Pathophysiology of autoimmune and allergic diseases

Hypersensitivity reactions type II – type IV

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Hypersensitivity reactions

1. Immunology definition

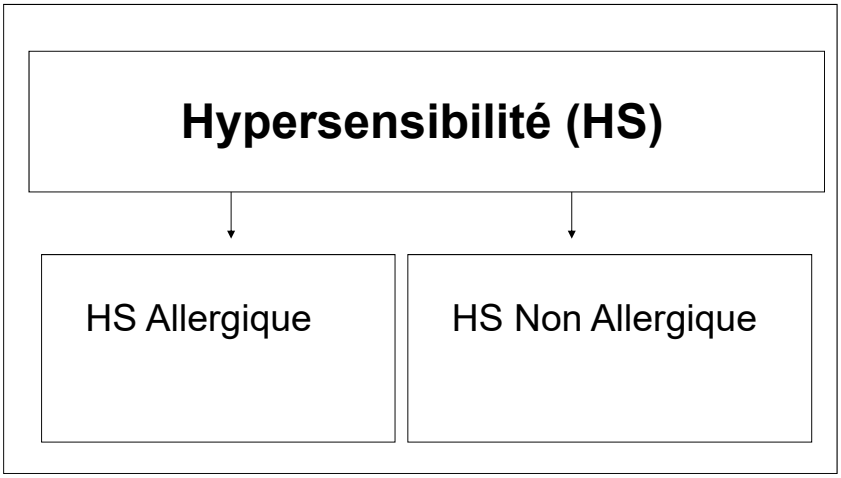
   Hypersensitivity reactions = inappropriate and damaging immune response to an antigen caused by adaptive immunity (Igs and/or T cells)

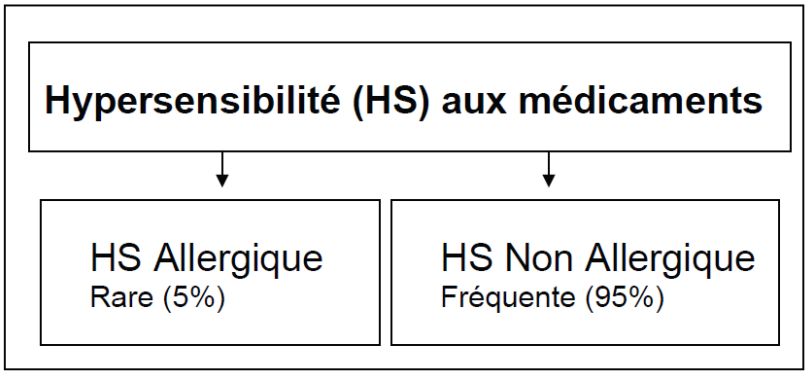
   - Allergic diseases
   - Autoimmune diseases

2. Allergy définition

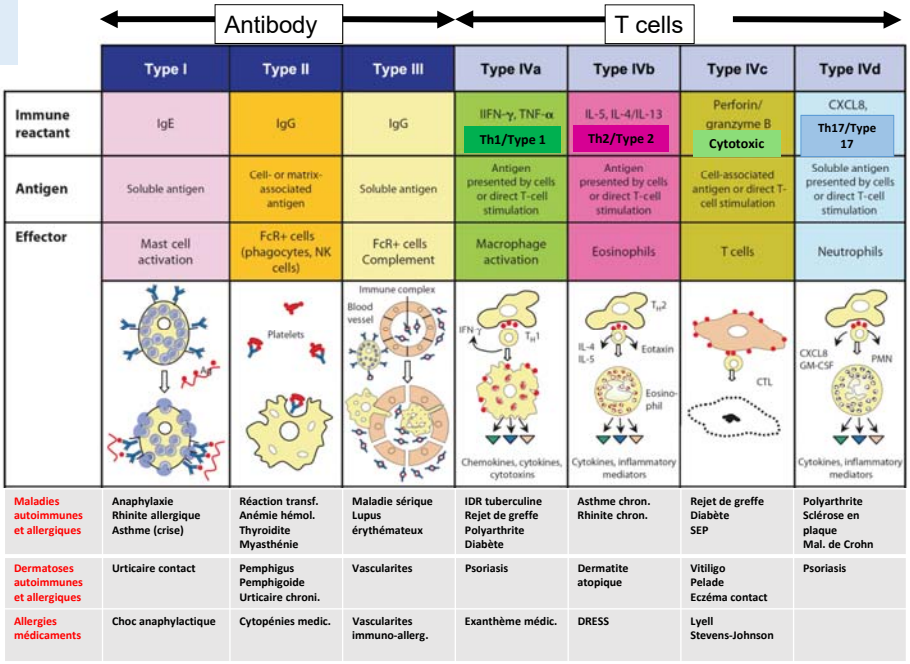
   Hypersensitivity reactions = inappropriate and damaging immune response to a molecule caused by both innate and/or adaptive immunity

   - Allergic HS
   - Non allergic HS


Hypersensibilité (HS)
HS Allergique
HS Non Allergique

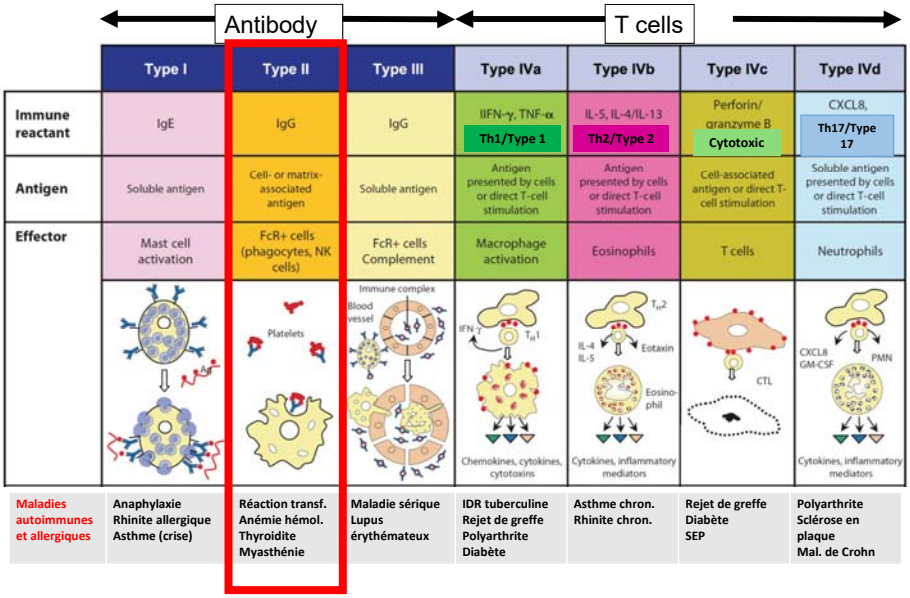

Hypersensibilité (HS) aux médicaments
HS Allergique
Rare (5%)
HS Non Allergique
Fréquente (95%)

Hypersensibilités
Classification de Gell & Coombs



Maladies autoimmunes et allergiques	Anaphylaxie Rhinite allergique Asthme (crise)	Réaction transf. Anémie hémol. Thyroidite Myasthénie	Maladie sérique Lupus érythémateux	IDR tuberculine Rejet de greffe Polyarthrite Diabète	Asthme chron. Rhinite chron.	Rejet de greffe Diabète SEP	Polyarthrite Sclérose en plaque Mal. de Crohn
Dermatoses autoimmunes et allergiques	Urticaire contact	Pemphigus Pemphigoide Urticaire chroni.	Vascularites	Psoriasis	Dermatite atopique	Vitiligo Pelade Eczéma contact	Psoriasis
Allergies médicaments	Choc anaphylactique	Cytopénies medic.	Vascularites immuno-allerg.	Exanthème médic.	DRESS	Lyell Stevens-Johnson	

Hypersensibilités
Classification de Gell & Coombs



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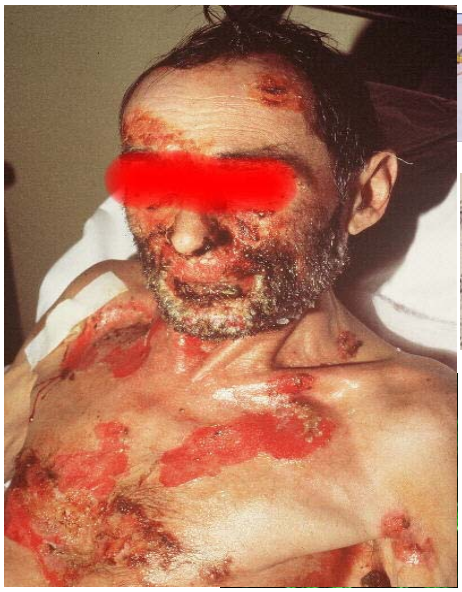
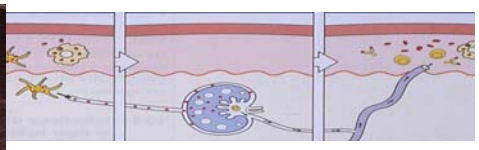
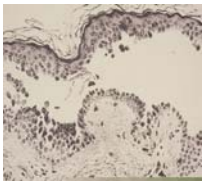
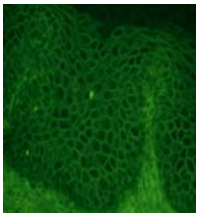
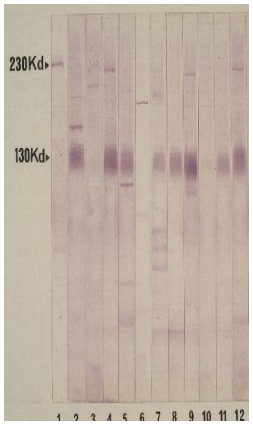
Hypersensibilité de type II due à des IgG spécifiques
PEMPHIGUS

Hypersensibilités
Classification de Gell & Coombs

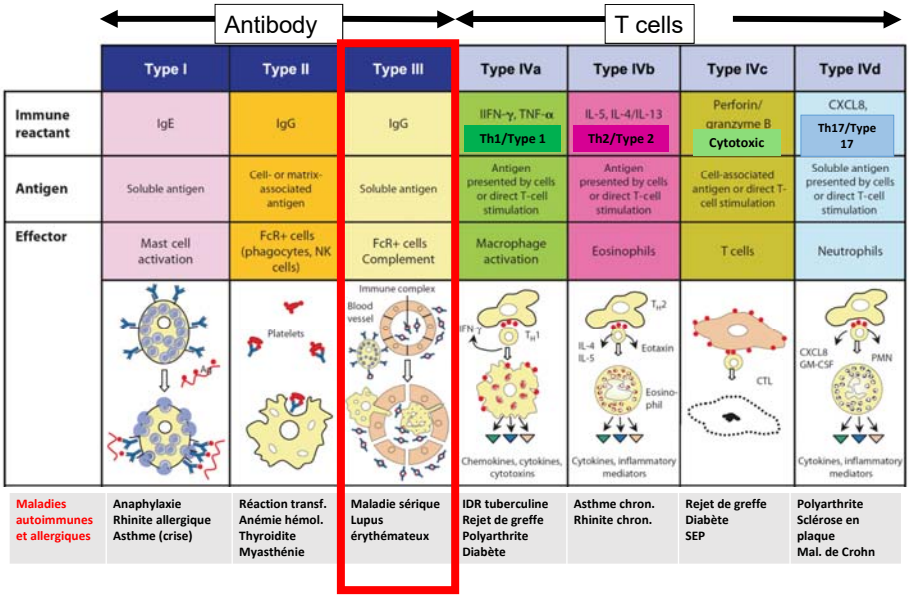


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Fig

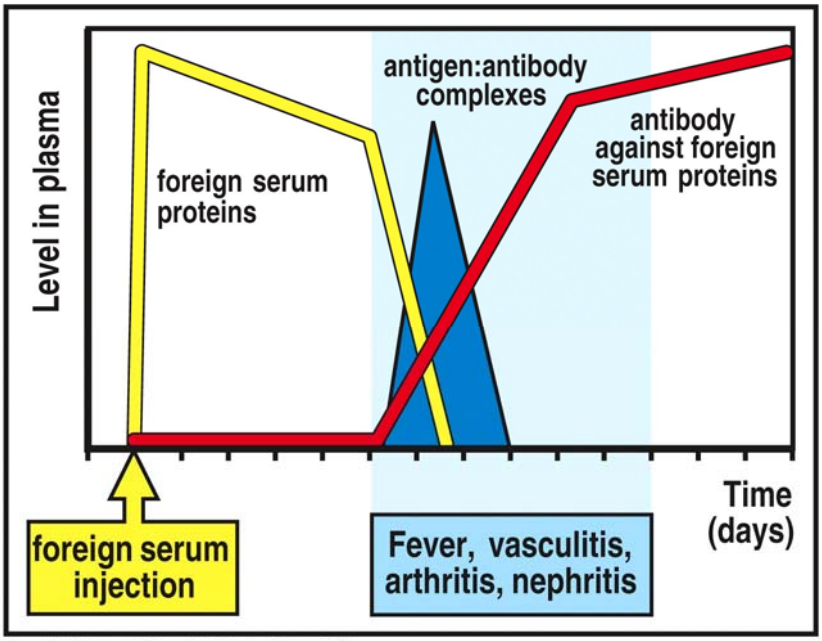
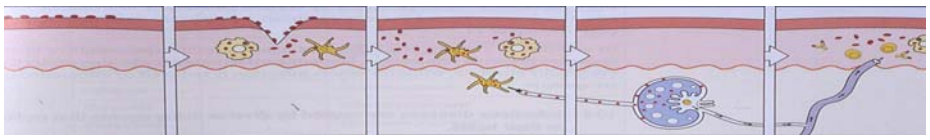
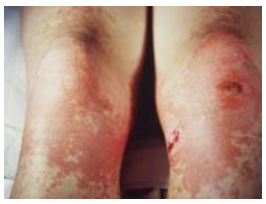
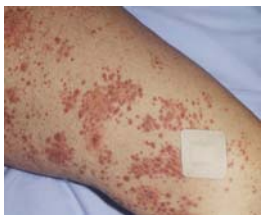


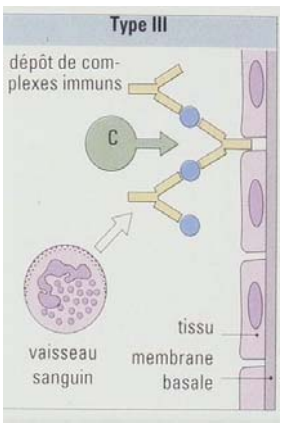
Figure 12-23 Immunobiology, 6/e. (© Garland Science 2005)

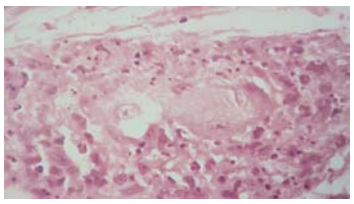
Hypersensibilité de type III due à des complexes immuns
VASCULITES – PURPURA RHUMATOIDE

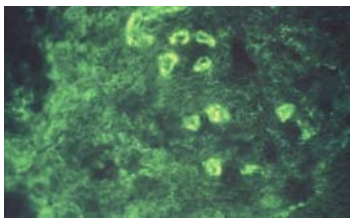




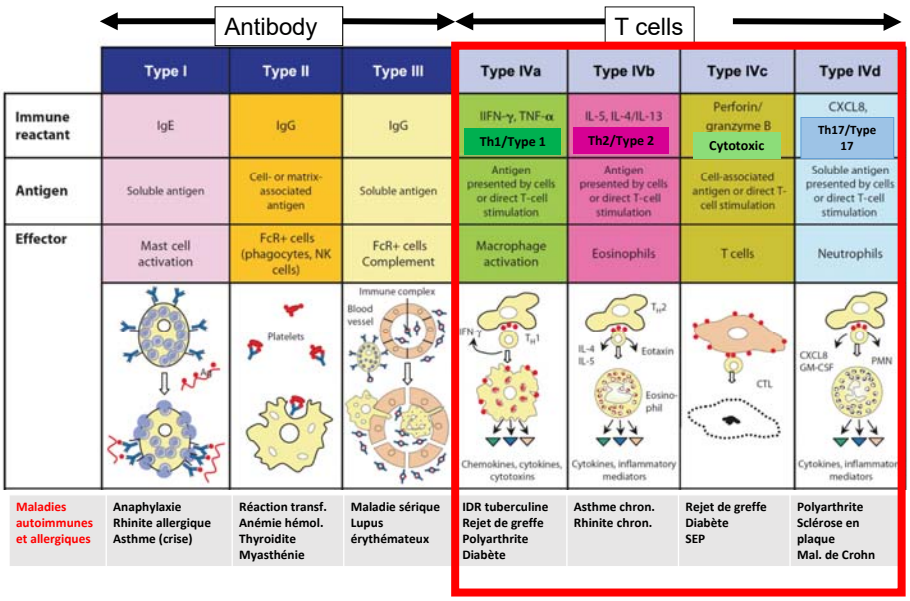








Hypersensibilités
Classification de Gell & Coombs



The 3 major types of innate and adaptive cell-mediated effector immunity

Francesco Annunziato, PhD,[a] Chiara Romagnani, MD, PhD,[b] and Sergio Romagnani, MD[a] *Florence, Italy, and Berlin, Germany*

The immune system has tailored its effector functions to optimally respond to distinct species of microbes. Based on emerging knowledge on the different effector T-cell and innate lymphoid cell (ILC) lineages, it is clear that the innate and adaptive immune systems converge into 3 major kinds of cell-mediated effector immunity, which we propose to categorize as type 1, type 2, and type 3. Type 1 immunity consists of T-bet$^+$ IFN-γ–producing group 1 ILCs (ILC1 and natural killer cells), CD8$^+$ cytotoxic T cells (T_C1), and CD4$^+$ T_H1 cells, which protect against intracellular microbes through activation of mononuclear phagocytes. Type 2 immunity consists of GATA-3$^+$ ILC2s, T_C2 cells, and T_H2 cells producing IL-4, IL-5, and IL-13, which induce mast cell, basophil, and eosinophil activation, as well as IgE antibody production, thus protecting against helminthes and venoms. Type 3 immunity is mediated by retinoic acid–related orphan receptor γt$^+$ ILC3s, T_C17 cells, and T_H17 cells producing IL-17, IL-22, or both, which activate mononuclear phagocytes but also recruit neutrophils and induce epithelial antimicrobial responses, thus protecting against extracellular bacteria and fungi. On the other hand, type 1 and 3 immunity mediate autoimmune diseases, whereas type 2 responses can cause allergic diseases. (J Allergy Clin Immunol 2015;135:626-35.)

Key words: *Type 1 immunity, type 2 immunity, type 3 immunity, innate lymphoid cells, T_H1, T_C1, T_H2, T_C2, T_H17/T_H22, T_C17/T_C22*

Abbreviations used
APC: Antigen-presenting cell
CRTH2: Chemoattractant receptor-homologous molecule expressed on T_H2 cells
DC: Dendritic cell
Eomes: Eomesodermin
IBD: Inflammatory bowel disease
IL-7R: IL-7 receptor
ILC: Innate lymphoid cell
LT: Lymphotoxin
MP: Mononuclear phagocyte
MS: Multiple sclerosis
NK: Natural killer
NKp: Natural killer progenitor
PB: Peripheral blood
RA: Rheumatoid arthritis
ROR: Retinoic acid–related orphan receptor
STAT: Signal transducer and activator of transcription
T_C: Cytotoxic T
TSLP: Thymic stromal lymphopoietin

whereas T_H2 cells produce IL-4, IL-5, and IL-13.[3] Subsequently, a similar dichotomy within the CD8$^+$ cytotoxic T (T_C) cell population was discovered in both mice and human subjects, and the 2 subsets were named T_C1 and T_C2,

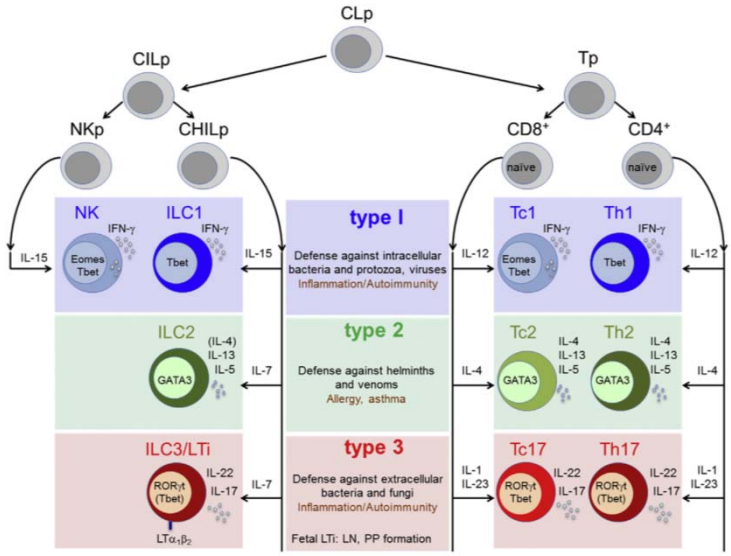


FIG 1. The 3 major types of innate and adaptive cell-mediated effector immunity. Type 1 immunity is composed of T-bet$^+$ IFN-γ–producing CD4$^+$ T_H1 cells and ILC1s and T-bet$^+$Eomes$^+$CD8$^+$ T_C1 and NK cells. Type 2 immunity is composed of GATA-3$^+$CD4$^+$ T_H2 cells, CD8$^+$ T_C2 cells, and ILC2s, which produce IL-4, IL-5, and IL-13. Type 3 immunity is composed of RORγt *(RORC)*$^+$CD4$^+$$T_H17$ cells, CD8$^+$ T_C17 cells, and ILC3s, producing IL-17, IL-22, or both. *CILp*, Common innate lymphoid precursor; *CLp*, common lymphoid precursor; *LN*, lymph node; *LTi*, lymphoid tissue inducer; *PP*, Peyer patch; *Tp*, T-cell progenitor.

Type 1 Immunity

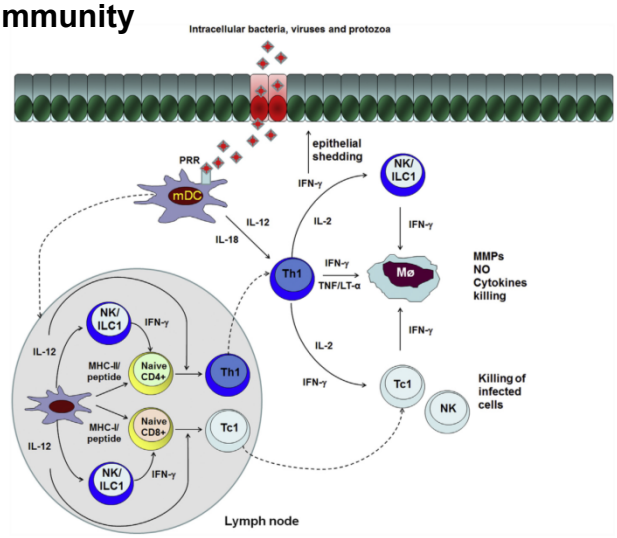


FIG 2. Cells, cytokines, and effectors of type 1 immunity. Intracellular microbes interacting with pathogen recognition receptors *(PRR)* on DCs in the presence of DC-derived IL-12 and IL-18 and of NK/ILC1-derived IFN-γ induce T_H1 or T_C1 development from naive T cells. T_C1 and NK cells kill virus-infected cells. T_H1 cell–, T_C1 cell–, and ILC1-derived cytokines activate MPs to produce the matrix metallopeptidase *(MMPs)*, nitric oxide *(NO)*, and cytokines that allow engulfment and killing of microbial invaders. *mDC*, Myeloid dendritic cell.

Type 2 Immunity

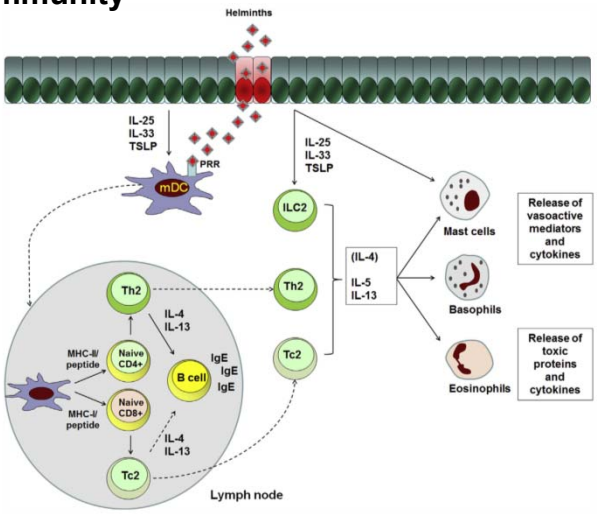


FIG 3. Cells, cytokines, and effectors of type 2 immunity. Helminths induce IL-25, IL-33, and thymic stromal lymphopoietin *(TSLP)* release by epithelial cells, which might directly activate mast cells, eosinophils, basophils, and ILC2s to produce IL-5, IL-13, and perhaps small amounts of IL-4. Activated DCs in the presence of IL-4 induce naive T cells to develop into T_H2 and T_C2 cells producing IL-4, IL-5, and IL-13. IL-4 and IL-13 allow IgE production by B lymphocytes, whereas IL-5 promotes eosinophil recruitment. *mDC*, Myeloid dendritic cell; *PRR*, pathogen recognition receptors.

Type 3/ type 17 Immunity

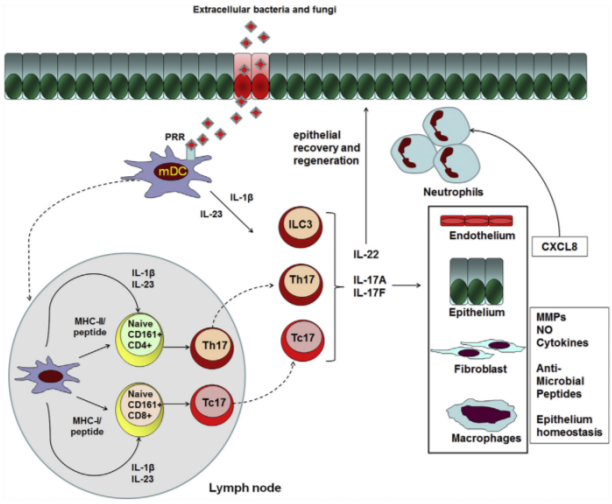
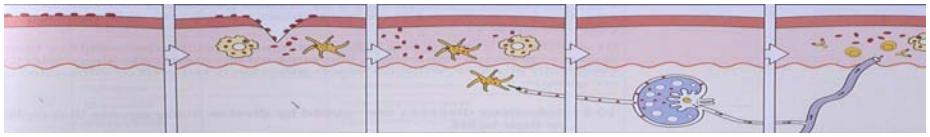
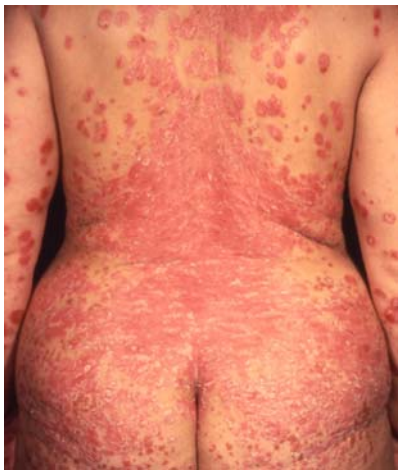


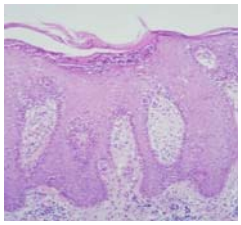
FIG 4. Cells, cytokines, and effectors of type 3 immunity. Extracellular bacteria and fungi induce myeloid dendritic cells *(mDC)* to produce IL-1β and IL-23, which allow T_H17 or T_C17 development from naive $CD161^+$ T cells and trigger cytokine production by ILC3s. IL-17A, IL-17F, and IL-22 from ILC3s and T_H17 and T_C17 cells activate nonimmune and immune cells to produce matrix metallopeptidases *(MMPs)*, nitric oxide *(NO)*, cytokines, antimicrobial peptides, and the neutrophil recruiter CXCL8. IL-22, especially that produced by ILC3s, promotes epithelial proliferation and restrains the gut microflora. *PRR*, Pathogen recognition receptors.

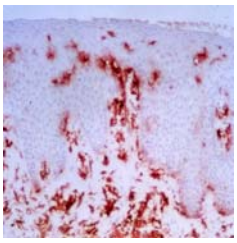
Hypersensibilité de type IV (HS retardée) due à des LT
PSORIASIS

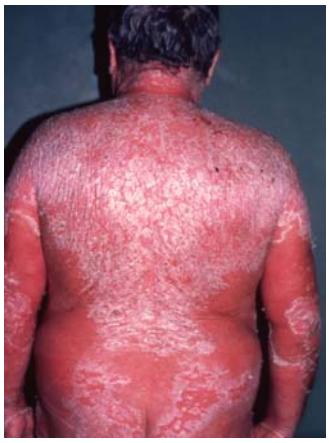
Th17
Type 17





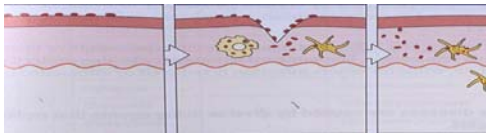


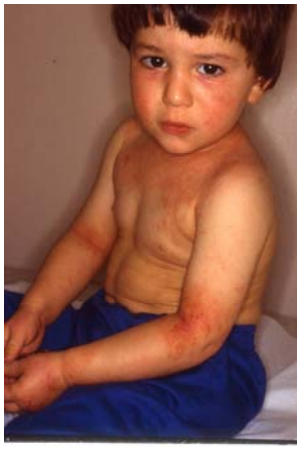


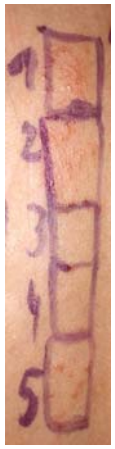


Hypersensibilité de type IV (HS retardée) due à des LT
DERMATITE ATOPIQUE

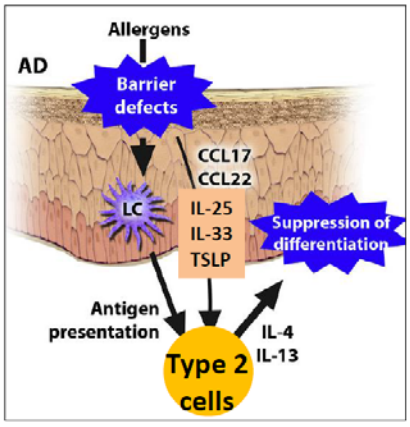
Th2
Type 2







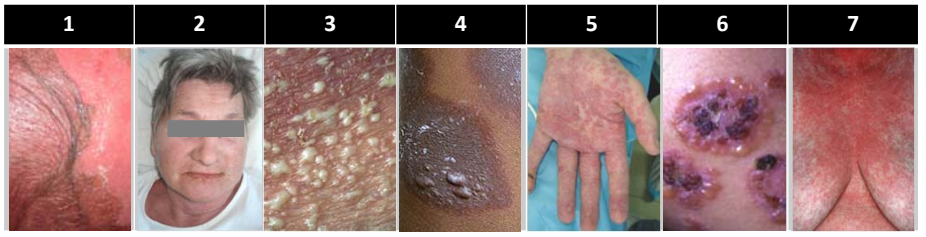
Type 2 phenotype



Type 2 inflammation
Type 2 immunity

Toxidermies – Drug allergy

Cytotoxic



SEVERE

1 - TEN: Toxic Epidermal Necrolysis

MODERATE

2 - DRESS: Drug Rash with Eosino &Systemic symptoms

3 - AGEP: Acute Generalized Exanthematous Pustulosis

4 - FDE: Fixed Drug Eruption

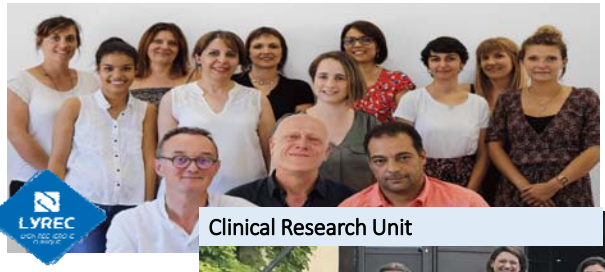
5 - Generalized Erythema multiform

6 - Linear IgA Dermatosis

MILD

7 - MPE: Maculo-papular exanthema

Département Allergologie et Immunologie Clinique



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