

Introduction to Allergy & Immunology



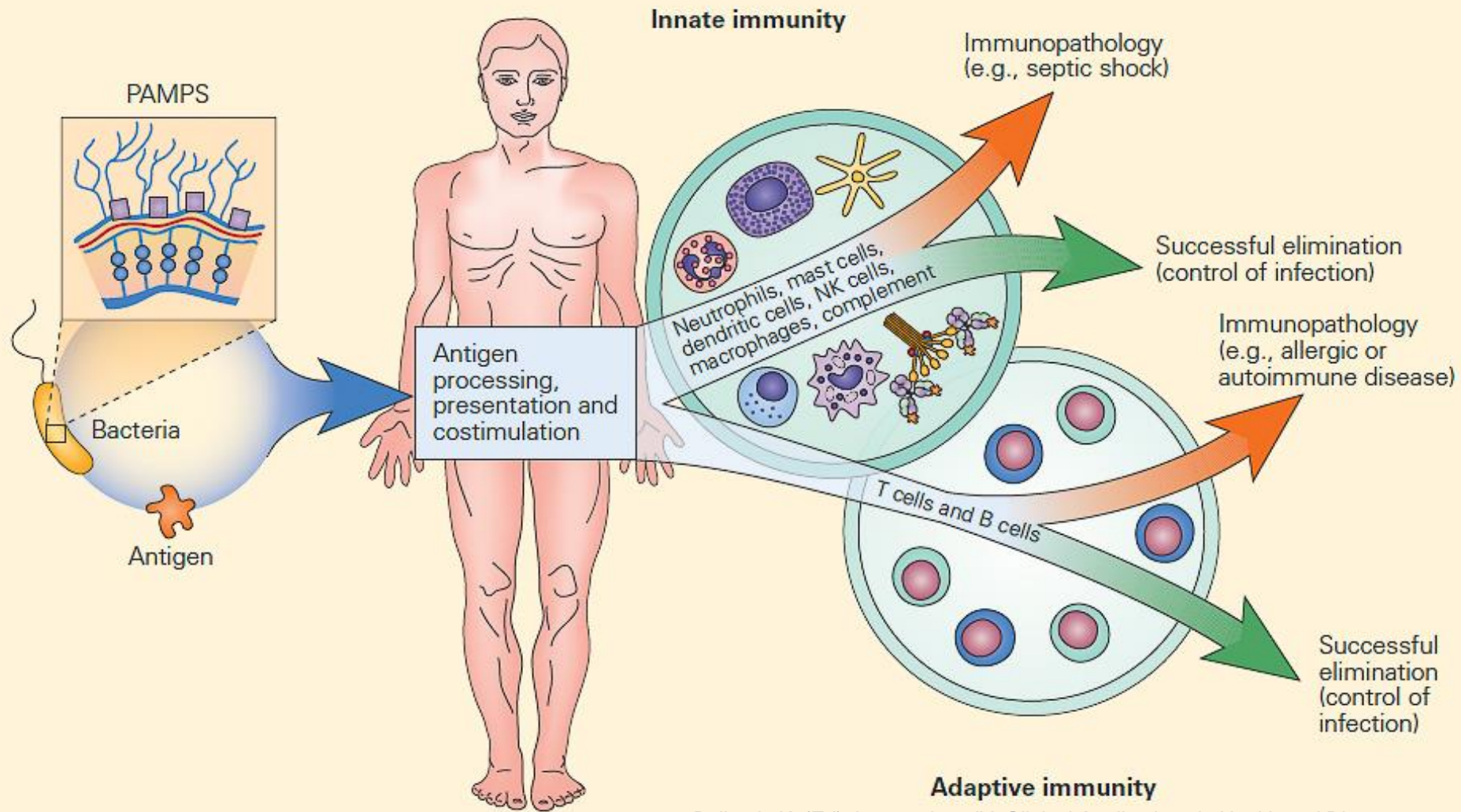
Aimee Lou M. Nano, MD, DPPS, DPSAAI

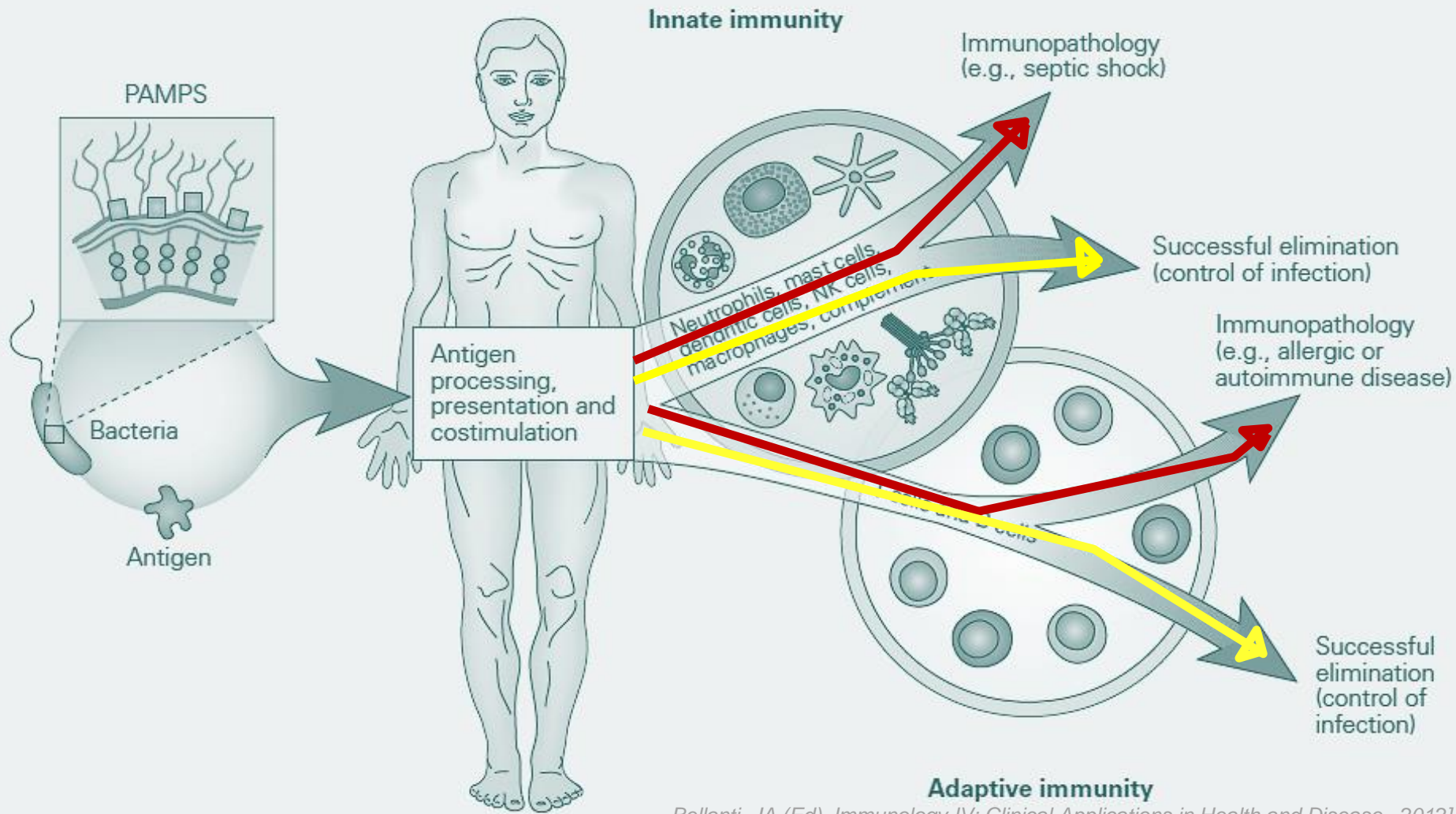
Allergy & Immunology

Hypersensitivity Reactions

- A. Mechanism
- B. Examples
- C. Diagnostics & Management

**What is
Hypersensitivity?**





The Immune Response

```
graph TD; A[The Immune Response] --> B[Host defense against microbes]; A --> C[Pathologic response: HYPERSENSITIVITY DISEASES]; C --> D[Autoimmunity]; C --> E[Reactions against microbes]; C --> F[Reactions against environmental antigens];
```

Host defense
against
microbes

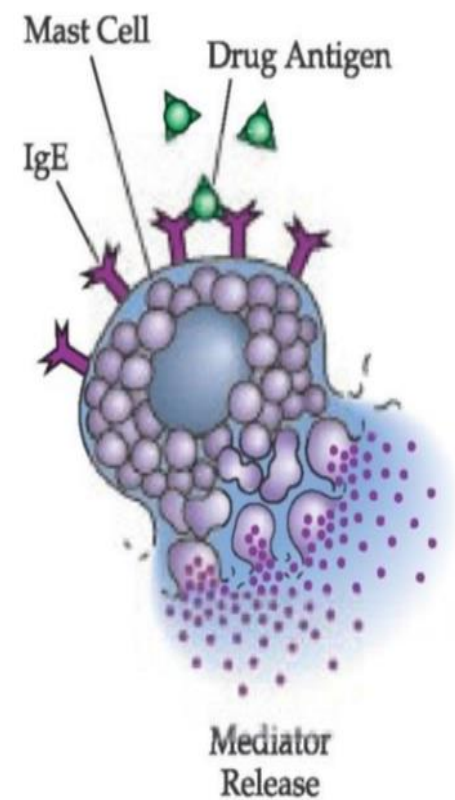
Pathologic response:
**HYPERSENSITIVITY
DISEASES**

Autoimmunity

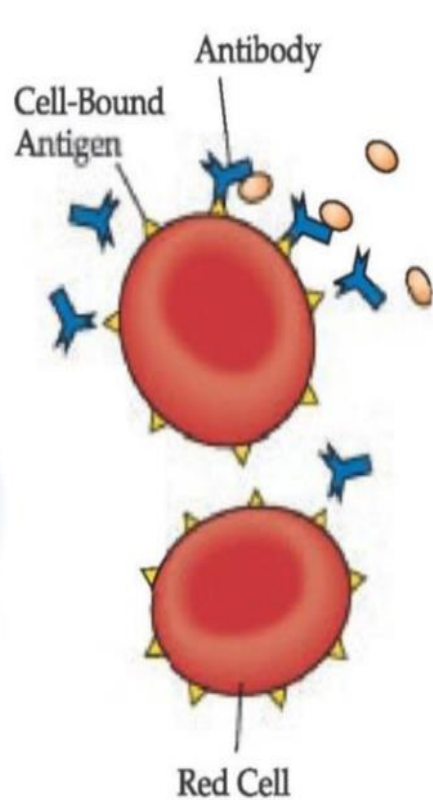
Reactions
against
microbes

Reactions against
environmental
antigens

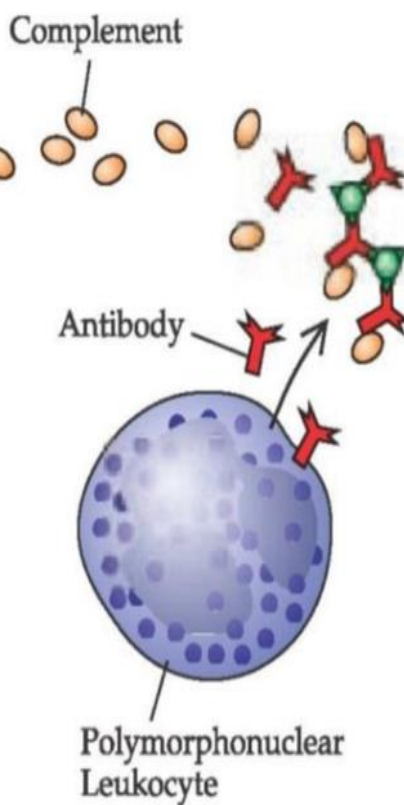
TYPE I



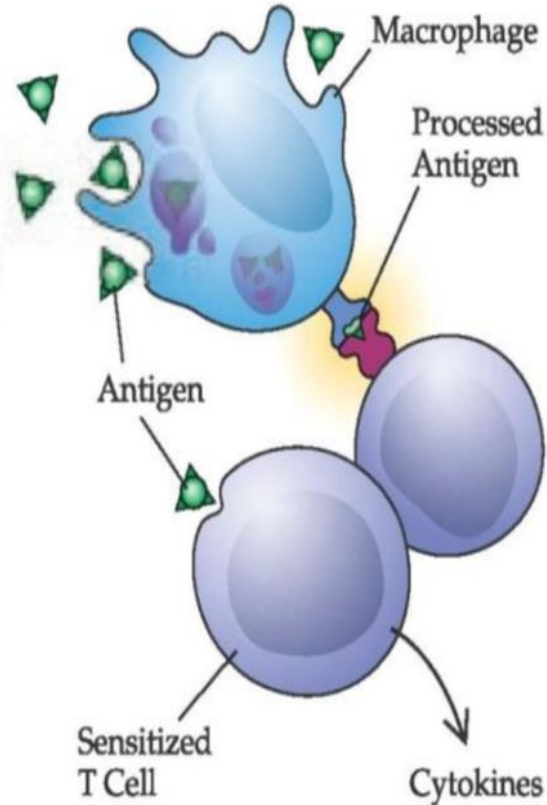
TYPE II

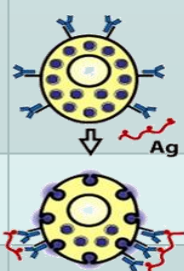
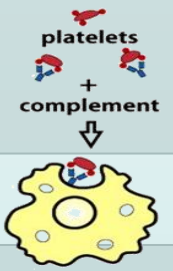
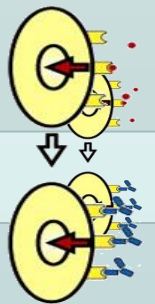
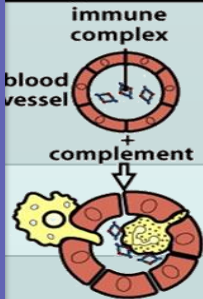
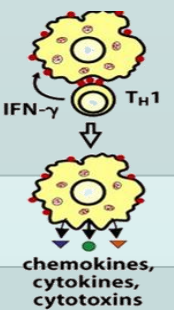
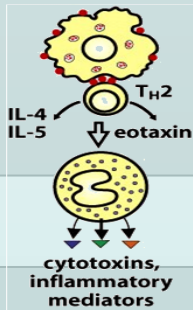

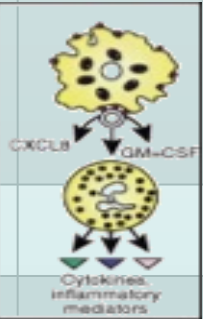


TYPE III



TYPE IV



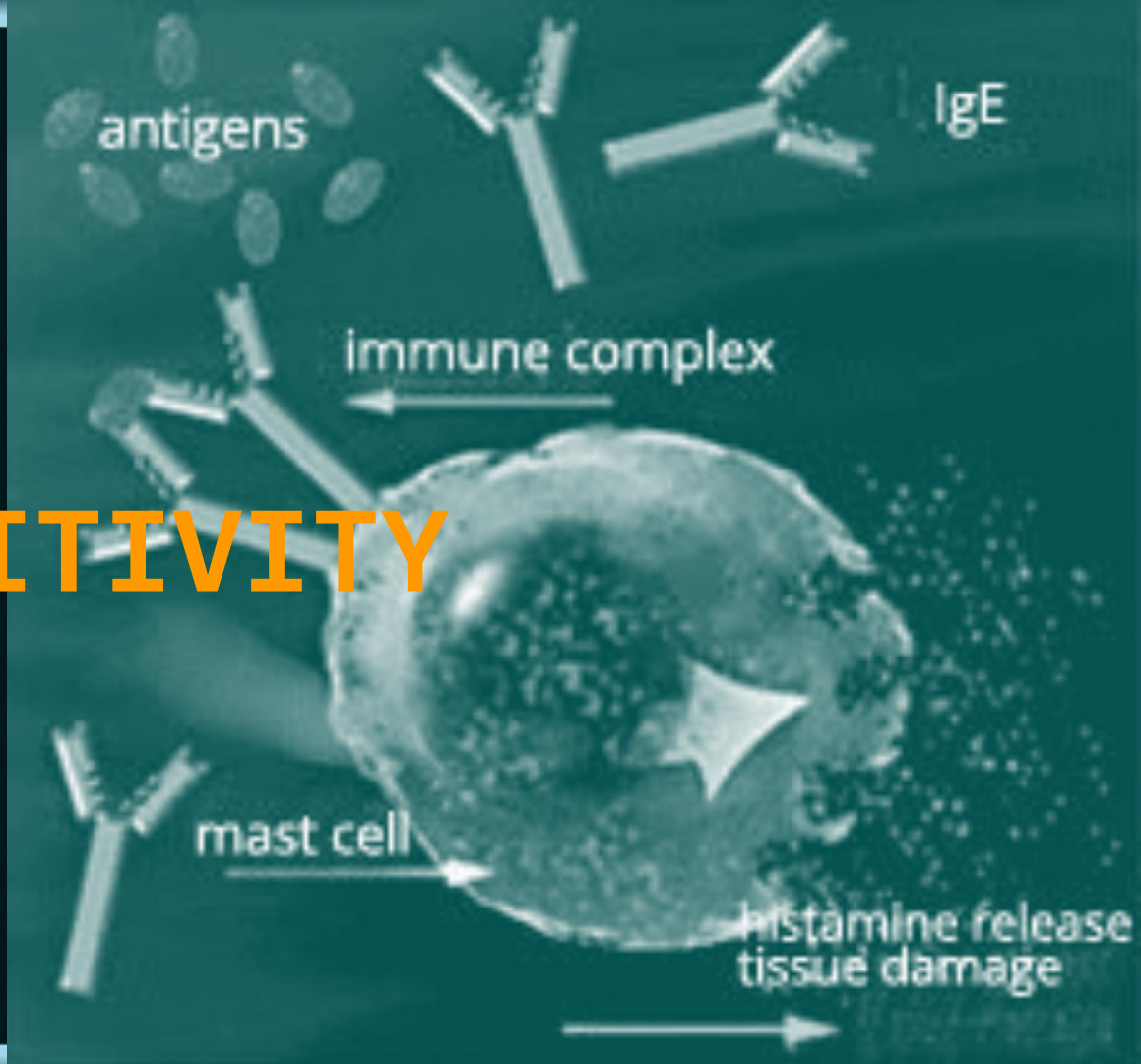
	Type I	Type IIa	Type IIb Type IIc	Type III	Type IVa	Type IVb	Type IVc	Type IVd
Immune reactant	IgE	IgG	IgG	IgG	TH1 cells	TH2 cells	Cytotoxic T cells (CD8+)	TH17 cells
Antigen (Ag)	Soluble Ag	Cell- or matrix-associated Ag	Cell-surface receptor	Soluble Ag	Soluble Ag	Soluble Ag	Cell-associated Ag	Soluble Ag
Effector cells	Mast-cell	Complement, phagocytes, NK cells	Antibody alters signaling (neutralizing/stimulatory)	Complement, phagocytes, immune complex	Macrophage	Eosinophils	T cells	Neutrophils
Diagram								
Example	AR, BA, anaphylaxis	Hemolytic anemia, thrombocytopenia	Chronic urticaria	Serum sickness	CD, Tuberculin reaction	Chronic asthma, chronic AR, MP exanthem with Eo	CD, MP & bullous exanthem, hepatitis	AGEP, Behçet's disease

	Type I	Type IIa	Type IIb Type IIc	Type III	Type IVa	Type IVb	Type IVc	Type IVd
Immune reactant	IgE	IgG	IgG	IgG	TH1 cells	TH2 cells	Cytotoxic T cells (CD8+)	TH17 cells
Antigen (Ag)	Soluble Ag	Cell- or matrix-associated Ag	Cell-surface receptor	Soluble Ag	Soluble Ag	Soluble Ag	Cell-associated Ag	Soluble Ag
Effector cells	Mast-cell	Complement, phagocytes, NK cells	Antibody alters signaling (neutralizing or stimulatory)	Complement, phagocytes, immune complex	Macrophage	Eosinophils	T cells	Neutrophils
Example	AR, BA, anaphylaxis	Hemolytic anemia, thrombocytopenia	Chronic urticaria	Serum sickness	CD, Tuberculin reaction	Chronic asthma, chronic AR, MP exanthem with Eo	CD, MP & bullous exanthem, hepatitis	AGEP, Behçet's disease

Revised from Janeway's Immunobiology 2008 & Middleton's Allergy 2009

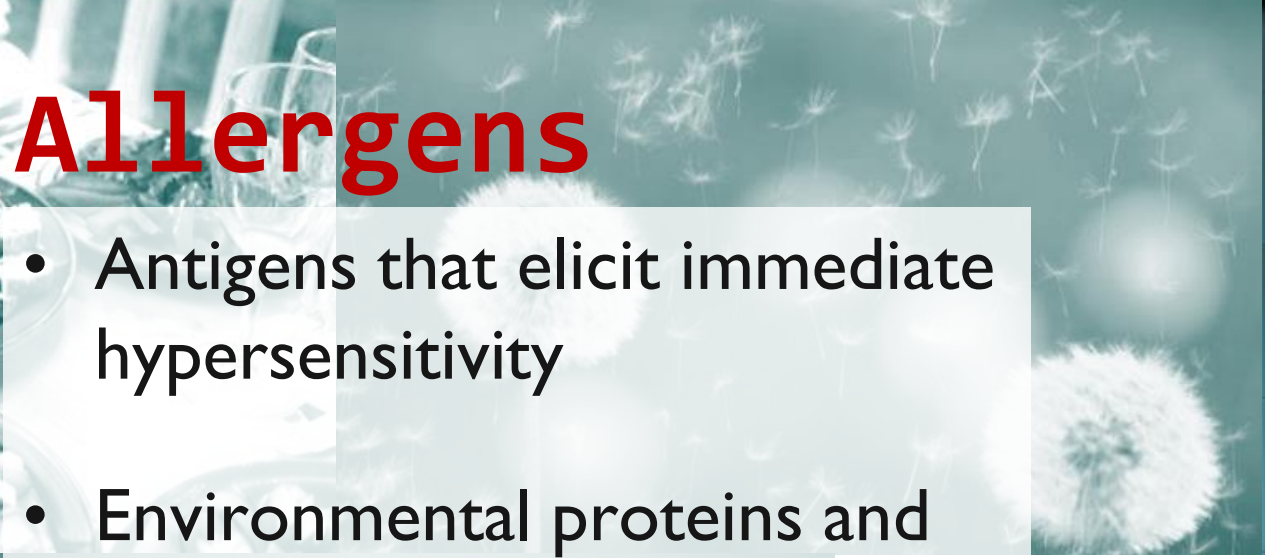
TYPE I: IMMEDIATE HYPERSENSITIVITY

IgE-mediated



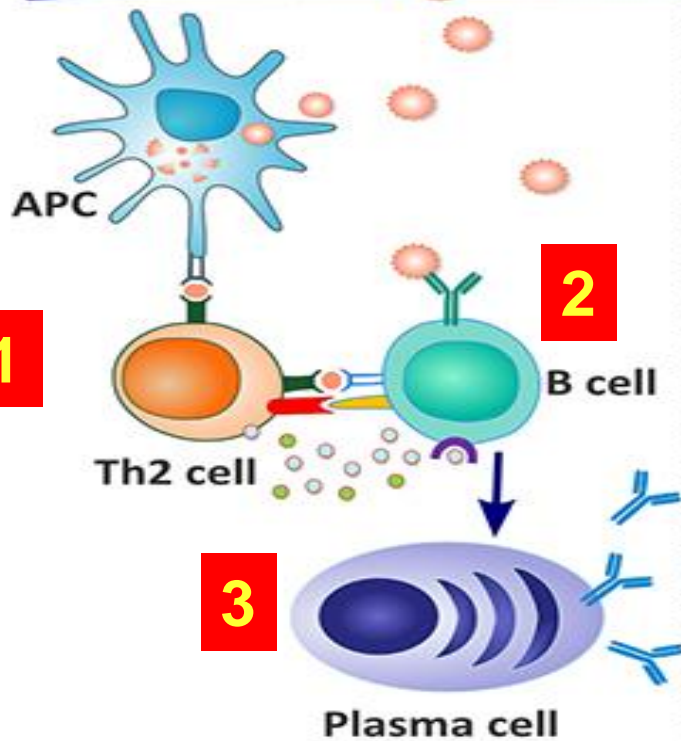
Allergens

- Antigens that elicit immediate hypersensitivity
- Environmental proteins and chemicals



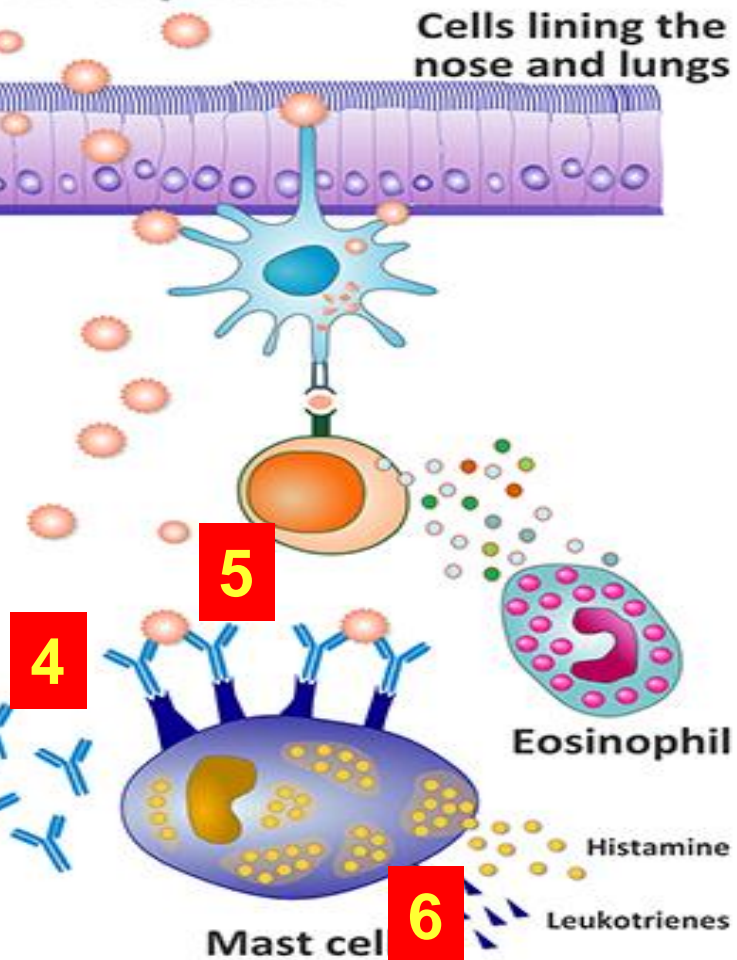
Sensitization

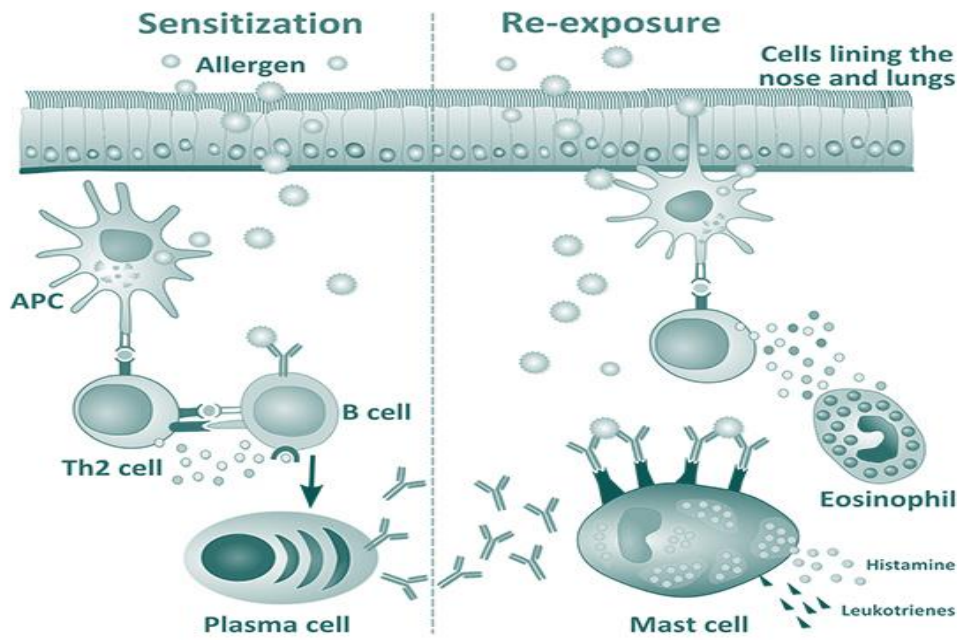
Allergen



Re-exposure

Cells lining the nose and lungs



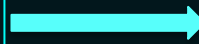


**Vasoactive amines,
Lipid mediators**



**Immediate
Hypersensitivity Reaction**
(minutes after repeat
exposure to allergen)

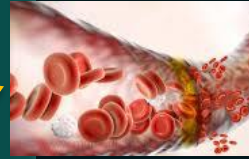
Cytokines



Late Phase Reaction
(2-4 hours after repeat
exposure to allergen)

Biologic Effects

Biogenic amines
(histamine)
Lipid mediators
(PAF, PGD₂, LTC₄)



Vascular leak

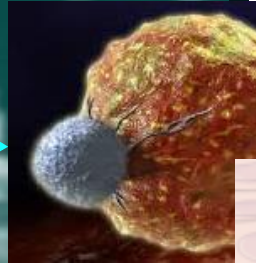


Broncho-
constriction



Intestinal
hypermotility

Cytokines
(TNF)
Lipid mediators
(PAF, PGD₂, LTC₄)



Inflammation

Enzymes
(tryptase)



Tissue
damage

**Immediate
Reaction**

**Late-phase
Reaction**



hives



itching



**wheezing or
shortness of breath**

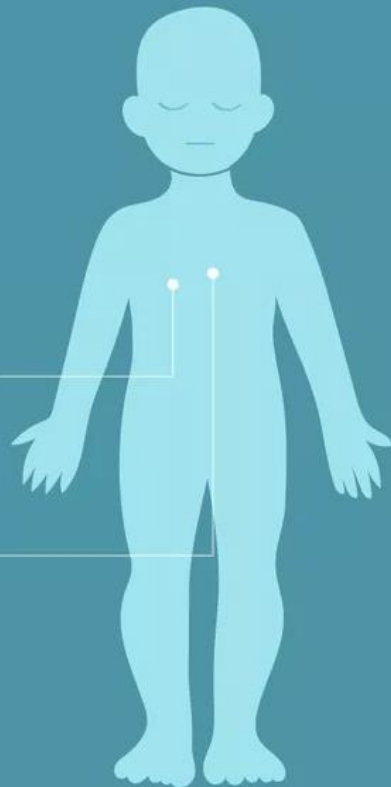


**low blood
pressure**



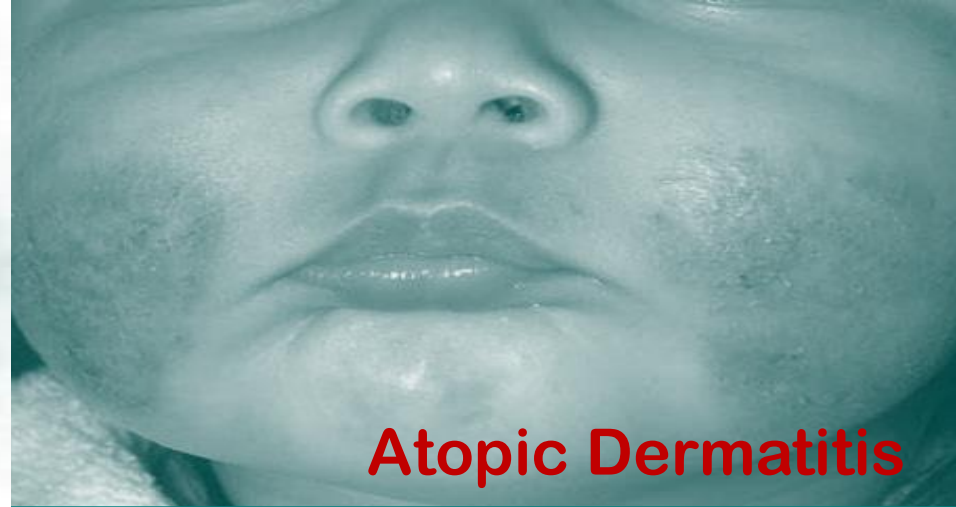
pale skin color

Anaphylaxis





Allergic Rhinitis



Atopic Dermatitis



Bronchial Asthma



Urticaria

Diagnostic Tests

- **Anaphylaxis**
 - Diagnosis is mostly clinical
 - Histamine
 - Total Tryptase

Allergy Tests

- Adjuncts to thorough exposure history that indicates the presence of relevant IgE-mediated symptoms or signs & the physical exam



Skin Allergy Test

<http://bit.ly/PAwuN>

In Vivo Allergy Skin Test

- Mast cell degranulation
- Skin exposed to specific allergens
- Wheal & flare reaction
- Documentation of allergic sensitivity to specific allergens

In Vitro Testing of Total Serum IgE

- Identify persons with high likelihood of atopy
- Not a diagnostic or screening test on its own
- Measures total circulating IgE
- Variations of levels with age

Antigen-Specific IgE

- ELISA
- Quantitatively measures IgE antibodies to specific allergens

<http://bit.ly/OnFiFA>

Management

Pharmacologic

Non-pharmacologic

Immunotherapy

Antihistamines
Antileukotrienes

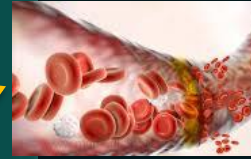
Biogenic amines
(histamine)
Lipid mediators
(PAF, PGD_2 , LTC_4)

Bronchodilators

Cytokines
(TNF)
Lipid mediators
(PAF, PGD_2 , LTC_4)

Steroids

Enzymes
(tryptase)



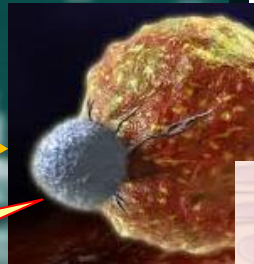
Vascular leak



**Broncho-
constriction**



**Intestinal
hypermotility**



Inflammation



**Tissue
damage**

**Immediate
Reaction**

**Late-phase
Reaction**

Management

Epinephrine IM

0.01 mg/kg of a 1 mg/ml
(1:1000) aqueous dilution

Adults: 0.5 mg maximum

Children: 0.3 mg maximum



Management

Pharmacologic

Non-pharmacologic

Immunotherapy

Avoid your allergens



Management

Pharmacologic

Non-pharmacologic

Immunotherapy

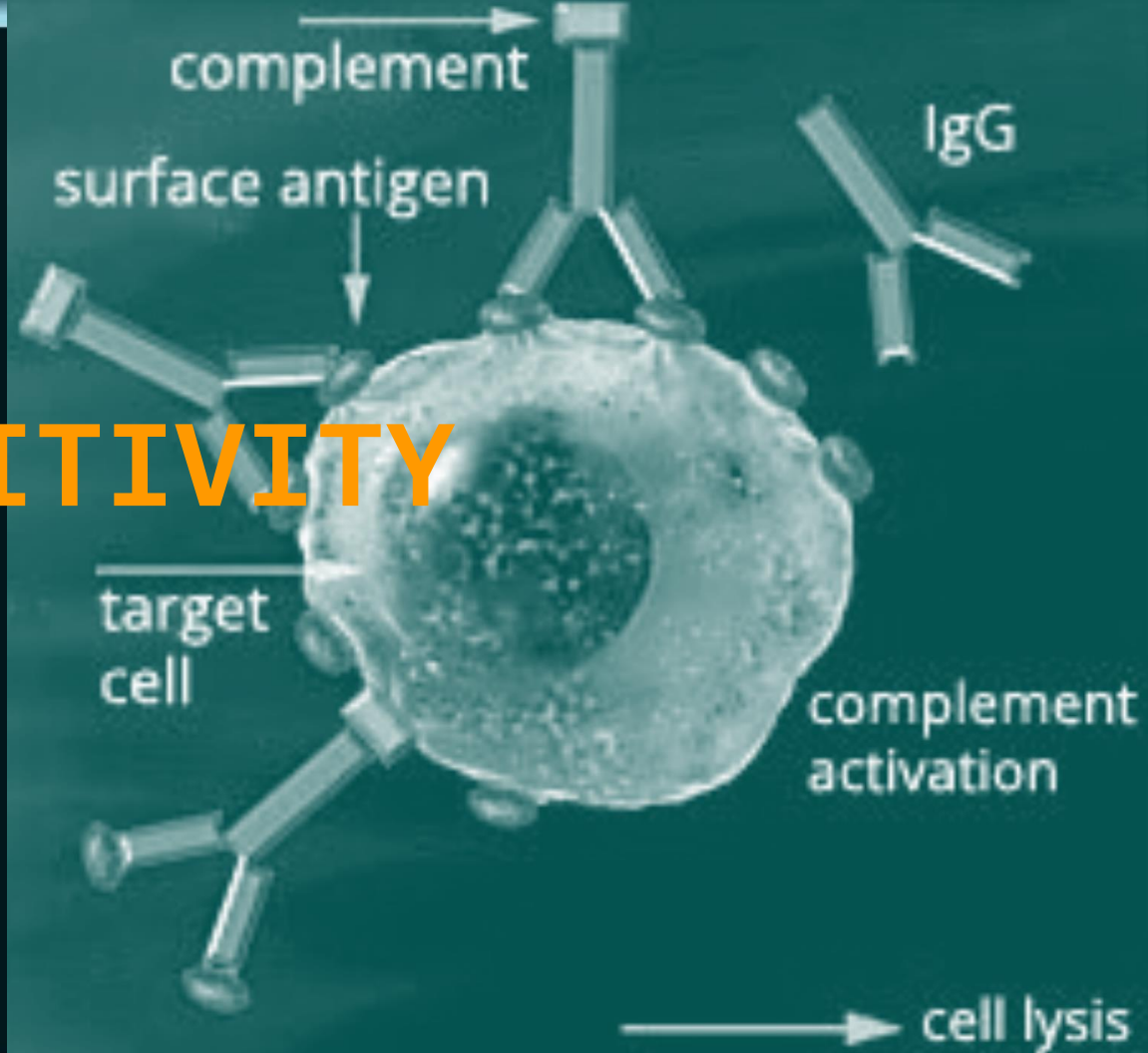


Immunotherapy

- For IgE-mediated reactions
- Induce a shift from TH2 to TH1 reactions

TYPE II HYPERSENSITIVITY

IgG Antibody
Mediated



Antibody-Mediated Diseases

- Produced by antibodies that bind to antigens
 - cells or extracellular tissues
- Often not systemic
- Usually autoantibodies

Mechanisms of Antibody-Mediated Diseases

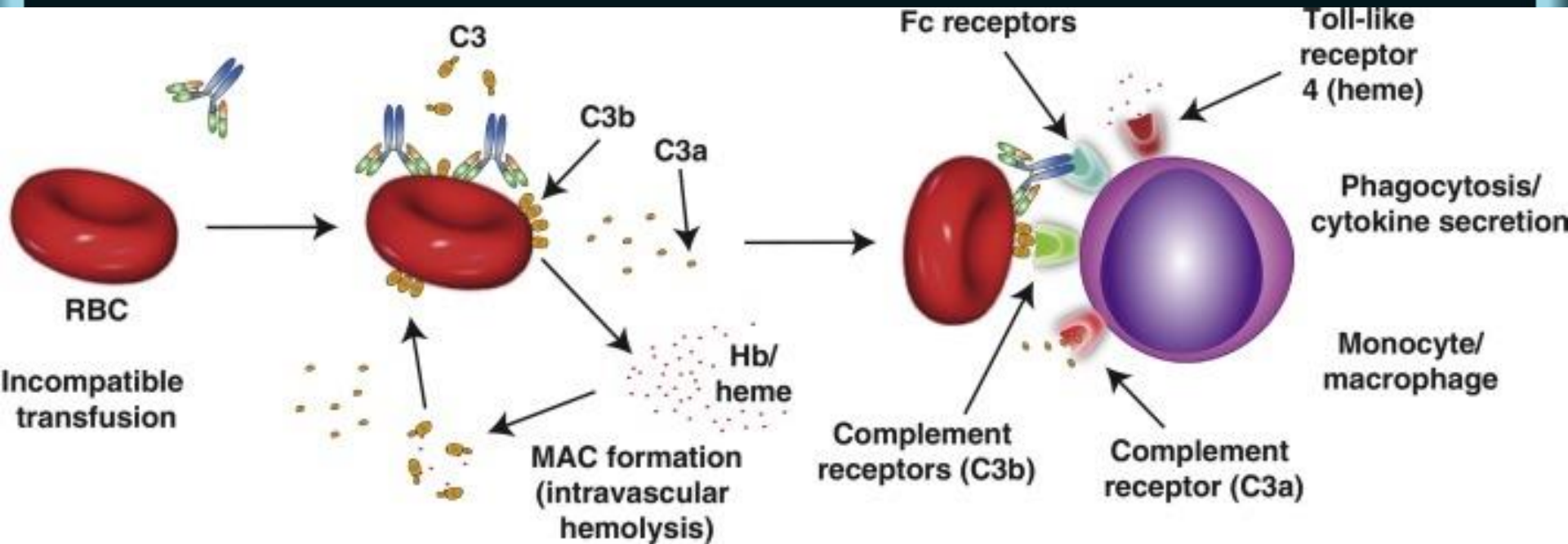
A. Cytolytic (*Type IIa*)

- Opsonization and phagocytosis
- Complement- and Fc receptor-mediated Inflammation

B. Abnormal physiologic responses without cell/tissue injury

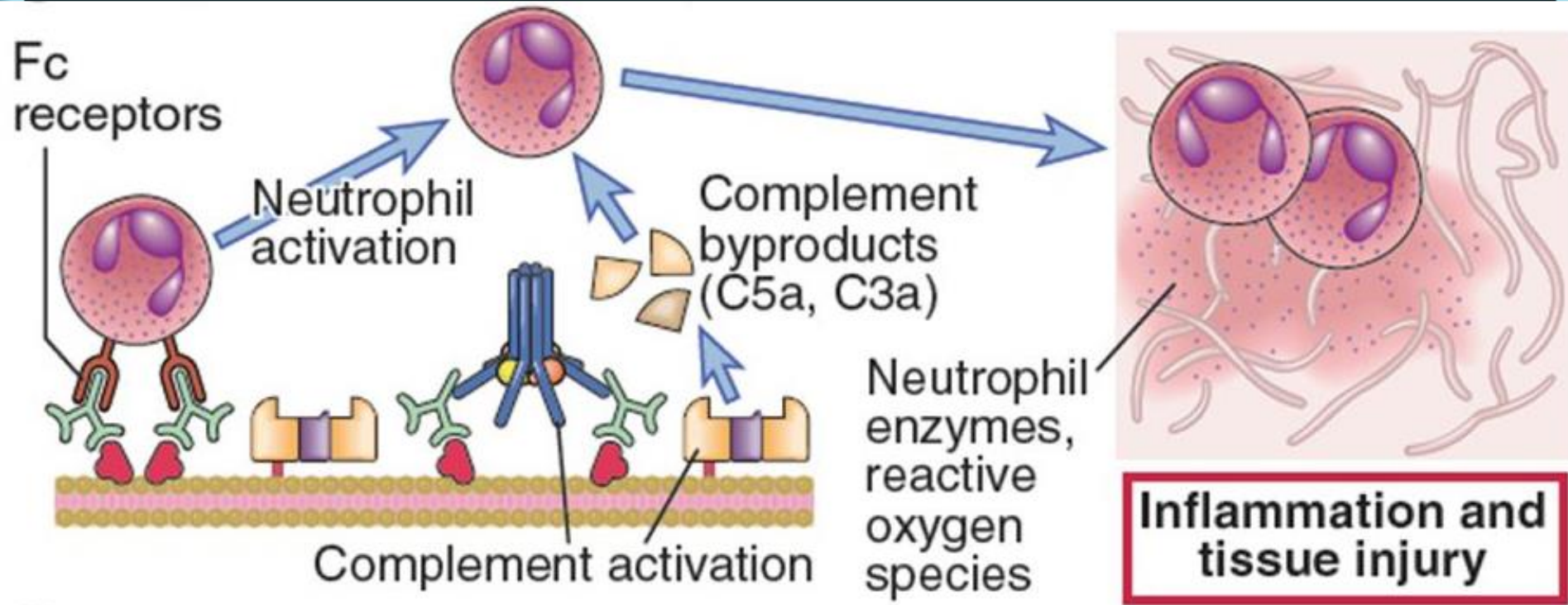
- Neutralizing (*Type IIb*)
- Stimulatory (*Type IIc*)

Opsonization and Phagocytosis



- Autoimmune hemolytic anemia
- Autoimmune thrombocytopenic purpura
- Hemolysis in transfusion reactions

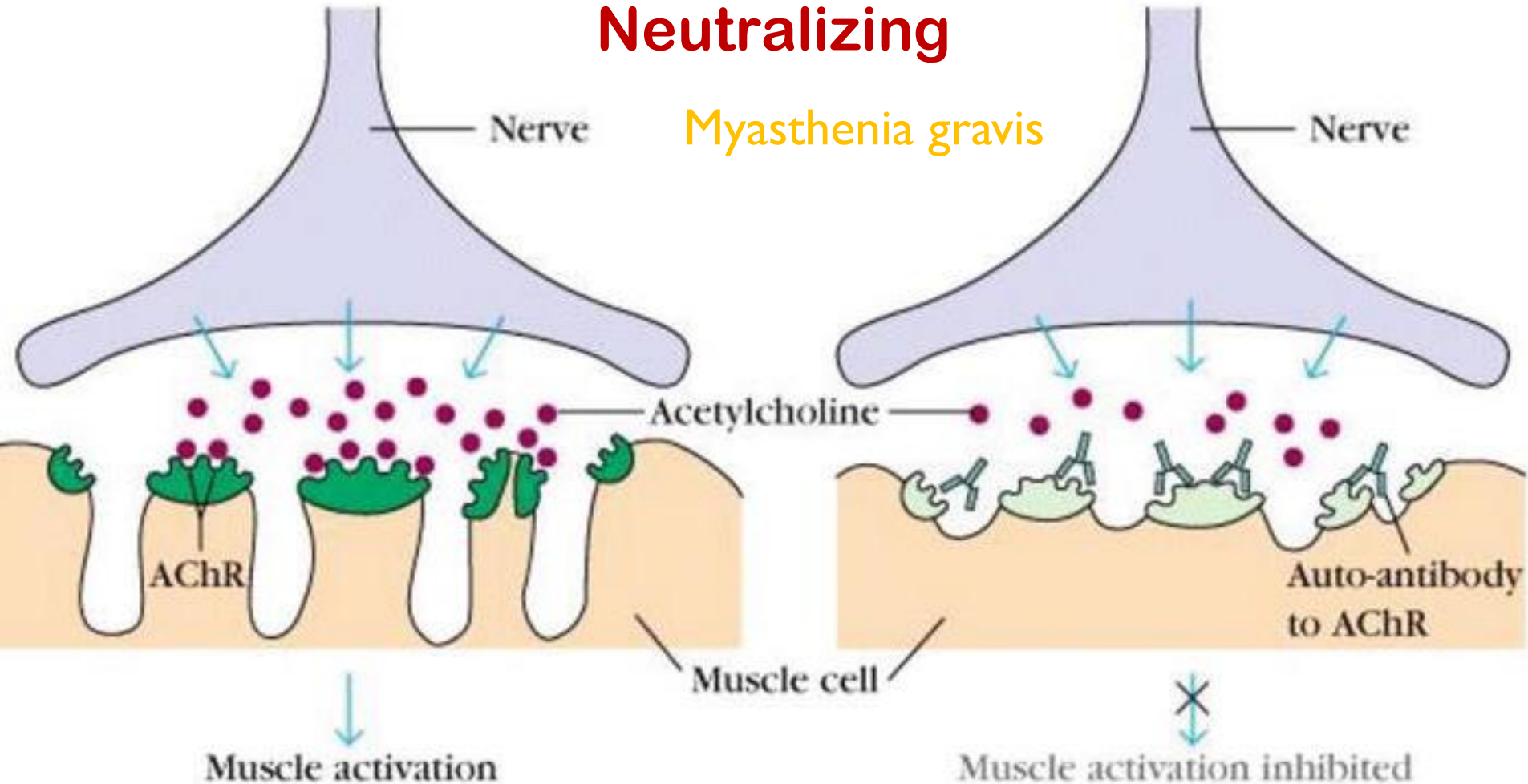
Complement- and Fc receptor-Mediated Inflammation



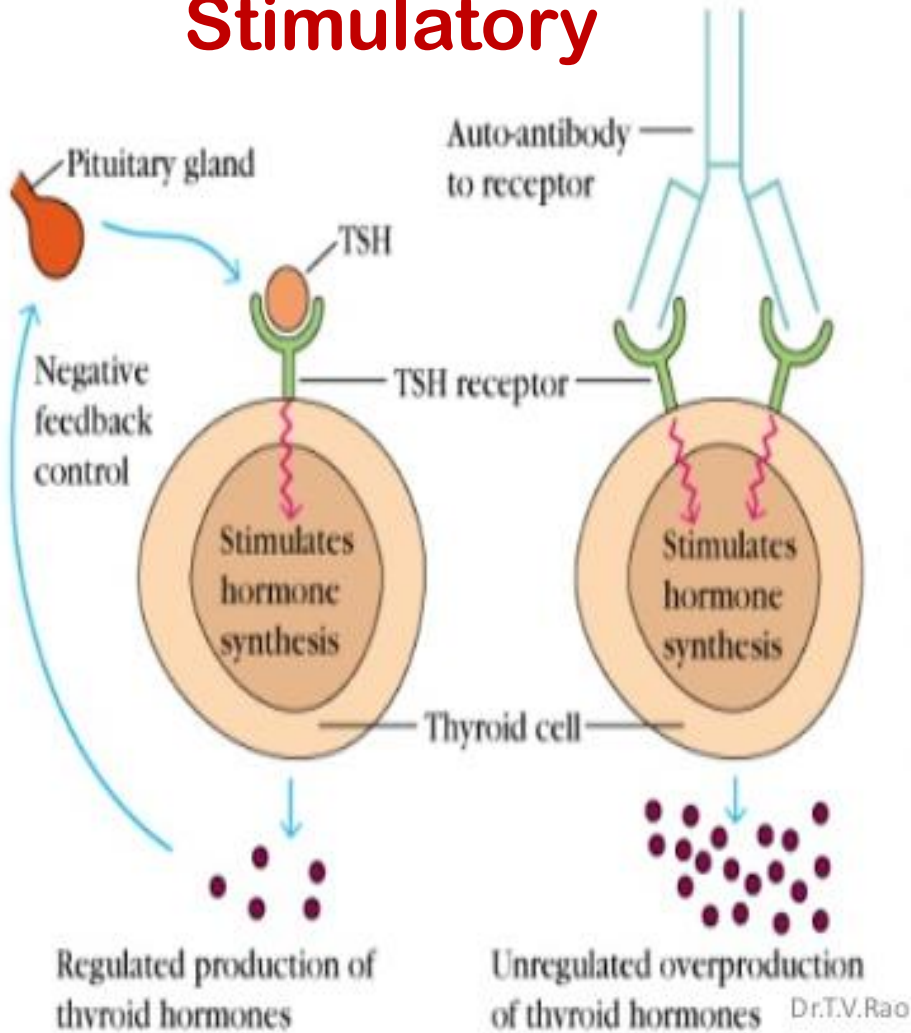
- Antibody-mediated glomerulonephritis (Goodpasture syndrome)

Neutralizing

Myasthenia gravis

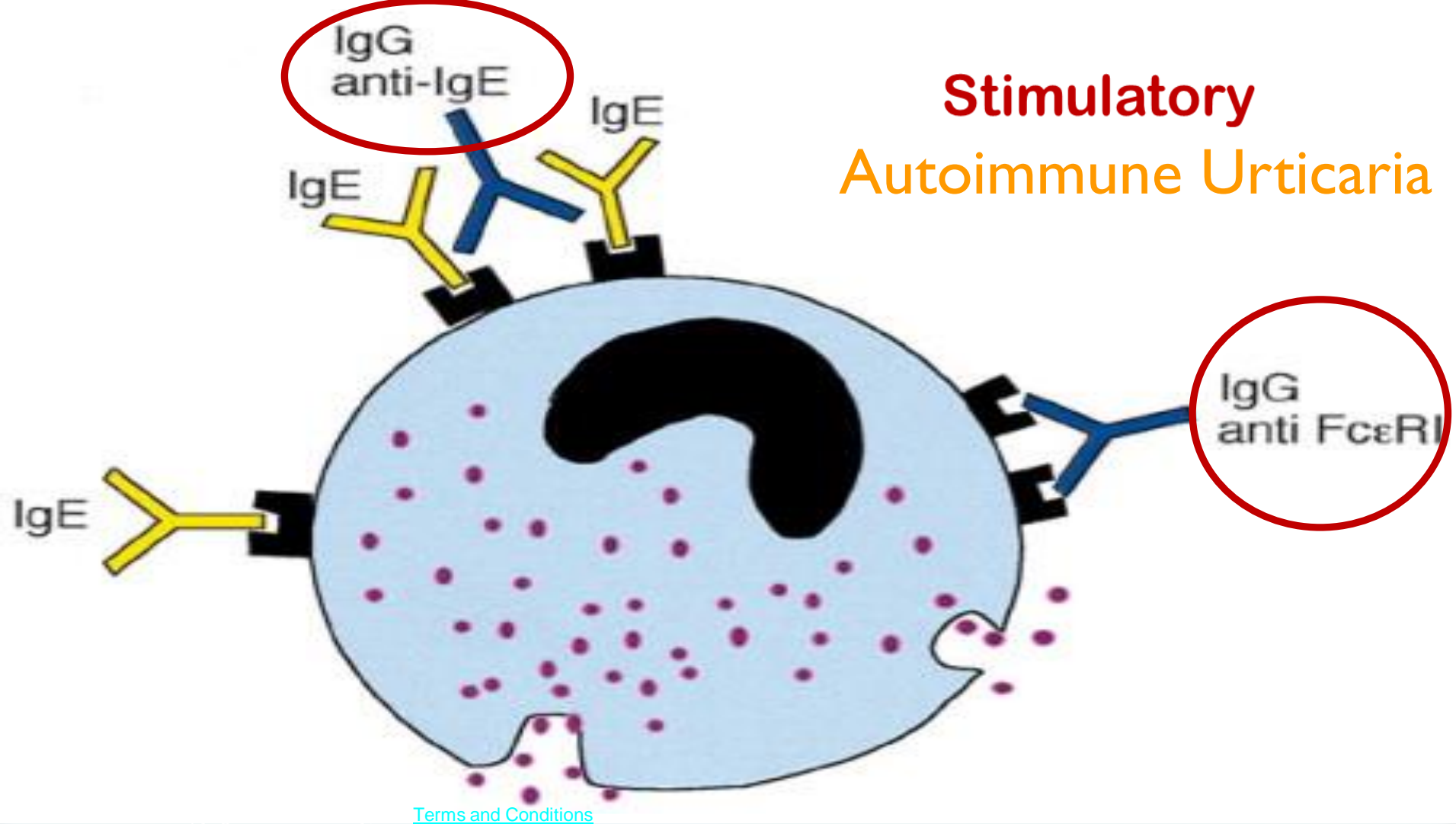


Stimulatory



Graves' disease

Stimulatory Autoimmune Urticaria



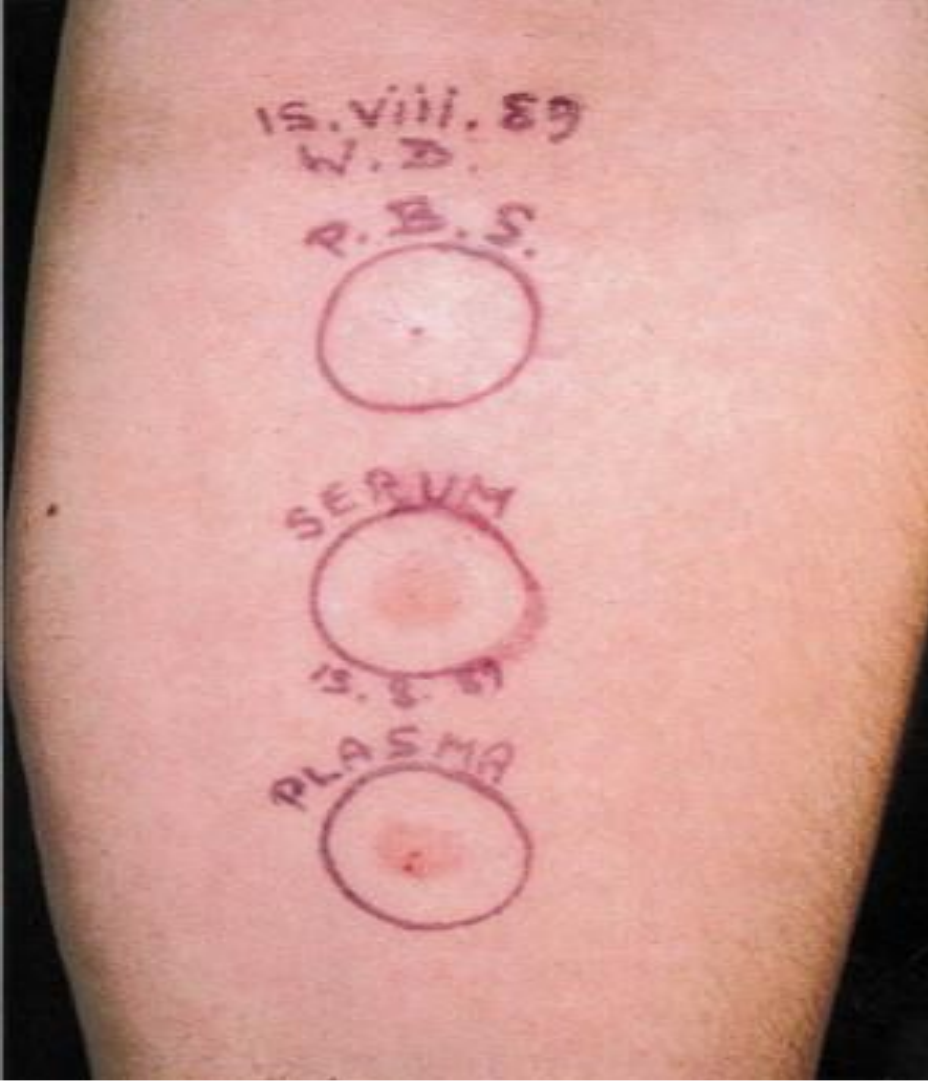
Stimulatory

Autoimmune Urticaria



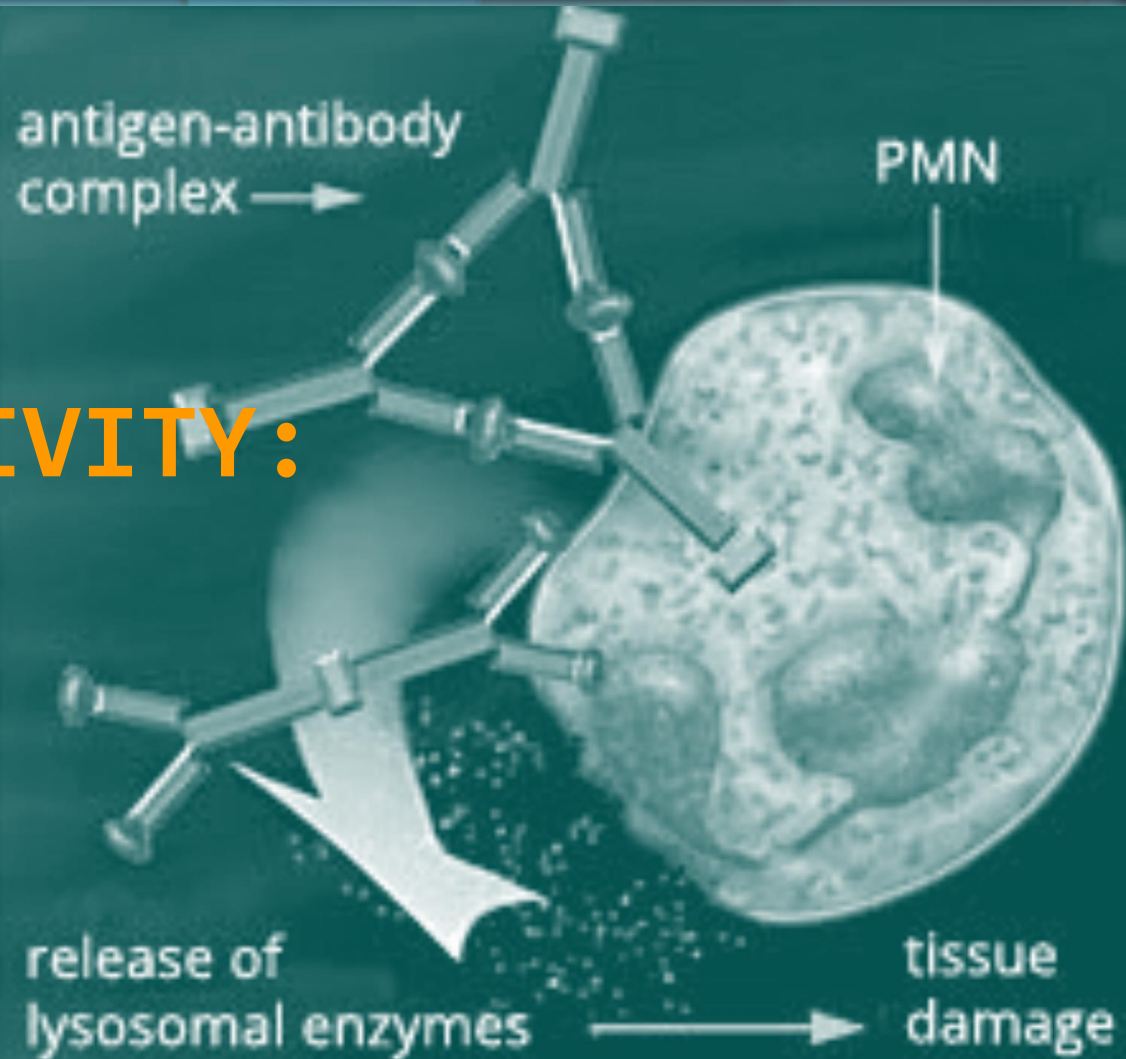
Autoimmune Urticaria

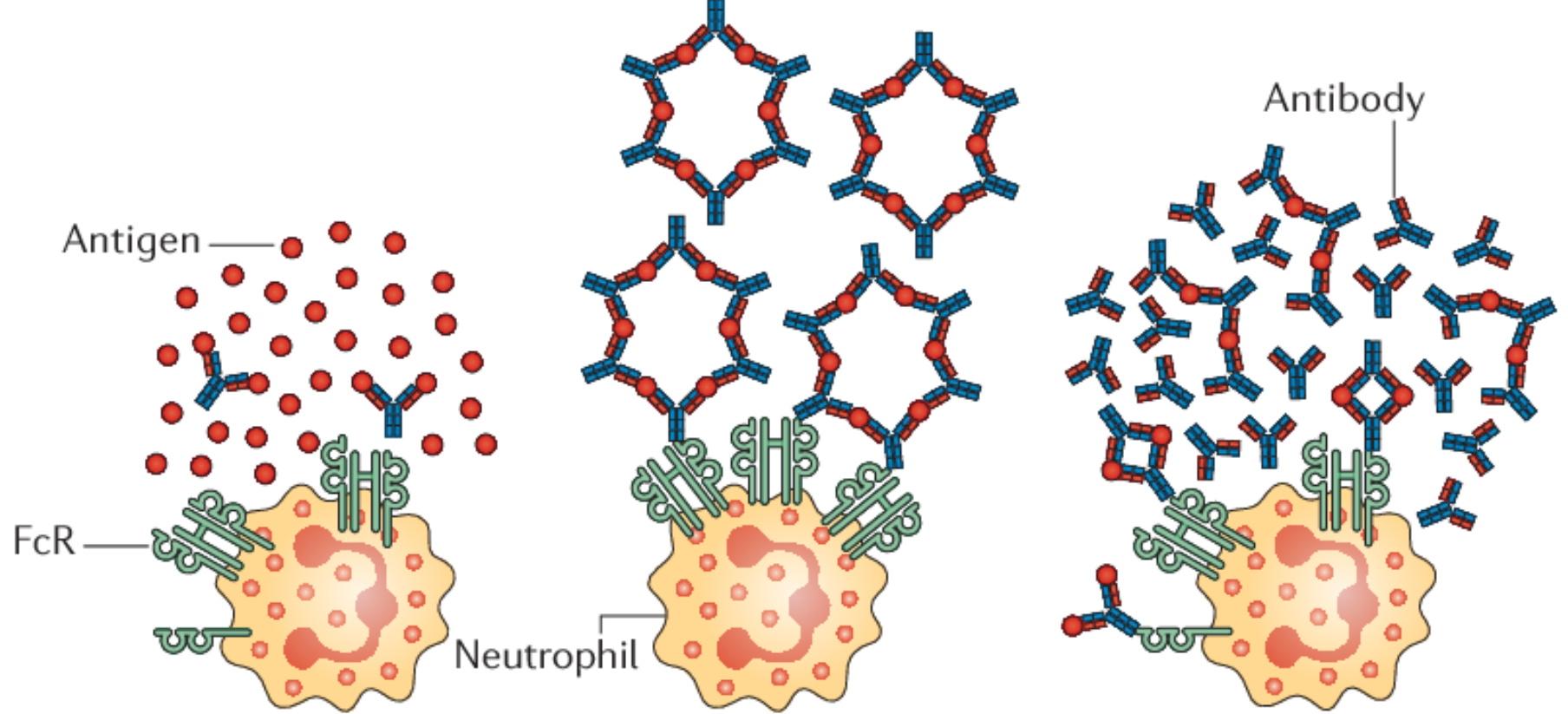
Autologous
serum- plasma
skin test



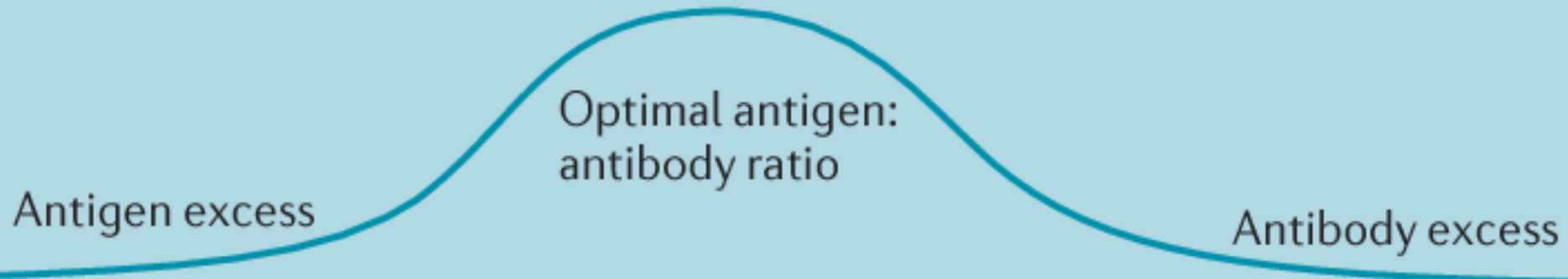
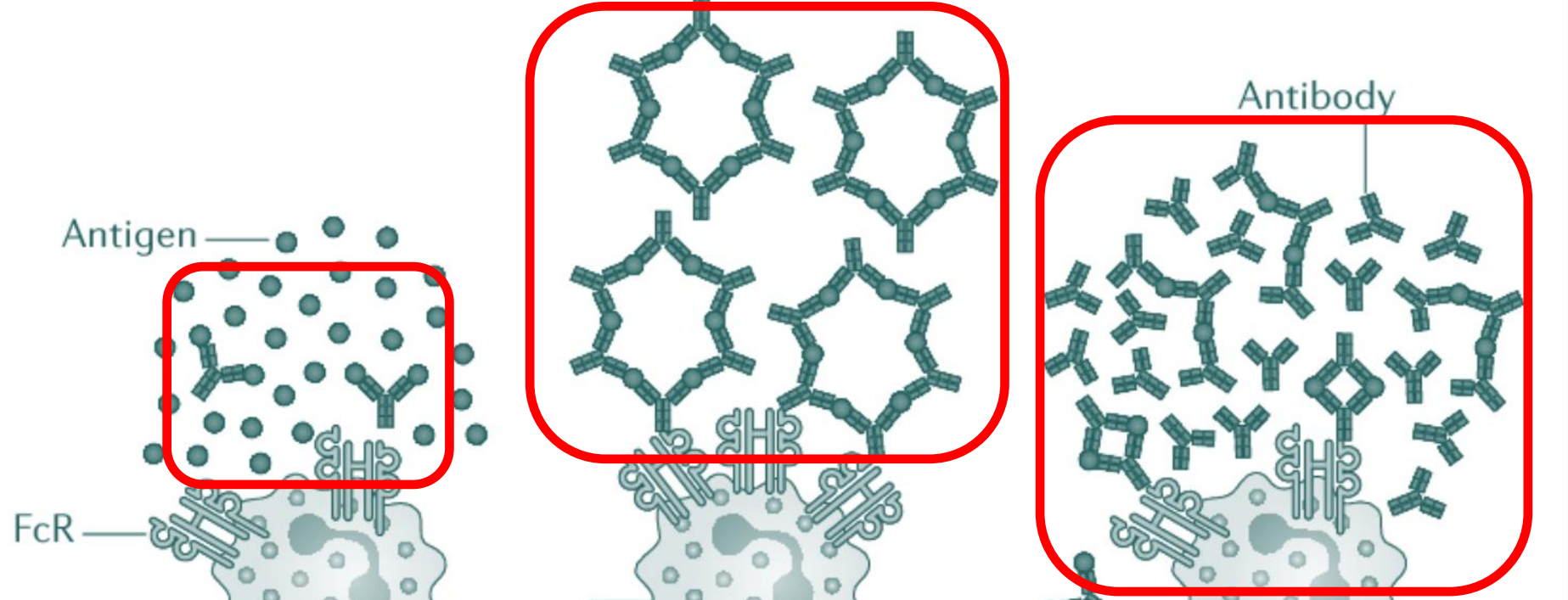
TYPE III HYPERSENSITIVITY:

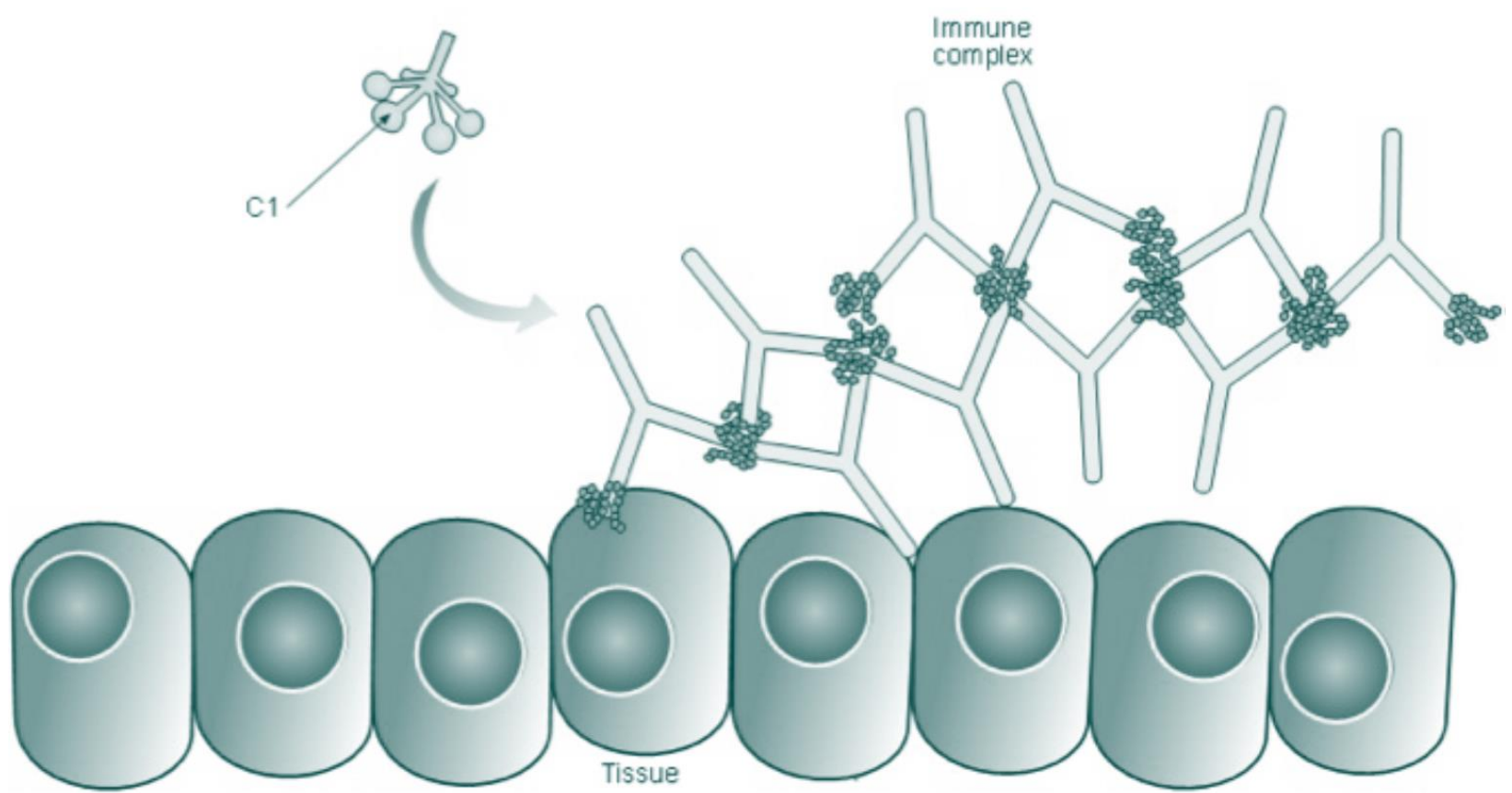
Immune Complex
Mediated



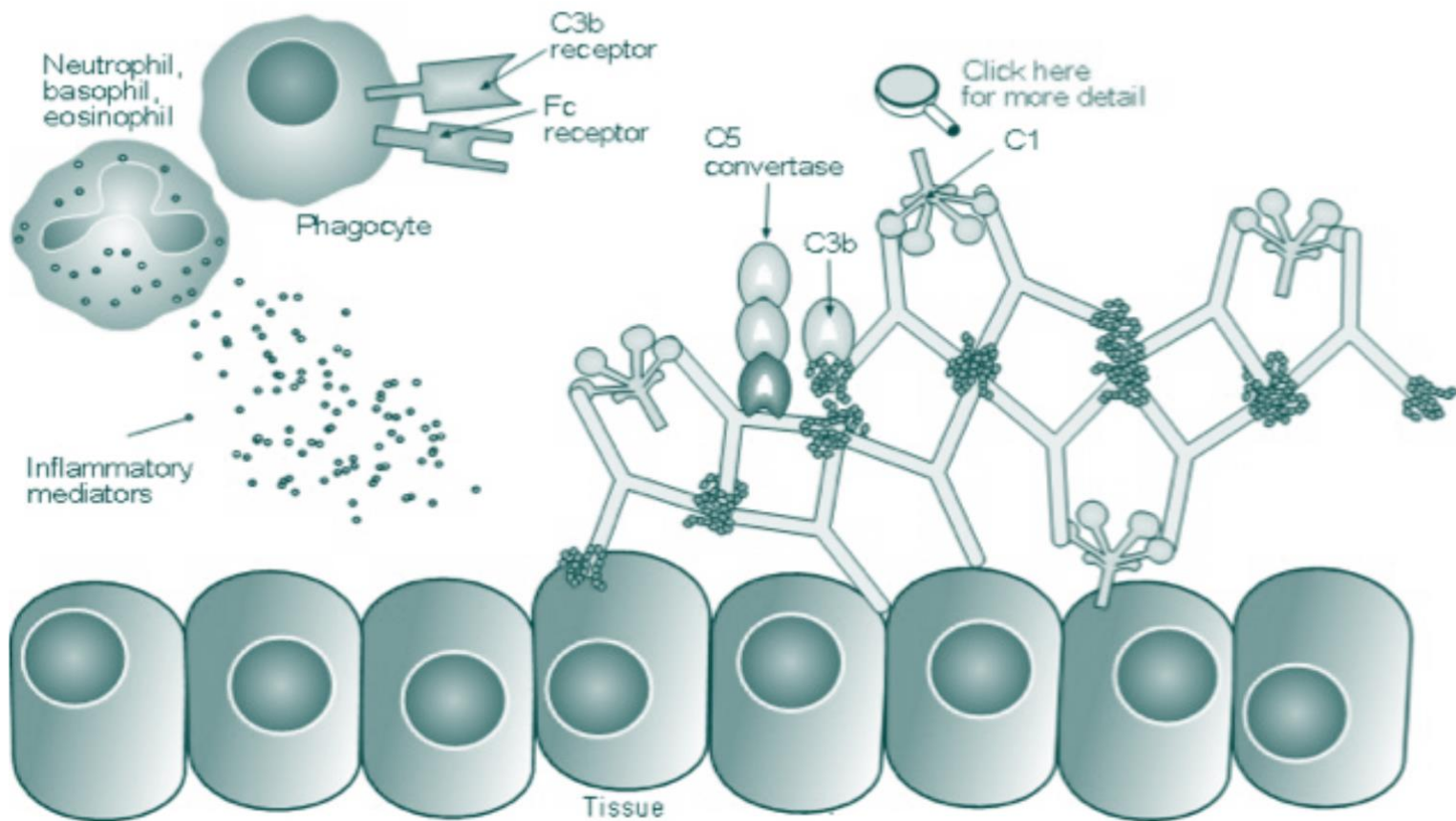


Immune Complex Formation





Deposition of Circulating Immune Complexes



Deposition of Circulating Immune Complexes

Type III Diseases

A. Local

- Arthus reaction
- Pneumonitis

B. Systemic

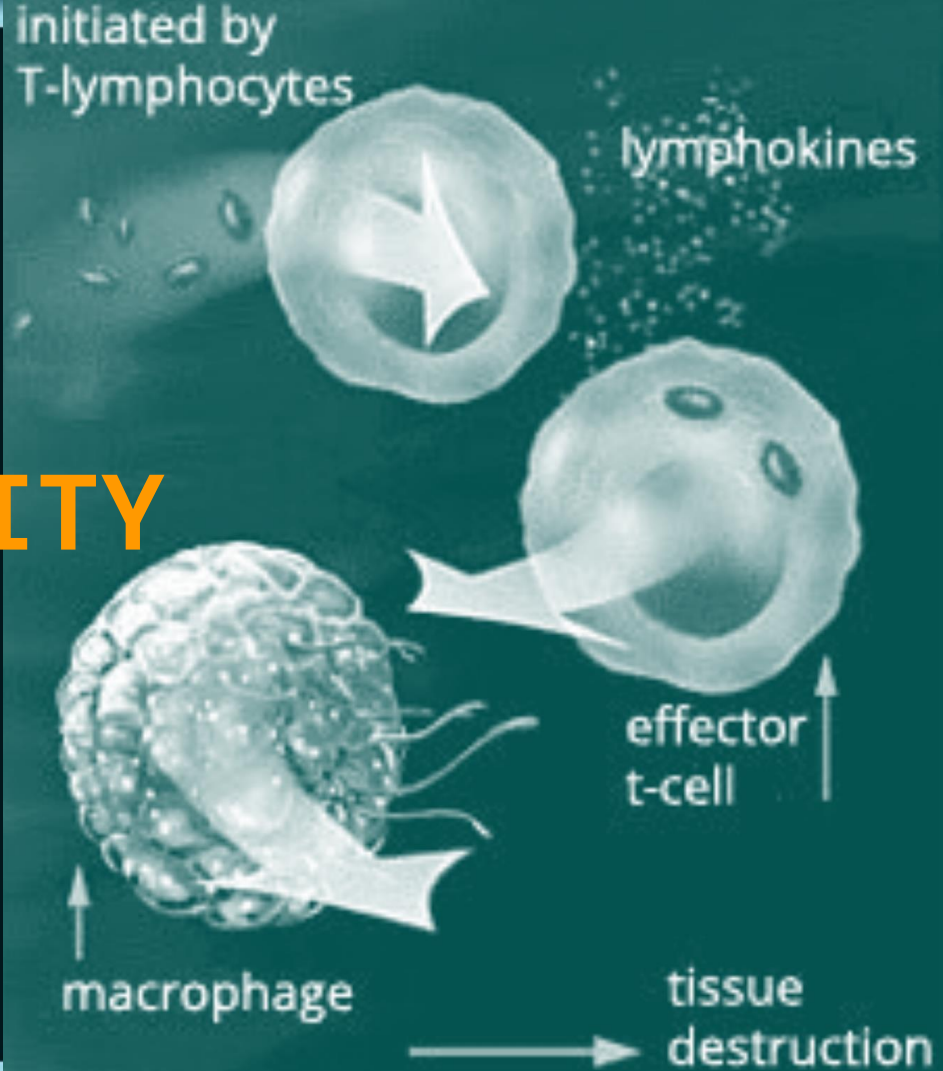
- Serum sickness
- SLE
- Post-streptococcal glomerulonephritis
- Vasculitis
 - Polyarteritis nodosa in chronic hepatitis B

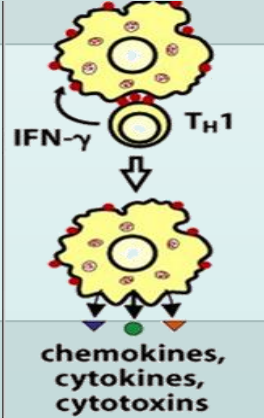
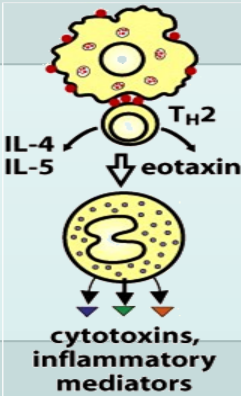
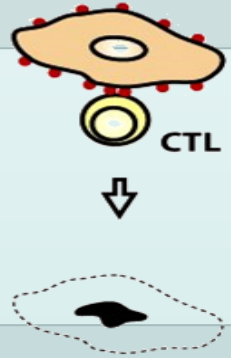
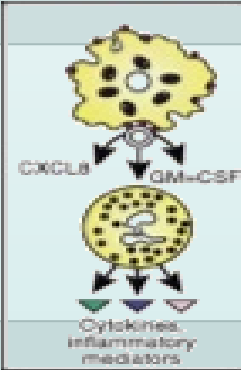
Management

- Remove the offending agent
- Anti-inflammatory agents
- Monoclonal anti-C5 antibody
- Intravenous immunoglobulin (IVIg)
 - In ITP
- Rituximab (anti-CD20 antibody)

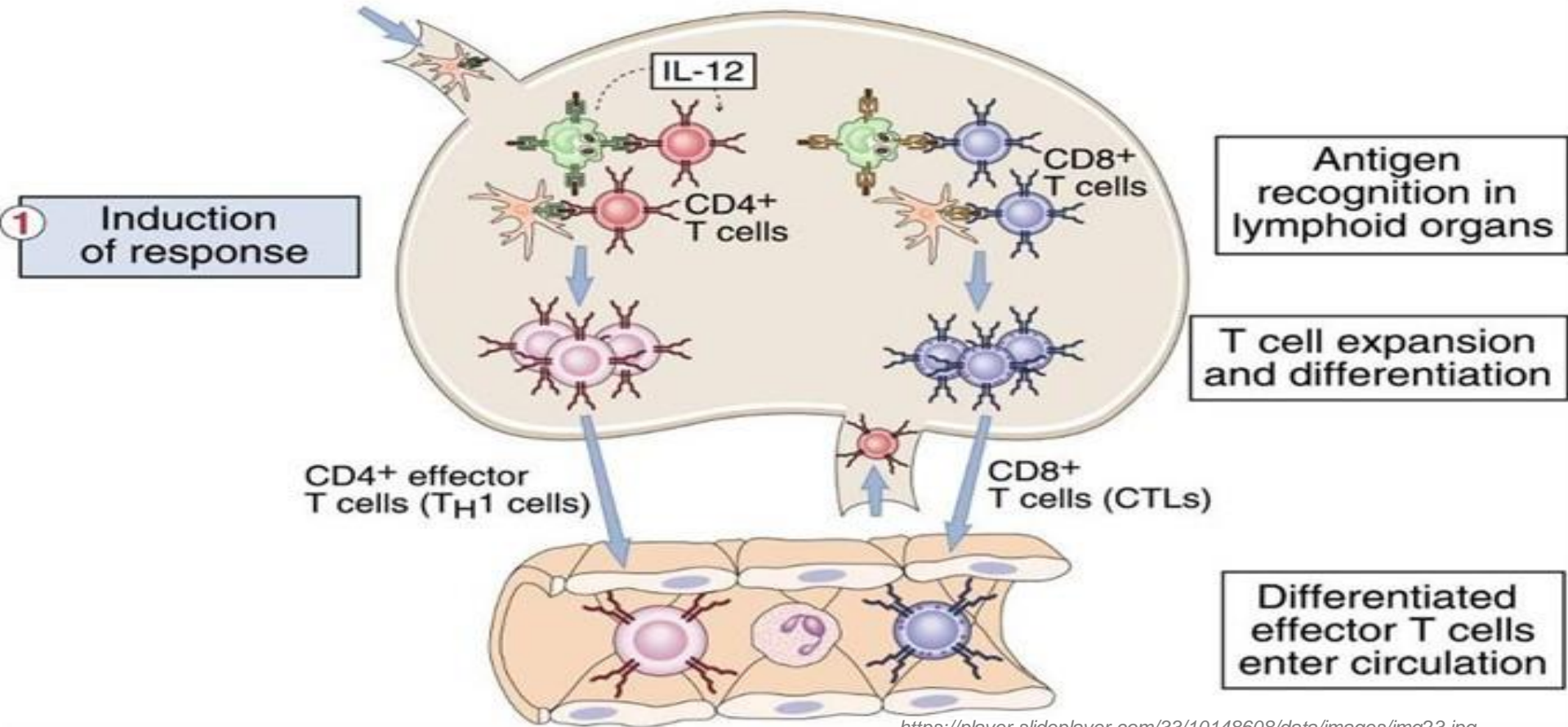
TYPE IV: DELAYED HYPERSENSITIVITY

T Cell-mediated

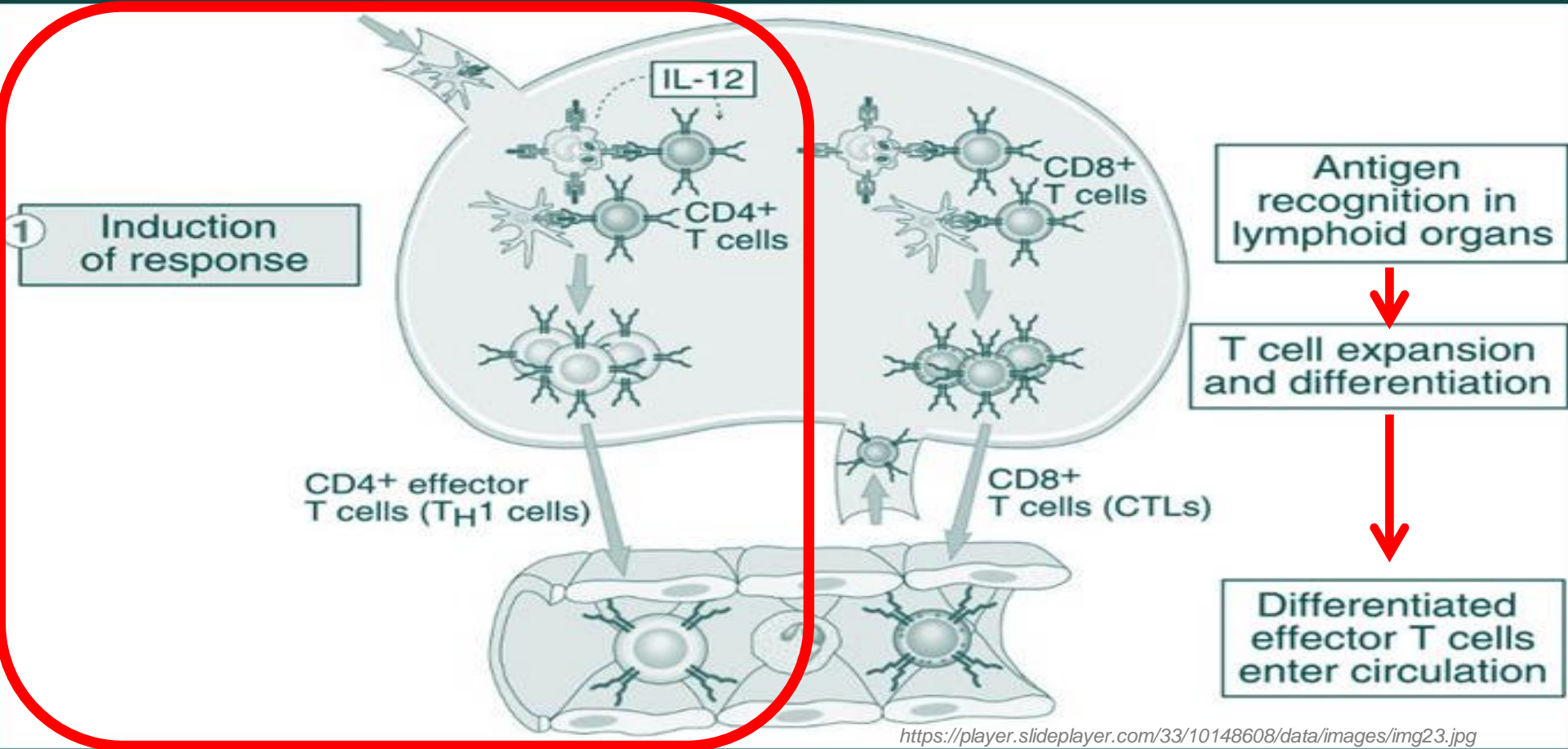


	Type IVa	Type IVb	Type IVc	Type IVd
Immune reactant	TH1 cells	TH2 cells	Cytotoxic T cells (CD8+)	TH17 cells
Antigen (Ag)	Soluble Ag	Soluble Ag	Cell-associated Ag	Soluble Ag
Effector cells	Macrophage	Eosinophils	T cells	Neutrophils
	 <p>chemokines, cytokines, cytotoxins</p>	 <p>cytotoxins, inflammatory mediators</p>		 <p>Cytokines, inflammatory mediators</p>
Example	CD, Tuberculin reaction	Chronic asthma, chronic AR, MP exanthem with Eo	CD, MP & bullous exanthem, hepatitis	AGEP, Behçet's disease

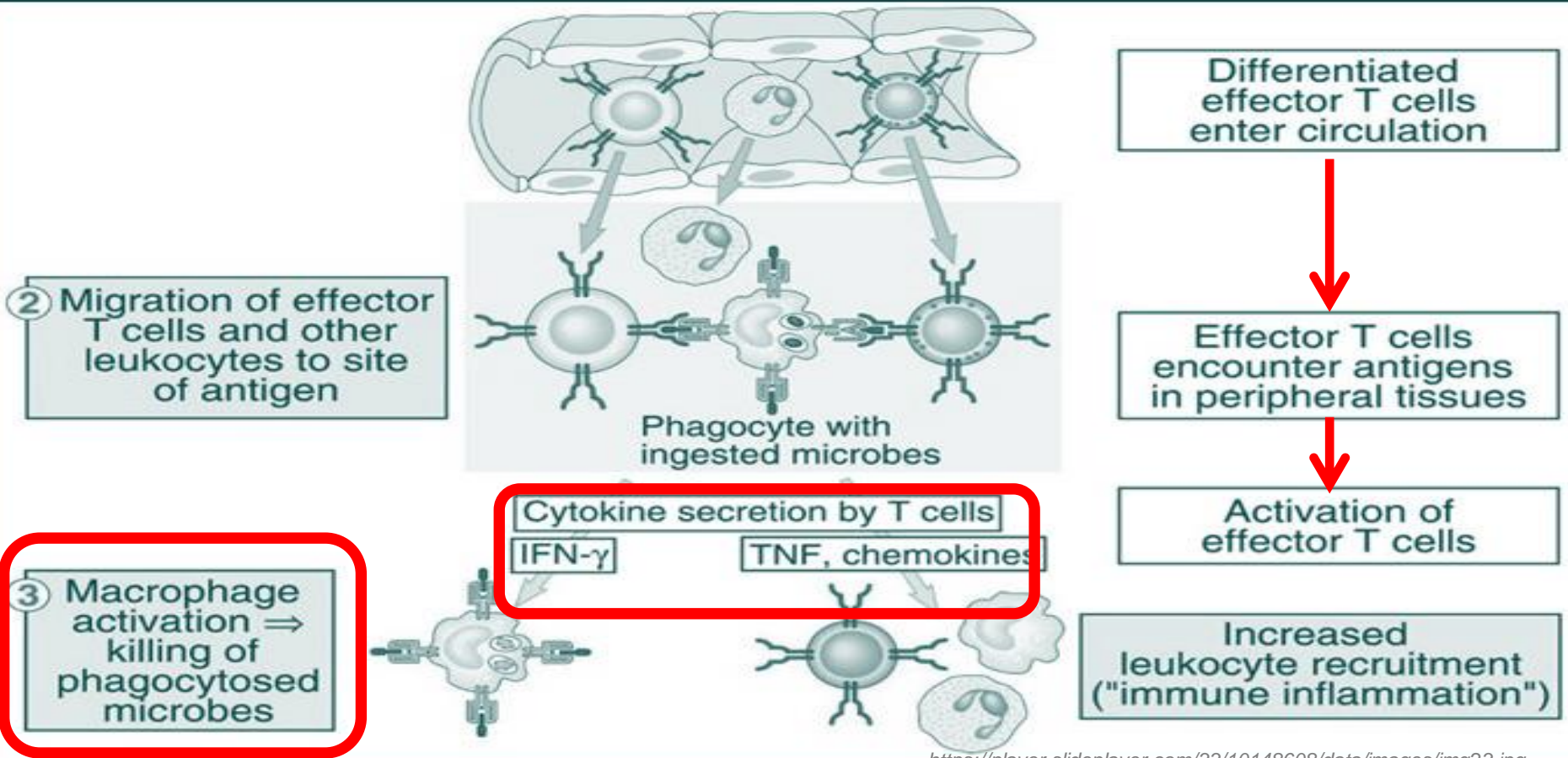
Th1 cell-mediated



Th1 cell-mediated



Th1 cell-mediated



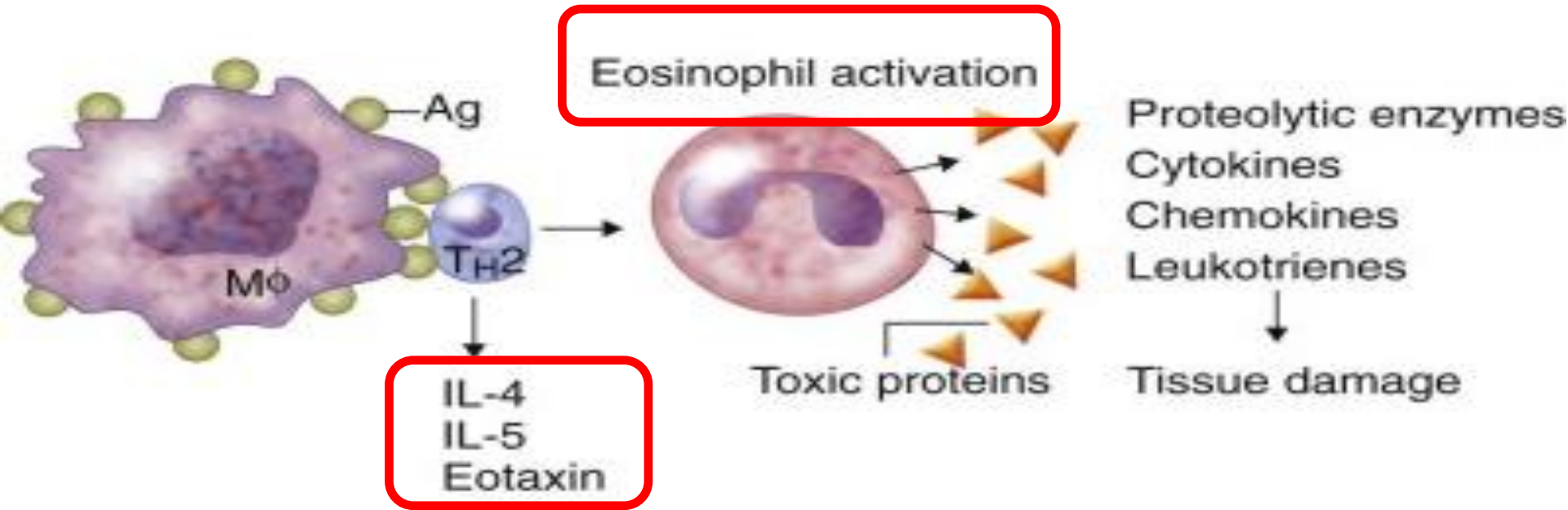


Contact Dermatitis

Tuberculin reaction



Th2 cytokine-mediated



<https://ars.els-cdn.com/content/image/3-s2.0-B9781437716047000464-f046-004-9781437716047.jpg>



Chronic Allergic Rhinitis



Atopic Dermatitis

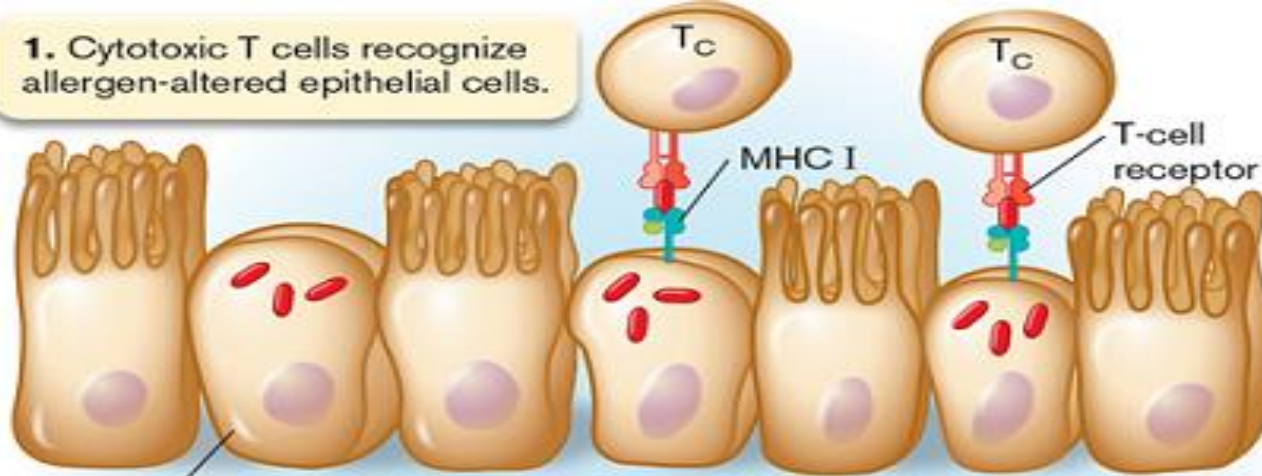


Chronic Asthma

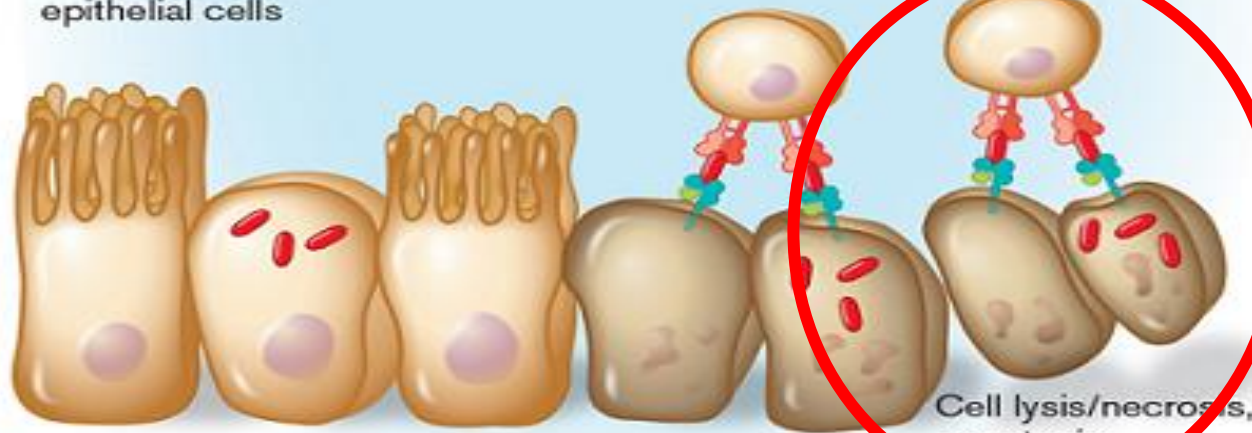


Maculopapular exanthem

1. Cytotoxic T cells recognize allergen-altered epithelial cells.



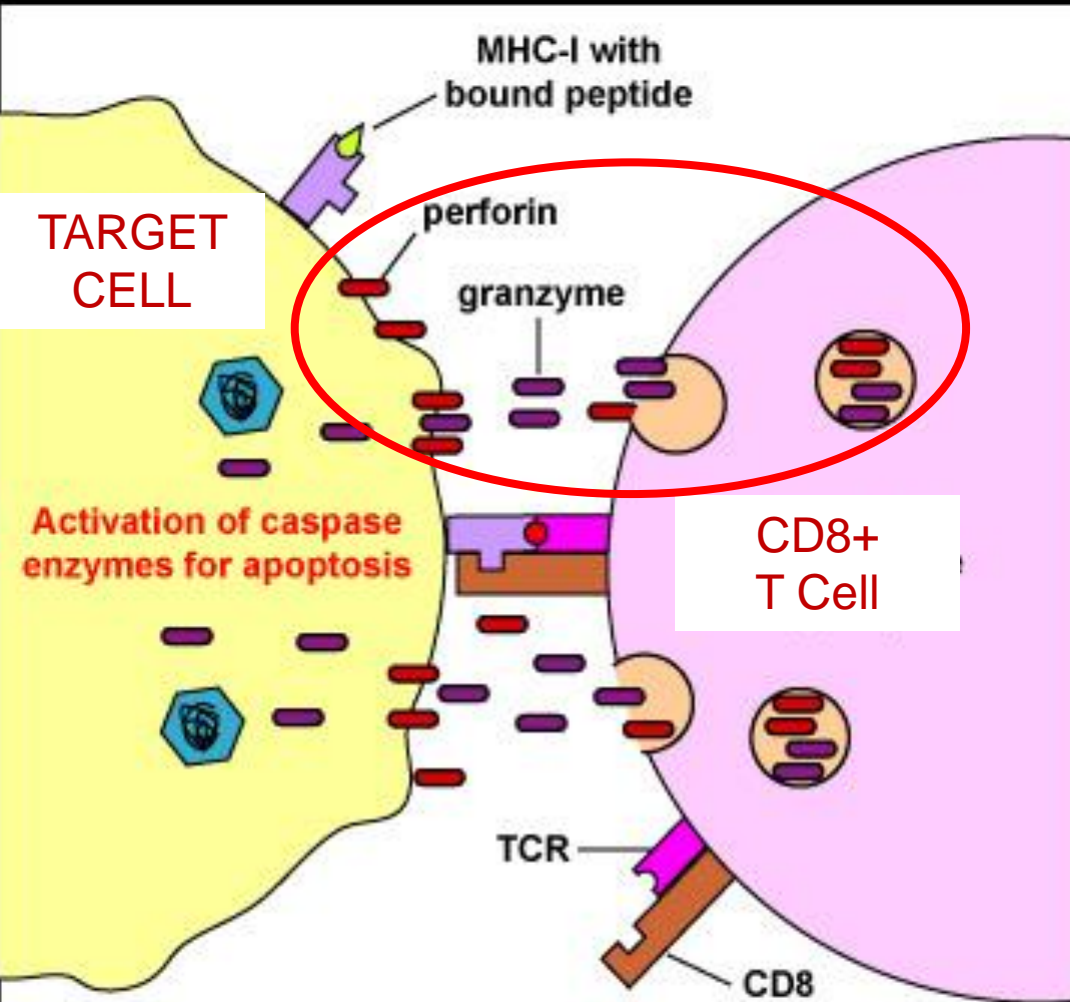
Antigen-altered epithelial cells



Cell lysis/necrosis,
apoptosis

2. Granzymes and cytokines trigger apoptosis.

CD8+
T cell
-mediated



CD8+ T cell-mediated Apoptosis

Stevens-Johnson Syndrome & Toxic Epidermal Necrolysis



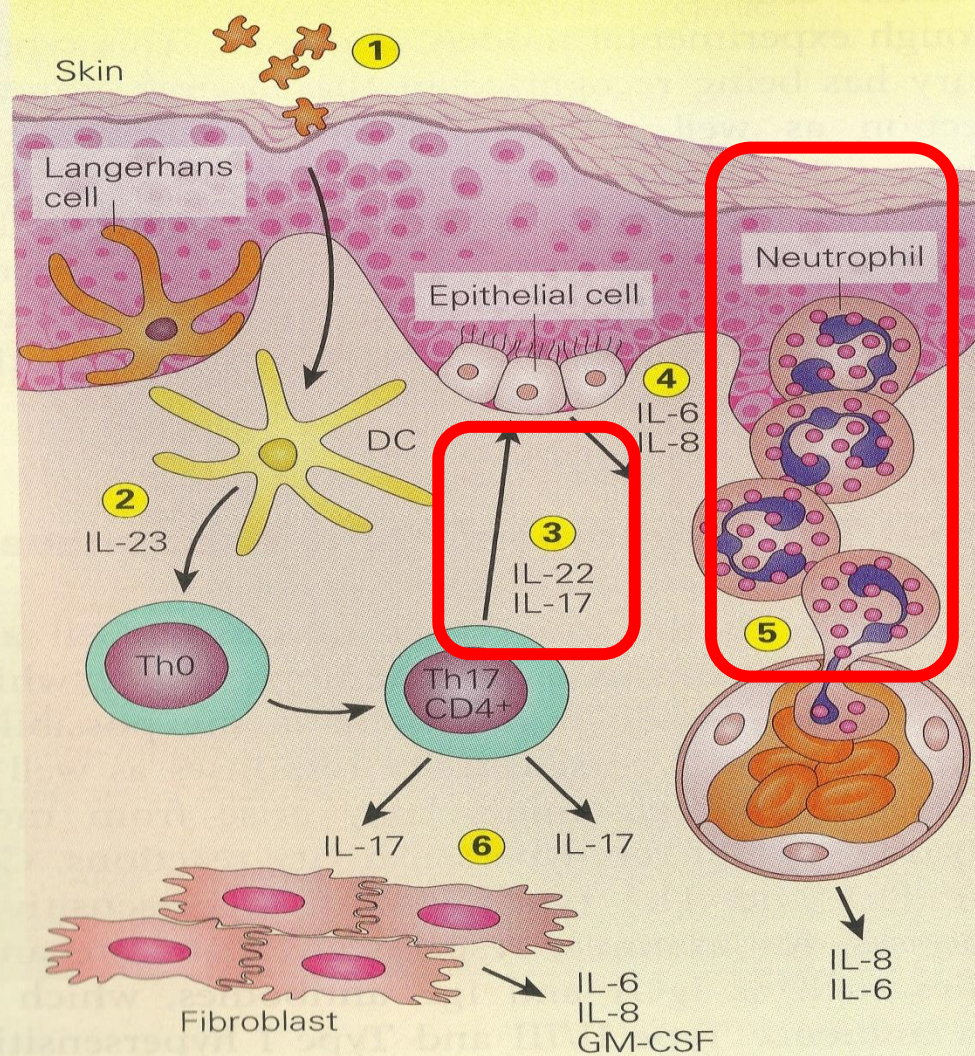
**Maculopapular &
bullous exanthems**



<http://bit.ly/PUCRKz>

Type IVD: Th17 cytokine- mediated

Bellant JA. *Immunology IV: Clinical Applications in Health & Disease*. Washington DC: I Care Press, 2012, p. 677



Psoriasis



<http://bit.ly/RnFd5S>



<https://jamanetwork.com/data/journals/derm/11773/dlv40012f2.png>

Behçet's Disease



<http://bit.ly/RR7Jiu>

**Acute Generalized
Exanthematous
Pustulosis (AGEP)**

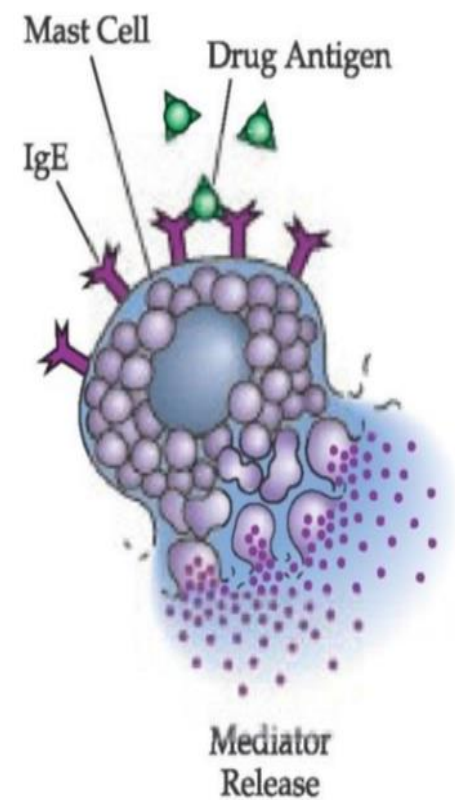


<http://allergyspecialist.com.au/wp-content/uploads/2014/07/patch-testing-300x240.jpg>

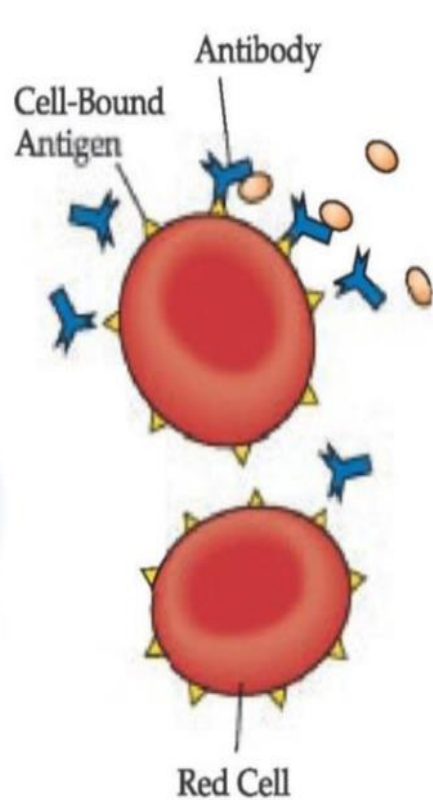
Patch Testing

- Measures delayed hypersensitivity reaction
- Determine antigens
 - Chemicals
 - Metals

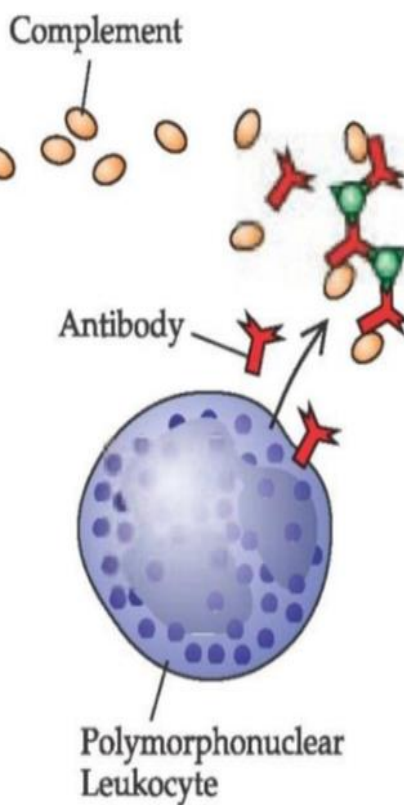
TYPE I



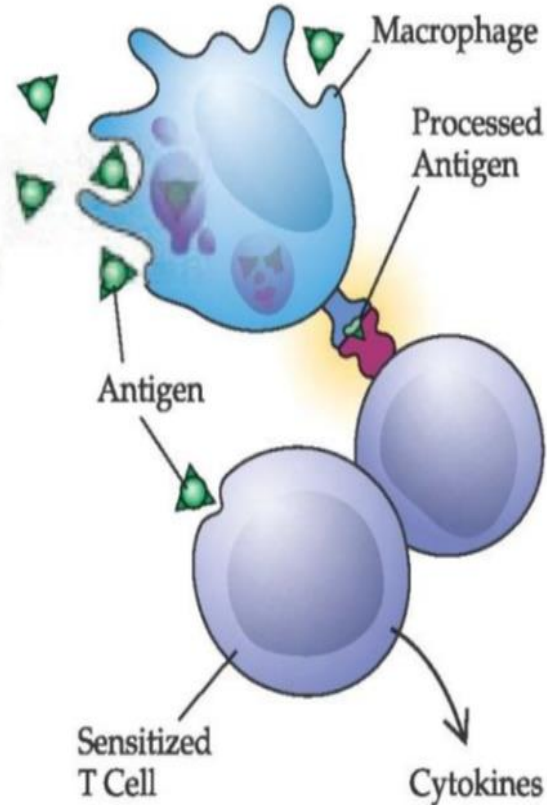
TYPE II

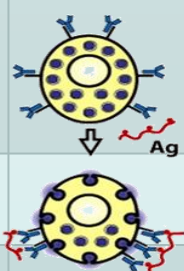
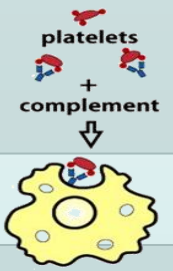
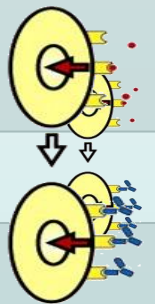
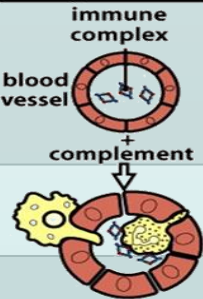
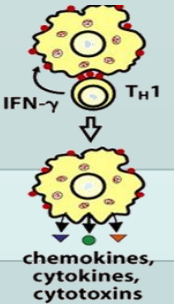
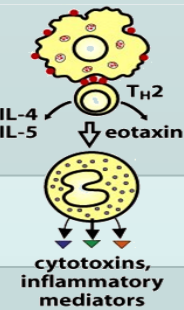

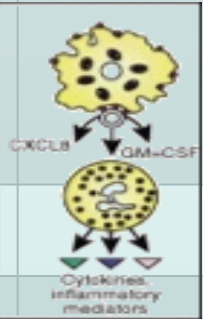


TYPE III



TYPE IV



	Type I	Type IIa	Type IIb Type IIc	Type III	Type IVa	Type IVb	Type IVc	Type IVd
Immune reactant	IgE	IgG	IgG	IgG	TH1 cells	TH2 cells	Cytotoxic T cells (CD8+)	TH17 cells
Antigen (Ag)	Soluble Ag	Cell- or matrix-associated Ag	Cell-surface receptor	Soluble Ag	Soluble Ag	Soluble Ag	Cell-associated Ag	Soluble Ag
Effector cells	Mast-cell	Complement, phagocytes, NK cells	Antibody alters signaling (neutralizing/stimulatory)	Complement, phagocytes, immune complex	Macrophage	Eosinophils	T cells	Neutrophils
								
Example	AR, BA, anaphylaxis	Hemolytic anemia, thrombocytopenia	Chronic urticaria	Serum sickness	CD, Tuberculin reaction	Chronic asthma, chronic AR, MP exanthem with Eo	CD, MP & bullous exanthem, hepatitis	AGEP, Behçet's disease