# Hypersensibilités et allergies aux médicaments

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## Gell & Coombs revisited

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# Hypersensitivity reactions

1. **Immunology definition – Gell & Coombs**

   Hypersensitivity reactions = inappropriate and damaging immune response to an antigen caused by adaptive immunity (Igs and/or T cells)

   - Allergic diseases

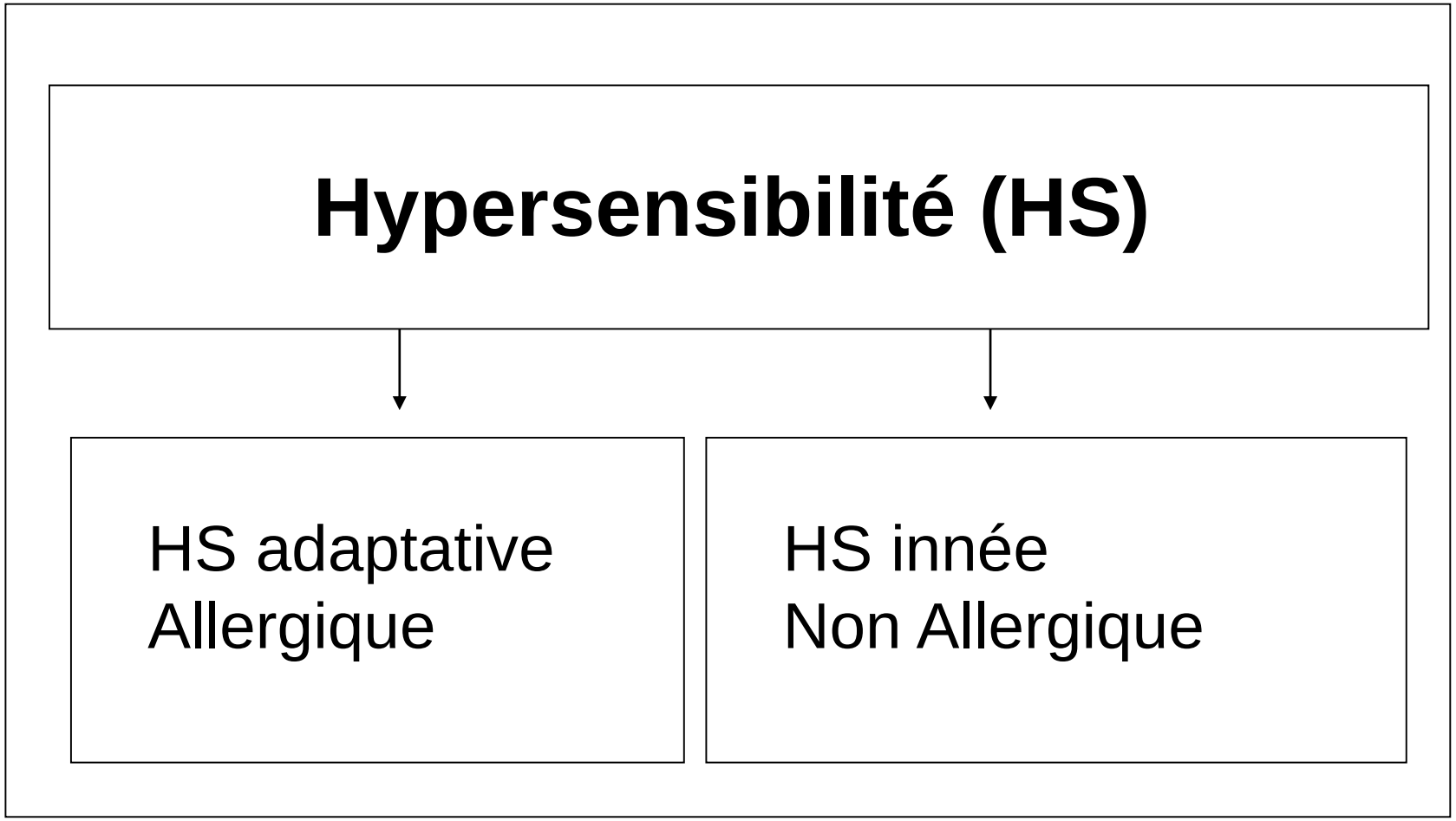
   - Autoimmune diseases

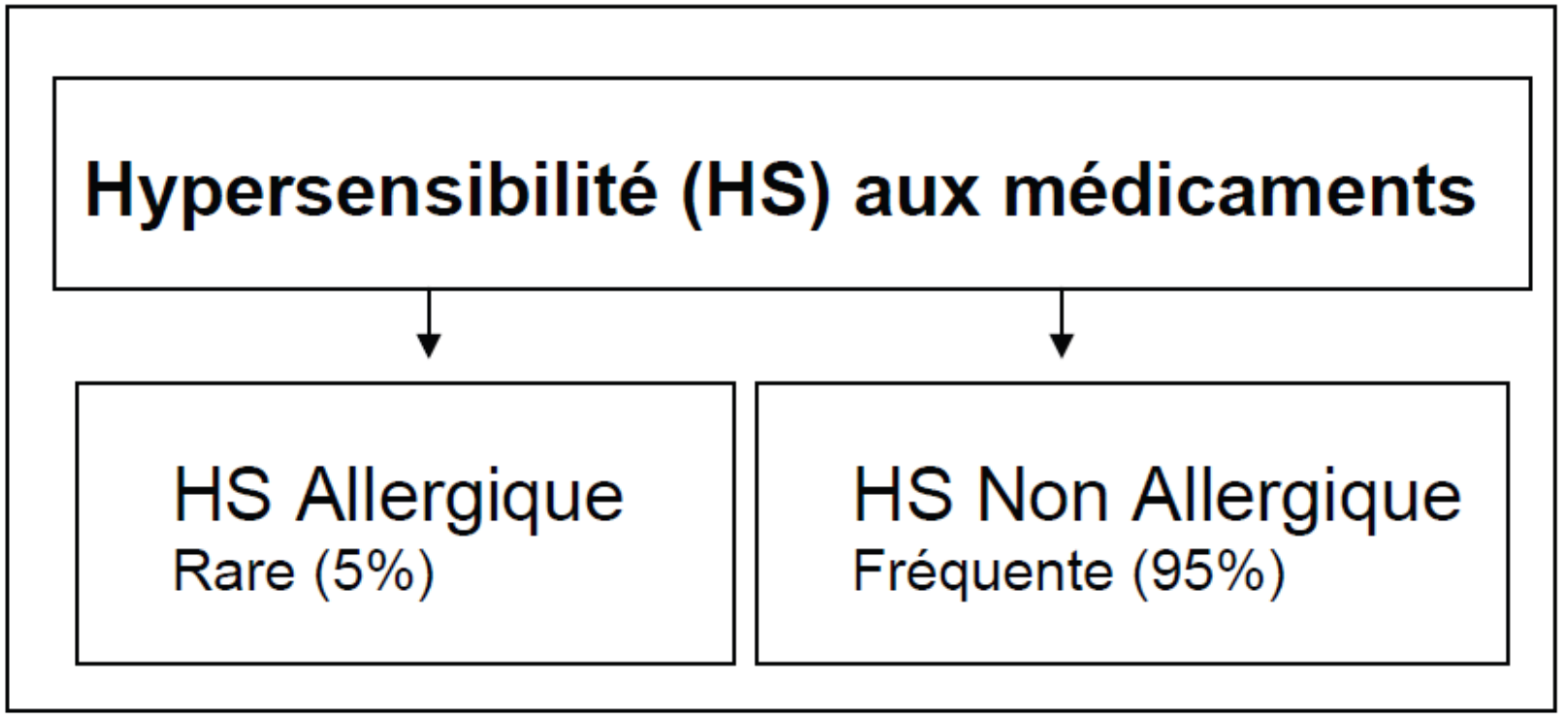
2. **Allergy définition**

   Hypersensitivity reactions = inappropriate and damaging immune response to a molecule caused by both innate and/or adaptive immunity

   - Allergic HS

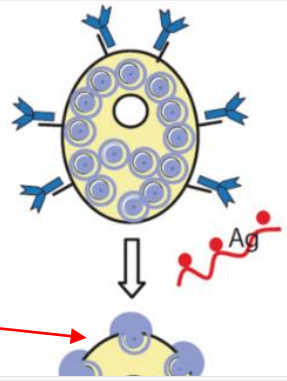
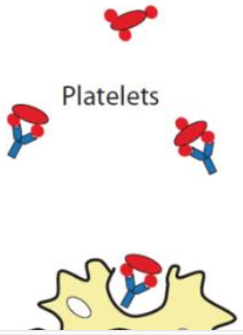
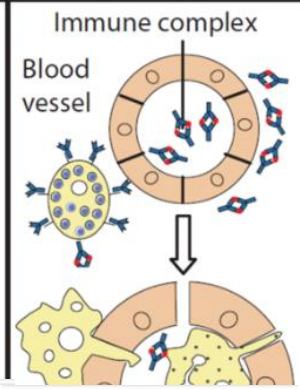
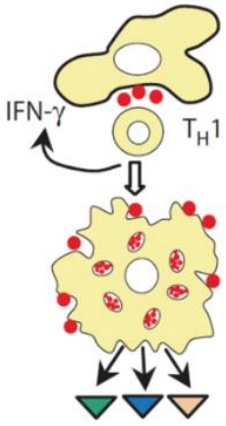
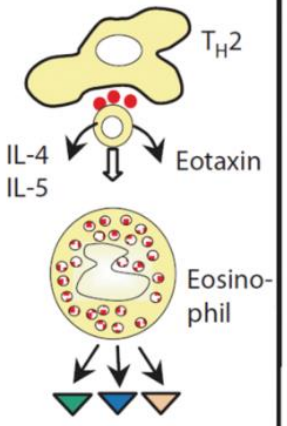
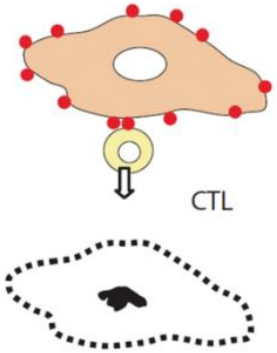
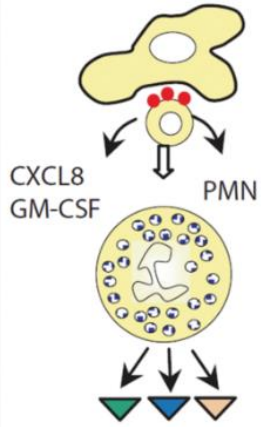
   - Non allergic HS


Hypersensibilité (HS)
HS adaptative
Allergique
HS innée
Non Allergique


Hypersensibilité (HS) aux médicaments
HS Allergique
Rare (5%)
HS Non Allergique
Fréquente (95%)
sévère
bénigne

# Hypersensibilités
Classification de Gell & Coombs

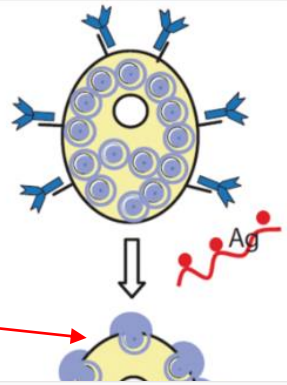
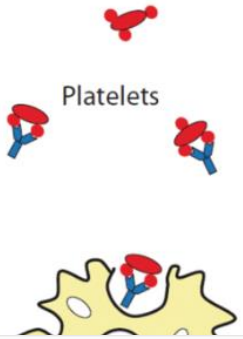
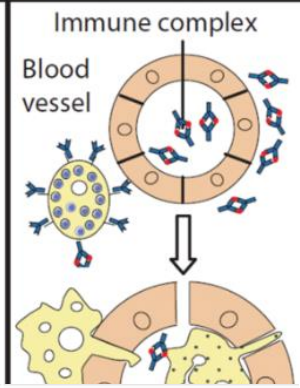
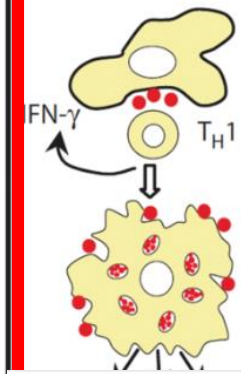
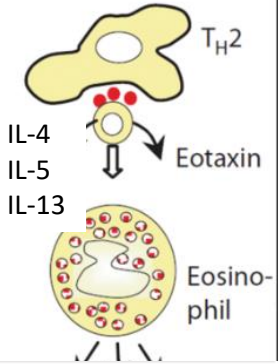
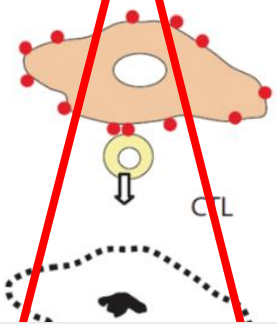
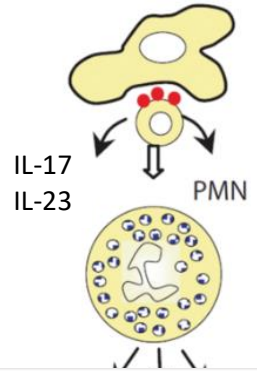
Antibody → T cells

| | Type I | Type II | Type III | Type IVa | Type IVb | Type IVc | Type IVd |
|---|---|---|---|---|---|---|---|
| **Immune reactant** | ~~IgE~~ | IgG | IgG | IIFN-γ, TNF-α ($T_H1$ cells) | IL-5, IL-4/IL-13 ($T_H2$ cells) | Perforin/ granzyme B (CTL) | IL-17, IL-22 (Th17) |
| **Antigen** | Soluble antigen | Cell- or matrix-associated antigen | Soluble antigen | Antigen presented by cells or direct T-cell stimulation | Antigen presented by cells or direct T-cell stimulation | Cell-associated antigen or direct T-cell stimulation | Soluble antigen presented by cells or direct T-cell stimulation |
| **Effector** | Mast cell activation | FcR+ cells (phagocytes, NK cells) | FcR+ cells Complement | Macrophage activation | Eosinophils | T cells | Neutrophils |
| |   |   |   |   Chemokines, cytokines, cytotoxins |   Cytokines, inflammatory mediators |   |   Cytokines, inflammatory mediators |
| | **Allergie et HS médicaments** | **Choc anaphylactique Urticaire aux médicaments** | **Cytopénies medic.** | **Vascularites immuno-allerg.** | | | |

HSI non allergique

# Hypersensibilités
Classification de Gell & Coombs

Antibody → ← Lymphocytes

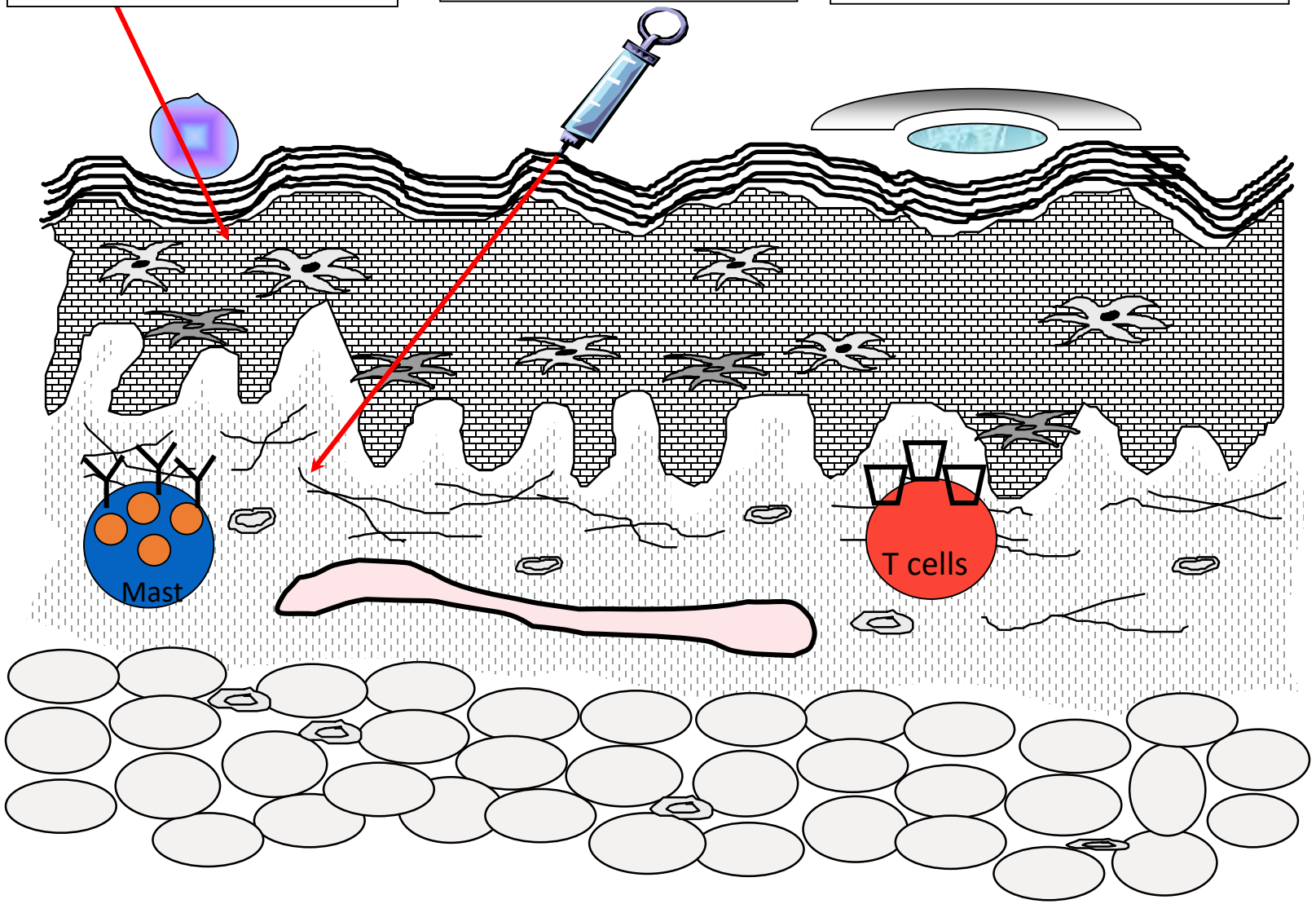
| | Type I | Type II | Type III | Type IVa | Type IVb | Type IVc | Type IVd |
|---|---|---|---|---|---|---|---|
| **Immune reactant** | ~~IgE~~ | IgG | IgG | IIFN-γ, TNF-α ($T_H1$ cells) | IL-5, IL-4/IL-13 ($T_H2$ cells) | Perforin/ granzyme B (CTL) | IL-17, IL-22 (Th17) |
| **Antigen** | Soluble antigen | Cell- or matrix-associated antigen | Soluble antigen | **Th1/Tc1/ILC1 Type 1 inflammation** | **Th2/Tc2/ILC2 Type 2 inflammation** | Cell-associated antigen or direct T-cell stimulation | **Th17/Tc17/ILC3 Type 3 (17) inflammation** |
| **Effector** | Mast cell activation | FcR+ cells (phagocytes, NK cells) | FcR+ cells Complement | Macrophage activation | Eosinophils | T cells | Neutrophils |
| |   |   |   |   |   |   |   |
| | **Allergie et HS médicaments** | **Choc anaphylactique<br>Urticaire aux médicaments** | **Cytopénies medic.** | **Vascularites immuno-allerg.** | **Exanthème Lyell<br>Stevens-Johnson** | **DRESS** | | **Pustulose exanthématique aigue généralisée** |

HSI non allergique

**Prick-test**
piqûre
superficielle au travers d'une goutte d'allergène

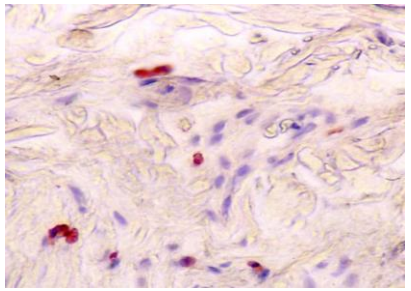
**IDR**
injection intradermique de l'allergène de façon stérile

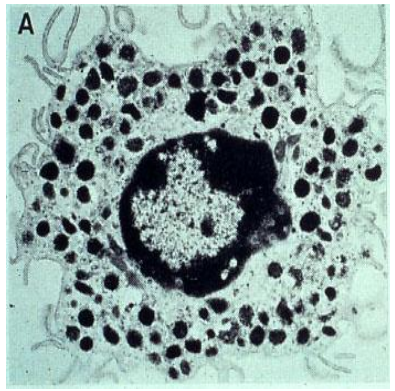
**Patch-test**
application de l'allergène sous occlusion par voie épicutanée

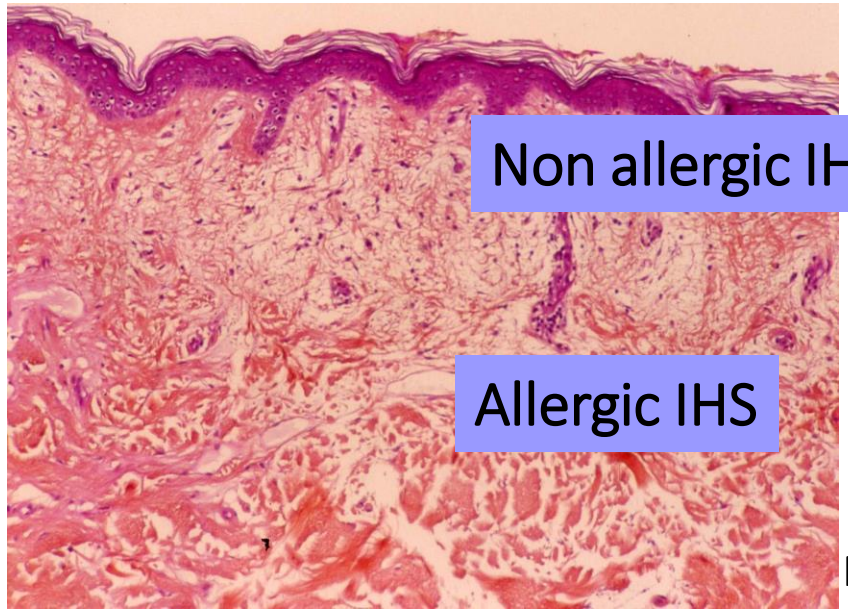


# TYPE I HYPERSENSITIVITY

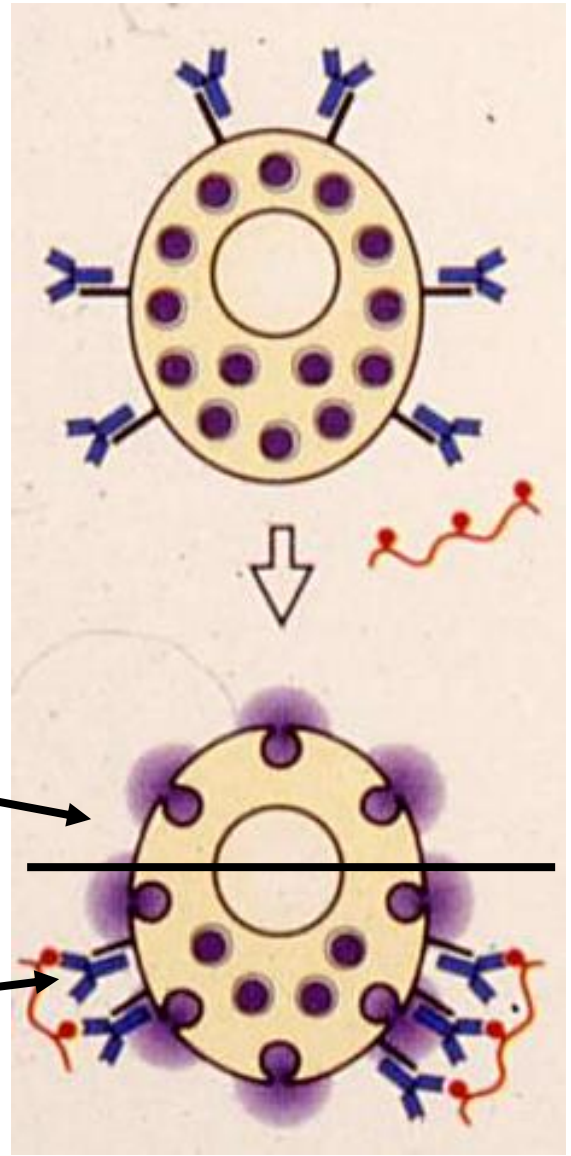
Œdème du derme / Vaisseaux



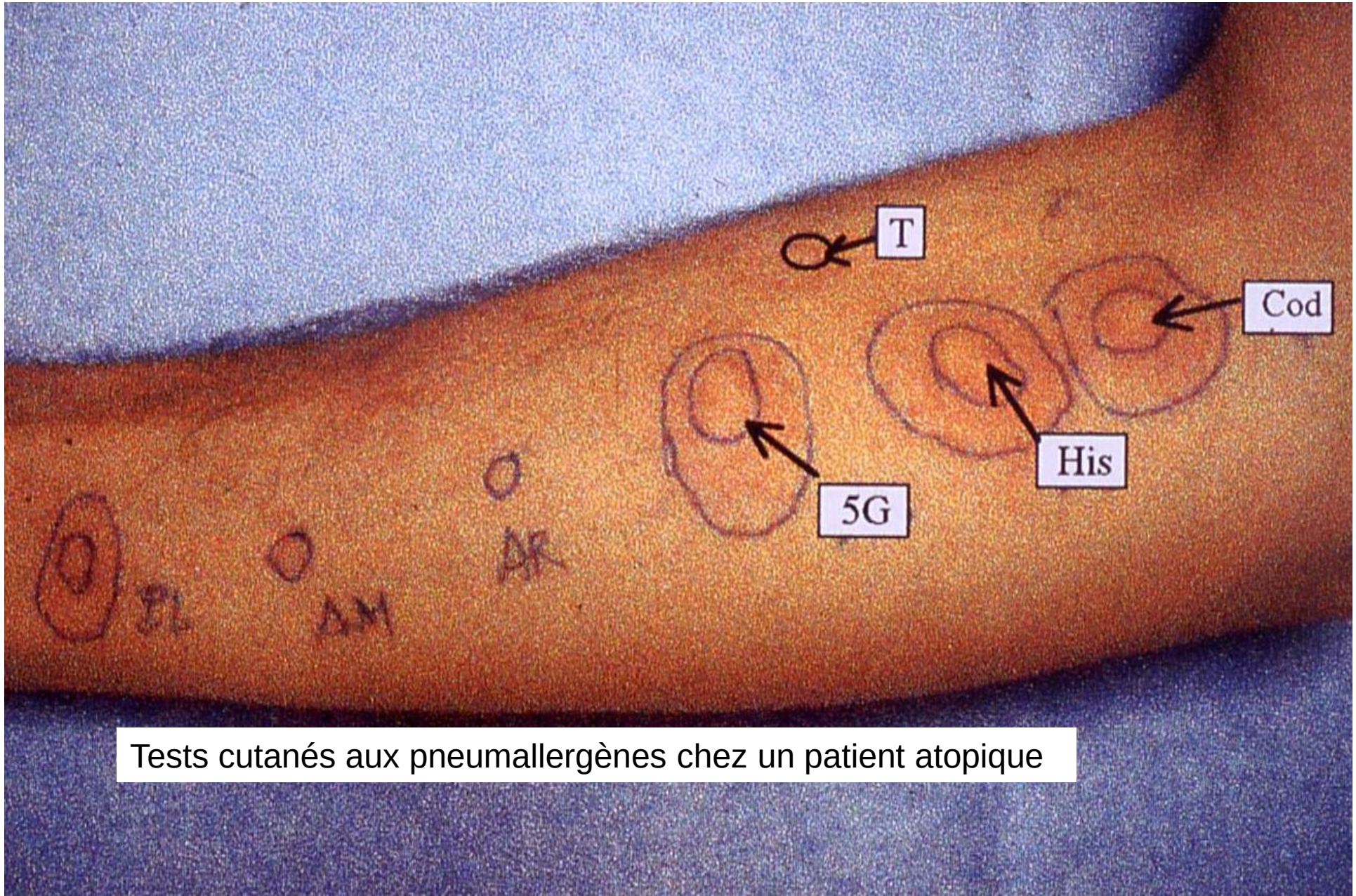



Mastocytes / Histamine



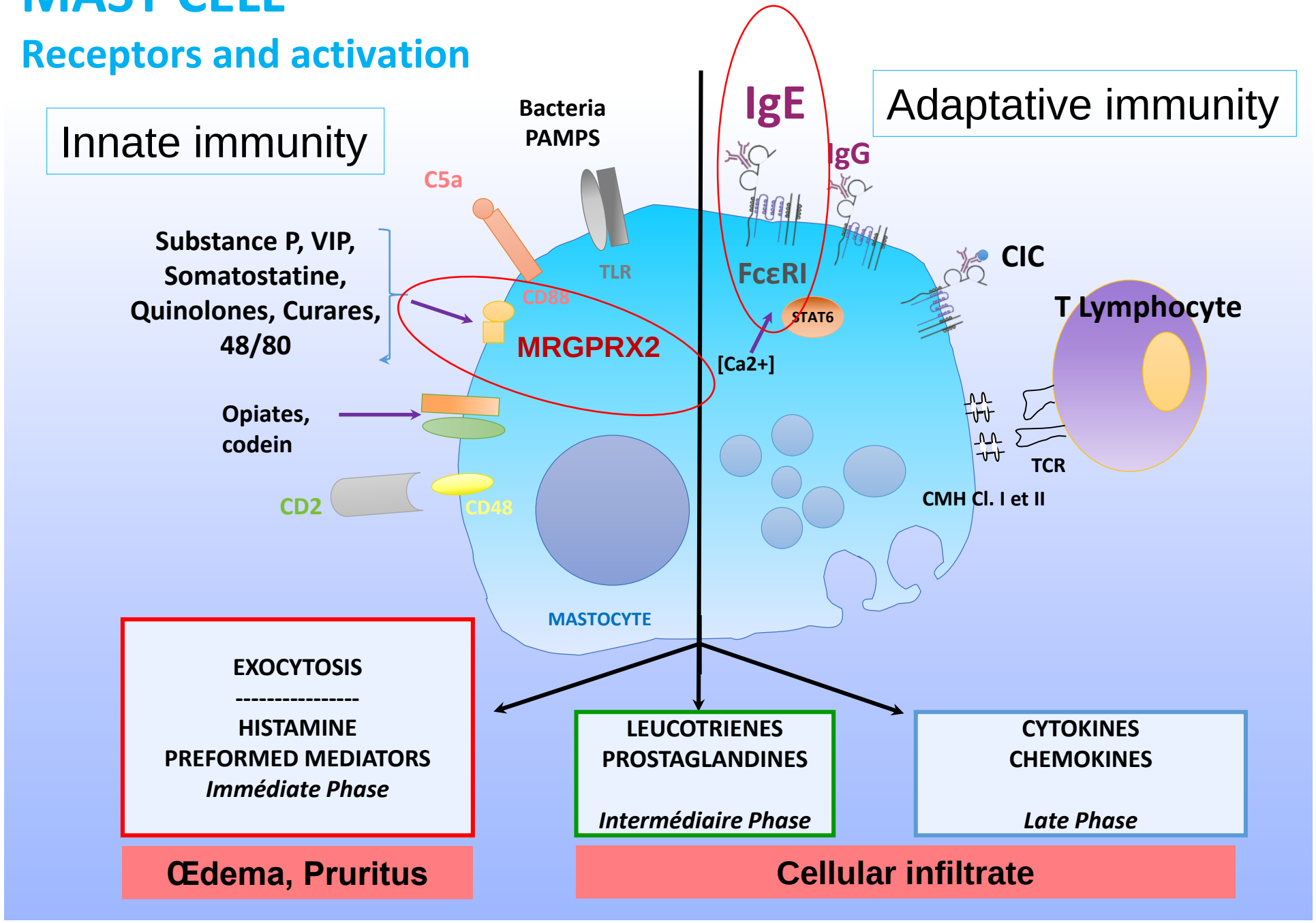
# HSI allergique et non allergique




Tests cutanés aux pneumallergènes chez un patient atopique

# MAST CELL

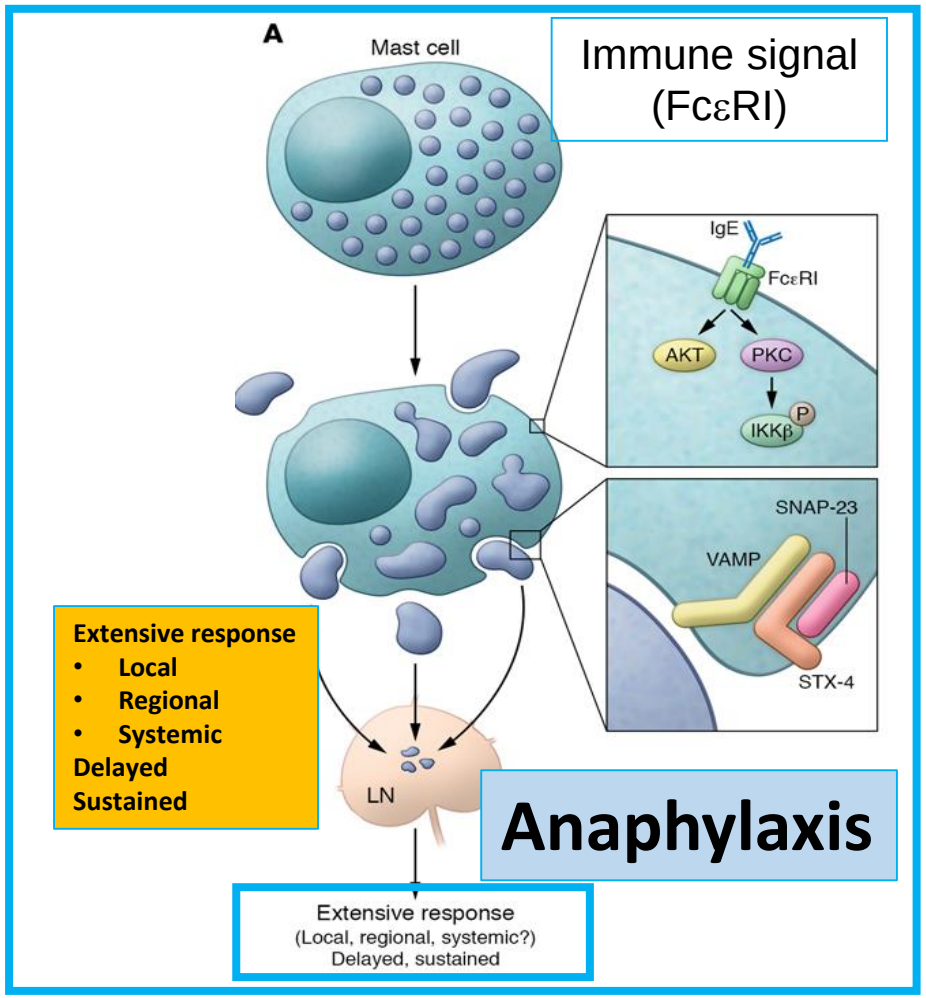
## Receptors and activation

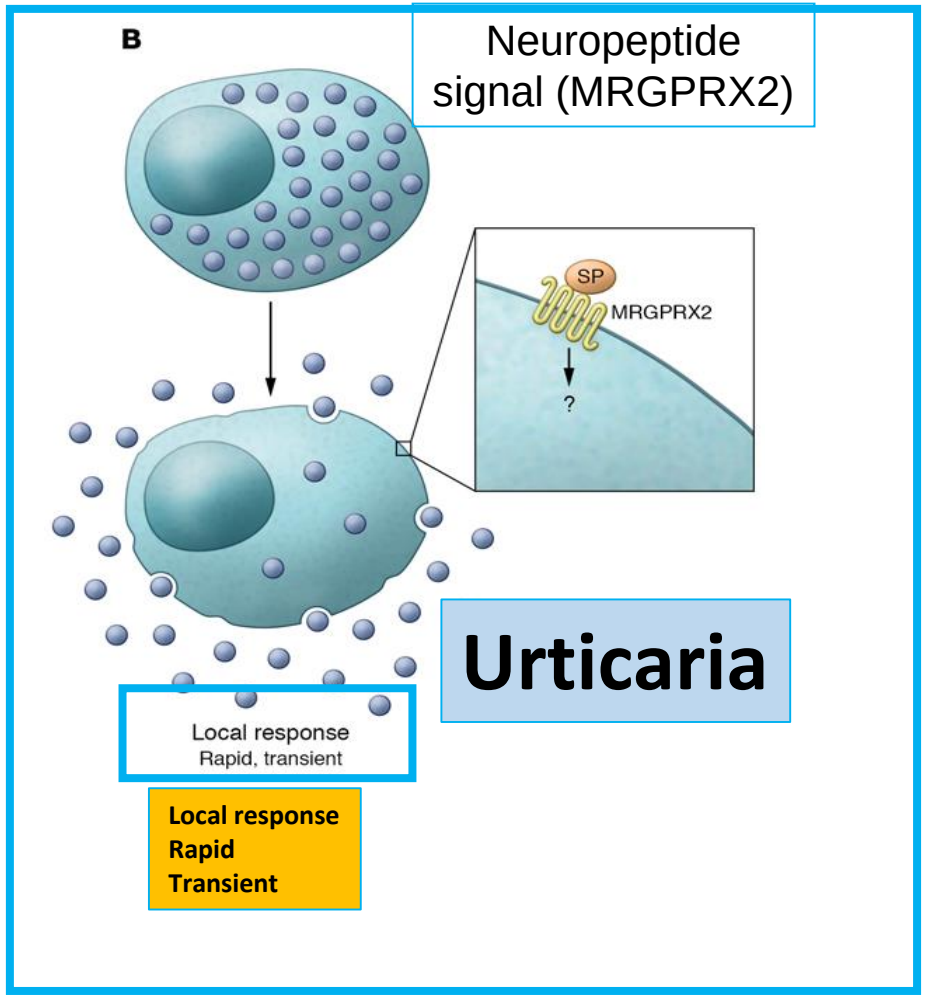


# Two fundamental degranulation pathways in mast cells

## IgE/FceRI

## Other receptor




*Gaudenzio et al.* ***J Clin Invest*** *2016*

# Drug-induced urticaria and angioedema

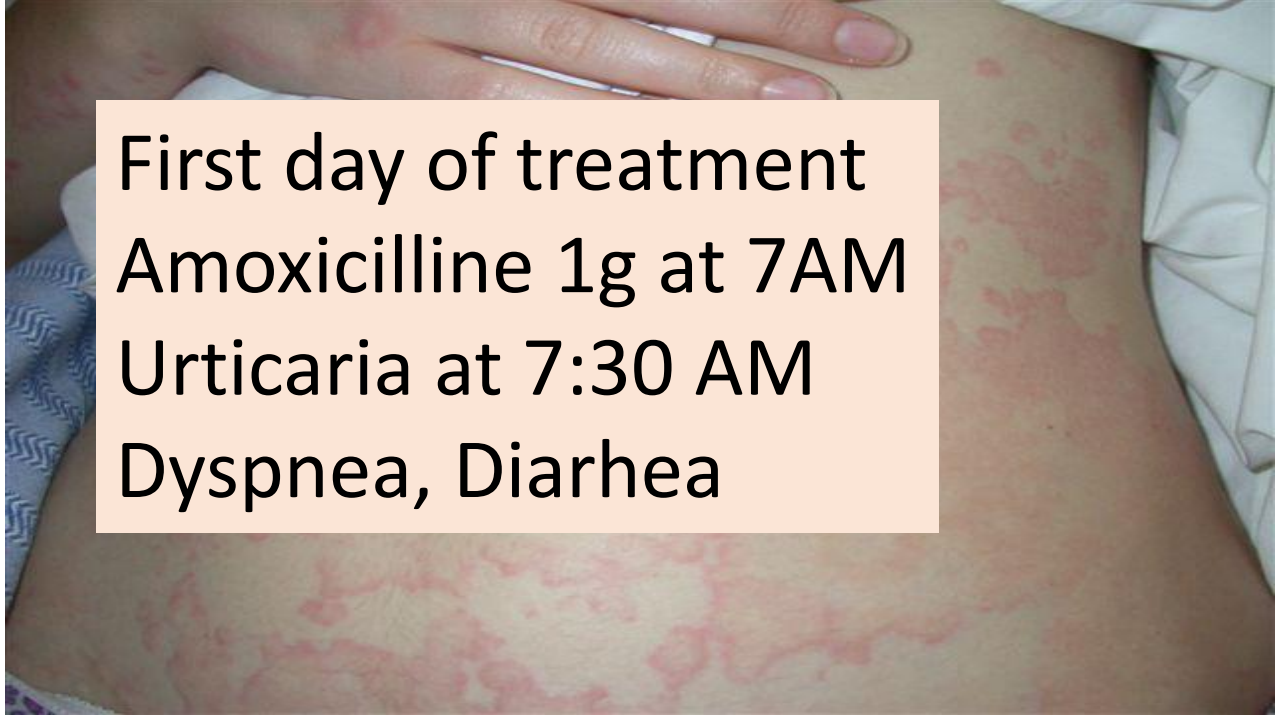
- **Allergic (IgE)**: rares (5%) and exceptionally isolated

- **Non allergic**: frequent (95%) and almost always benign


- Cousin F, Philips K, Favier B, Bienvenu J**,** Nicolas JF**.** Drug-induced urticaria. **Eur J Dermatol** 2001;11(3):181-7.


First day of treatment
Amoxicilline 1g at 7AM
Urticaria at 11 AM


Third day of treatment
Amoxicilline 1g at 7AM
Urticaria at 7:30 AM



First day of treatment
Amoxicilline 1g at 7AM
Urticaria at 7:30 AM
Dyspnea, Diarhea

**More a drug-induced reaction is severe, more it has a chance to be allergic**

# Département Allergologie et Immunologie Clinique

Clinical Research Unit

INSERM translational research team

Allergology & Clinical Immunology Department