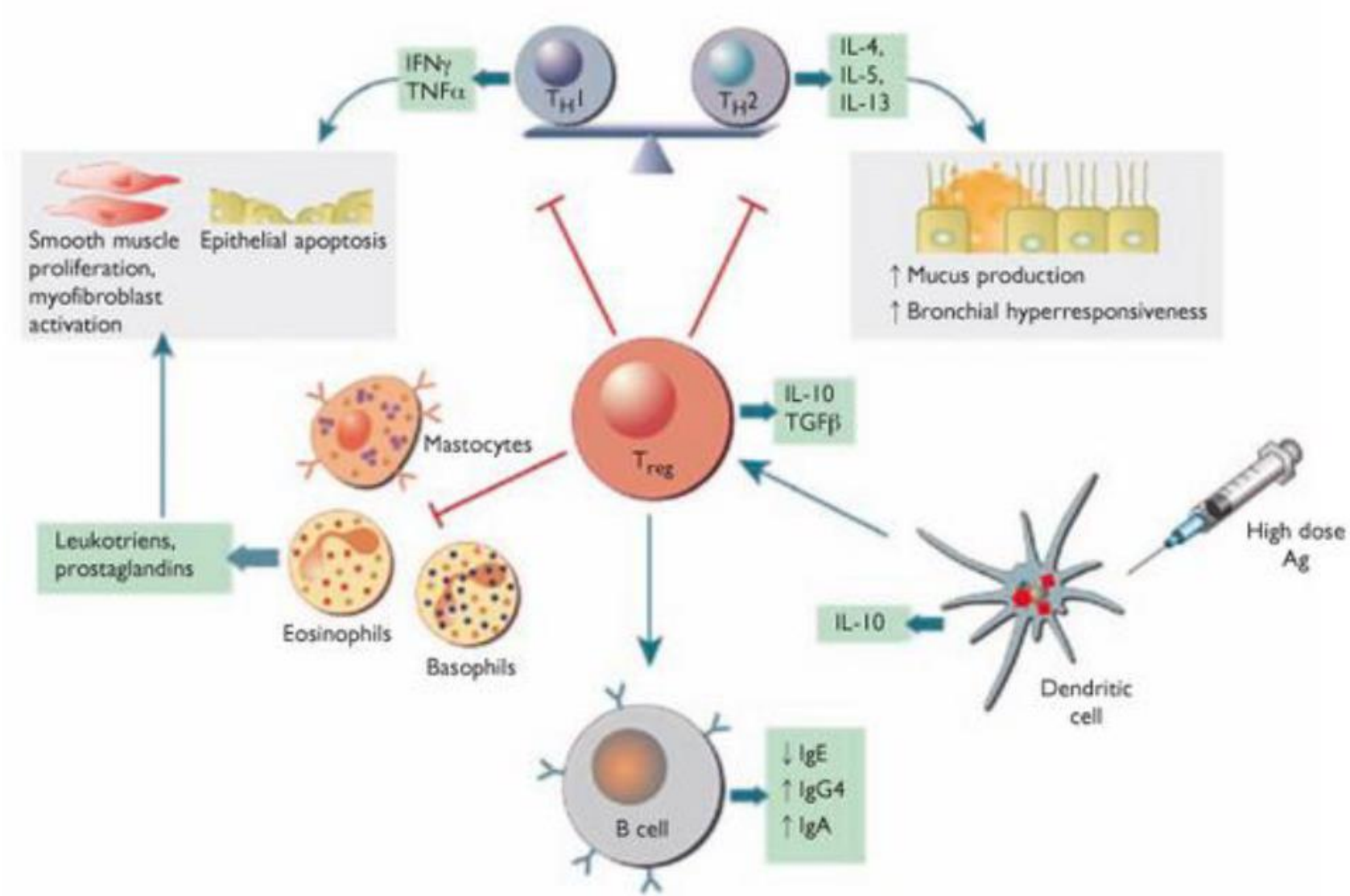
Allergen Immunotherapy

Allergen Immunotherapy

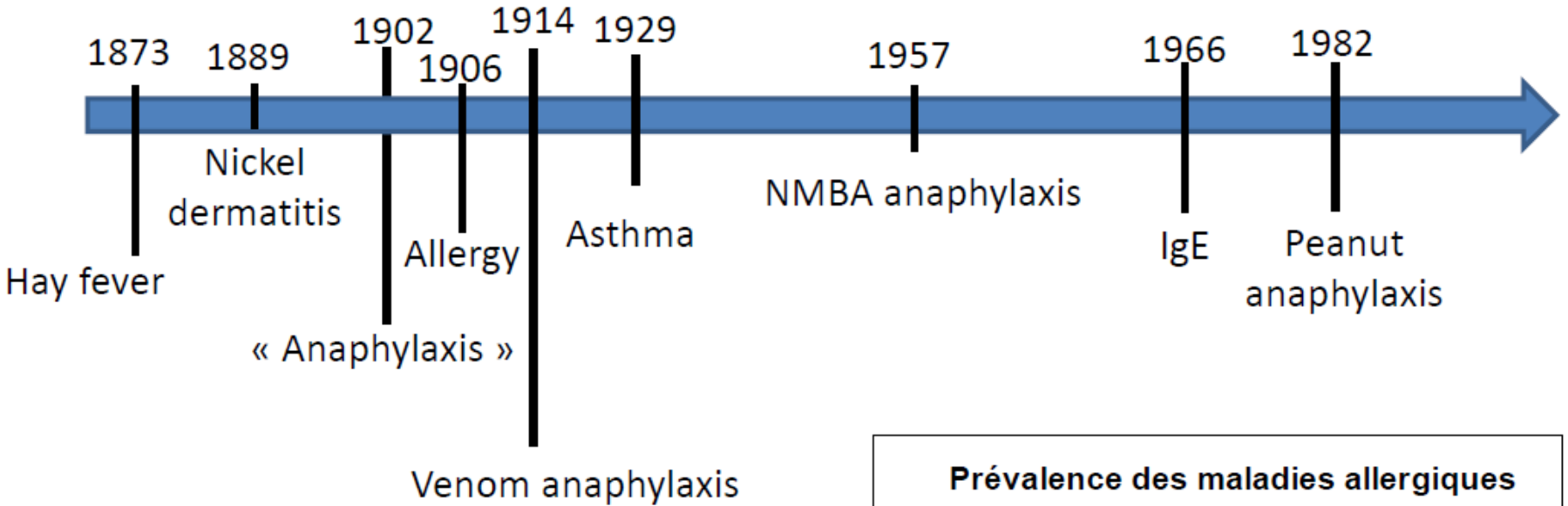
- Procedure : Initiation phase: increasing doses
  Maintenance phase : max dose for 3 to 5 years
- Administration route: SC, SL: drops or tablet
- CI :
  - Under 5 yo
  - Pregnancy
  - Immune dysfunction
  - Uncontrolled allergy
  - B-blockers
- Risk :
  - Allergic reaction +/- severe

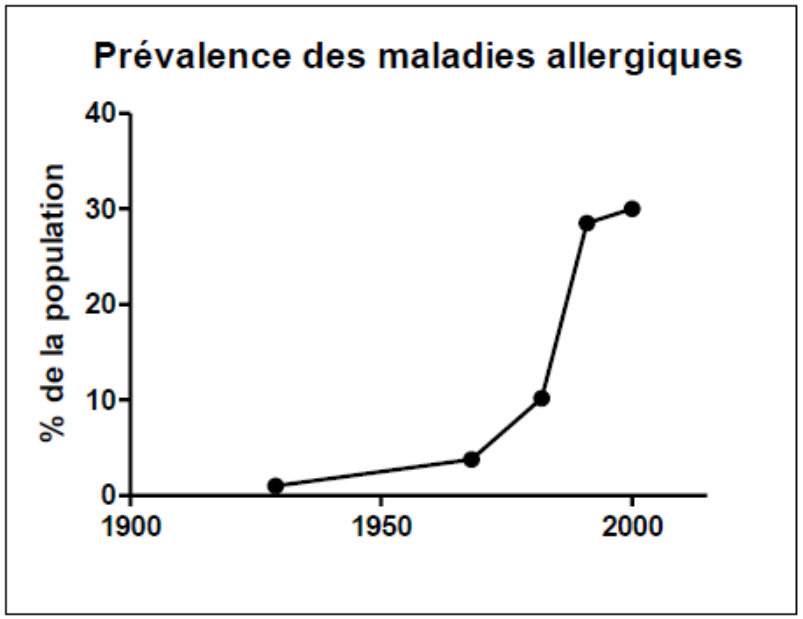
  Efficiency : wasp venom 95 %, honey bee 80 %, pollens and dust mites ~70 %

Mechanisms of AIT



Epidemiology





1929: Estimated prevalence: 1%

Epidemiologie

- Prevalence : 20% to 30% in Europe and North America
- 3 millions asthma patients in France

- Condordance between siblings:
  - 40% between **non-twins** or dizigotic twins
  - 50% between **monozygotic twins raised separately**
  - 80% between **monozygotic twins raised together**

Strong genetic influence

Strong environment influence

Genetic predisposition

Highly heritable disease

Risk to be atopic :

0 allergic parent	15%
1 allergic parent	25%
2 allergic parents	50% (80% if same disease)

Genes involved :

HLA: HLA-DR1 (cat) ; HLA-DR2 and 5 (ragweed)
TCR (dust mites)
Chrom. 11q13 : chaîne β du **FcεR1**
Chrom. 5q : **IL-3, IL-4, IL-13, IL-4R**, R β-adrenergics

Allergy and environment

Risk factors	Protective factors
-Prebirth stress	-Numerous siblings
-Pollutants exposure	-Countryside
-Tobacco	-Farm products
-Urban life	-Pet (dog++)
-Obesity	-Rich microbiota
-Excessive hygiene	-Long breast feeding
-Television?	-Early exposure

Modern lifestyle disease?

Conclusions

- Allergy is a type of hypersensitivity. It can be immediate or delayed
- Immediate allergy involves IgE production and histamine release by basophils and mast cells.
- Diagnosis relies on interview, skin tests and specific IgE measurement
- Allergy prevalence is increasing rapidly probably because of industrialization and urban lifestyle
- Treatment involves anti-histamines and allergen immunotherapy