Respiratory Block

Immunology

Lecture 1

Hypersensitivity reactions.

In this document you will find some main points gathered from the 1st lecture..This document is NOT a replacement for the lecture..If you need additional information go back to the lecture or use a book as a reference so you understand everything correctly.

Hopefully all the information is correct and Hope you find them Useful.

Good Luck to everyone.

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Immunology

Hypersensitivity reactions.

Some main points you can go through and revise from:

Note:
Hypersensitivity reactions → 'over reaction' of the immune system to environmental antigens

Note:
[H/S = Hypersensitivity]

Note:
Allergic Diseases→ Diseases caused by an immune responses to environmental antigens that lead to immediate reactions in the targeted tissues & rapid onset of symptoms.

Note:
An allergen → is an Antigen→
Allergen definition→Any substance that can cause an allergy.

Hypersensitivity reactions are classified into four types [by Coombs and Gell]:

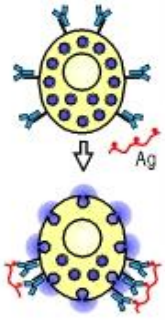
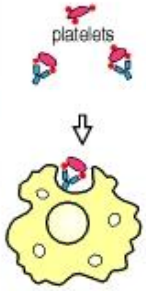
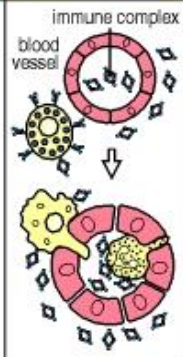
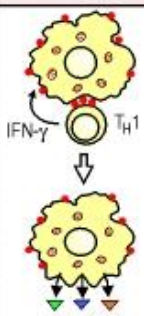
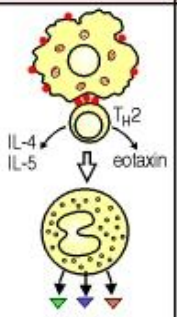
- Type I : Immediate H/S
- Type II : Cytotoxic H/S.
- Type III : Immune – complex H/S.
- Type IV : Delayed H/S.

Antibody-mediated	Cell-mediated
Type I / Immediate – IgE (Allergies & Anaphylactic Shock).	**Type-IV : Delayed- Type. - T cells, activated macrophages.**
Type II – IgG or IgM antibodies against tissue/cellular components.	
Type III – Immune complexes (IgG + soluble antigen).	

Note:
Soluble Antigen → A free antigen which binds to antibodies forming an immune complex.

Note: [Very Important to keep on mind]
One or more reaction may occur in the same patient.
e.g. : Type I and Type III.

Summary of Hypersensitivity types

	Type I	Type II	Type III	Type IV		
Immune reactant	IgE	IgG	IgG	T_H1 cells	T_H2 cells	CTL
Antigen	Soluble antigen	Cell- or matrix-associated antigen	Soluble antigen	Soluble antigen	Soluble antigen	Cell-associated antigen
Effector mechanism	Mast-cell activation	FcR^+ cells (phagocytes, NK cells)	FcR^+ cells Complement	Macrophage activation	Eosinophil activation	Cytotoxicity
						
Example of hypersensitivity reaction	Allergic rhinitis, asthma, systemic anaphylaxis	Some drug allergies (e.g., penicillin)	Serum sickness, Arthus reaction	Contact dermatitis, tuberculin reaction	Chronic asthma, chronic allergic rhinitis	Contact dermatitis

Type I Hypersensitivity.

(Immediate H/S)

Also termed (Other names for it):

- Immediate H/S.
- Anaphylactic reactions .
- Allergic reactions.

Note:

It can occur within minutes to hours)→ hence the term "Immediate"

Features:

- Antibody type → IgE.
- Cellular components:
- Mast cells, basophiles & eosinophils.

Antigens :

Allergens → antigens with low molecular weight & highly solubility

*Defense against parasitic infections → IgE
*Reactions towards harmless molecules → "atopy."

Explanation:

People who are "atopic" develop a reaction against substances that wouldn't harm normal individuals

The Hygiene Theory: *To help you understand*

In the high socio economical countries (ex: Switzerland) their IgE antibodies are directed against allergens so there is an increased rate of developing allergies.on the opposite side, the low socio economical countries (African countries where there is low heath care) their IgE antibodies are directed against parasitic infections.

Note:

Immediate allergy: an allergic reaction that becomes apparent in a sensitized person only minutes after contact.(Patiens show symptoms almost as soon as they come in contact with an allergen)

Type I Reaction occurs in 2 phases:

Phase I : *Sensitization phase*

- First contact with allergens. (Exposure to the allergen.)
- Activation of TH2 cells & stimulation of IgE class switching in B–cells = (B-Cells produce IgE)
- Sensitization =Binding of IgE to the Fc receptors on mast cells.

Note:

*Sensitization→ the state of being sensitive (as to an antigen)
*How sensitization happens→ By the attachment of specific IgE to Fc receptors on the mast cells.

Phase II : *Challenge phase*

- Subsequent contact with allergens (Repeated exposure to the allergen)
- Activation of mast cells (by cross linking) which will lead to
- its degranulation and the release of mediators.

Note:

*Cross linking→ Is when 1 antigen binds to 2 antibodies

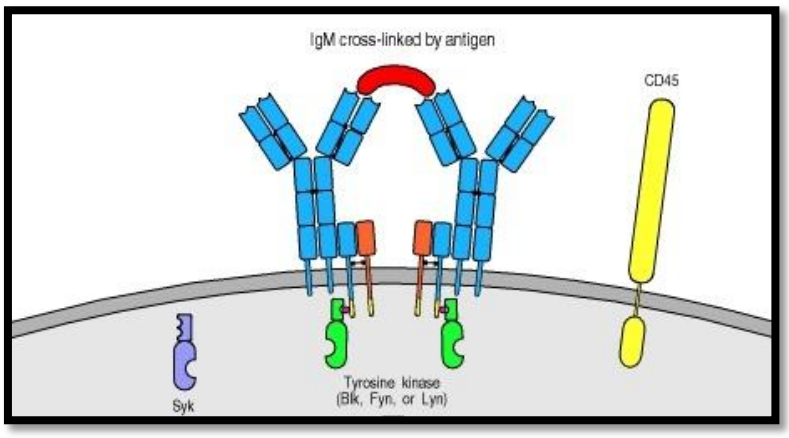
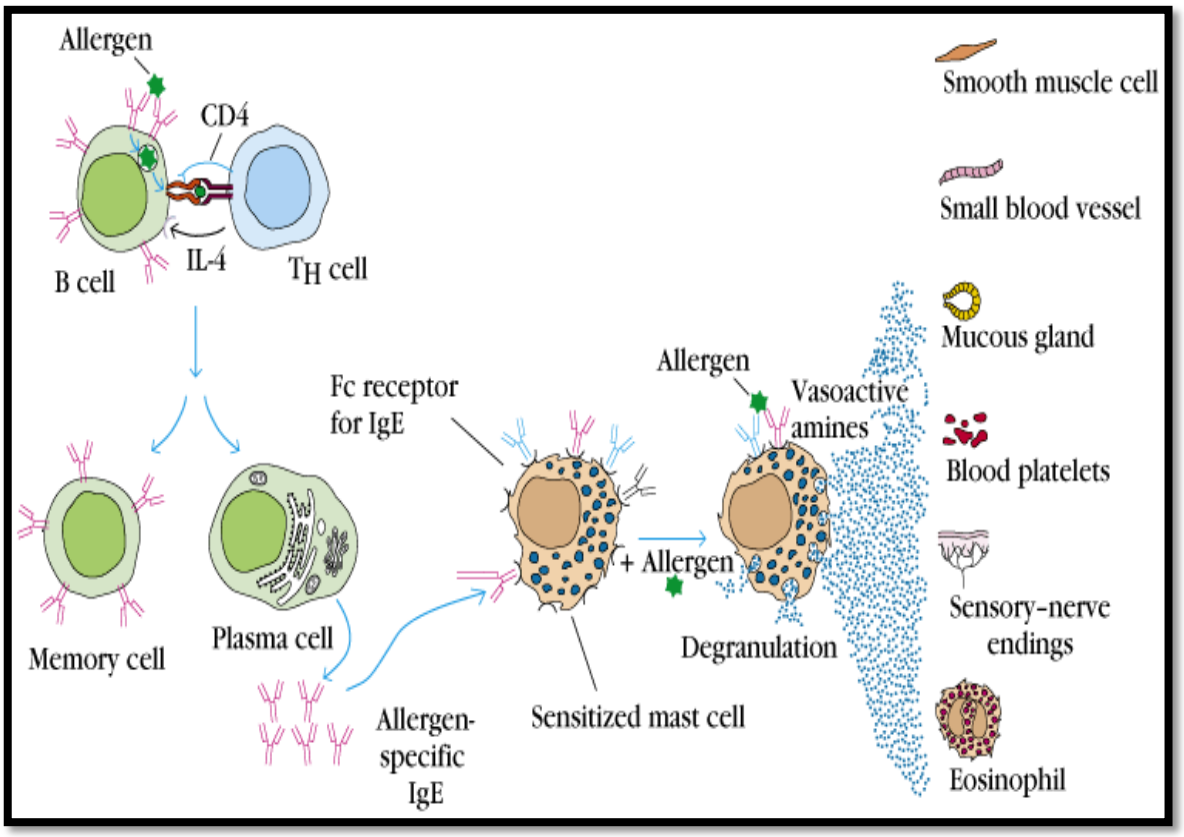
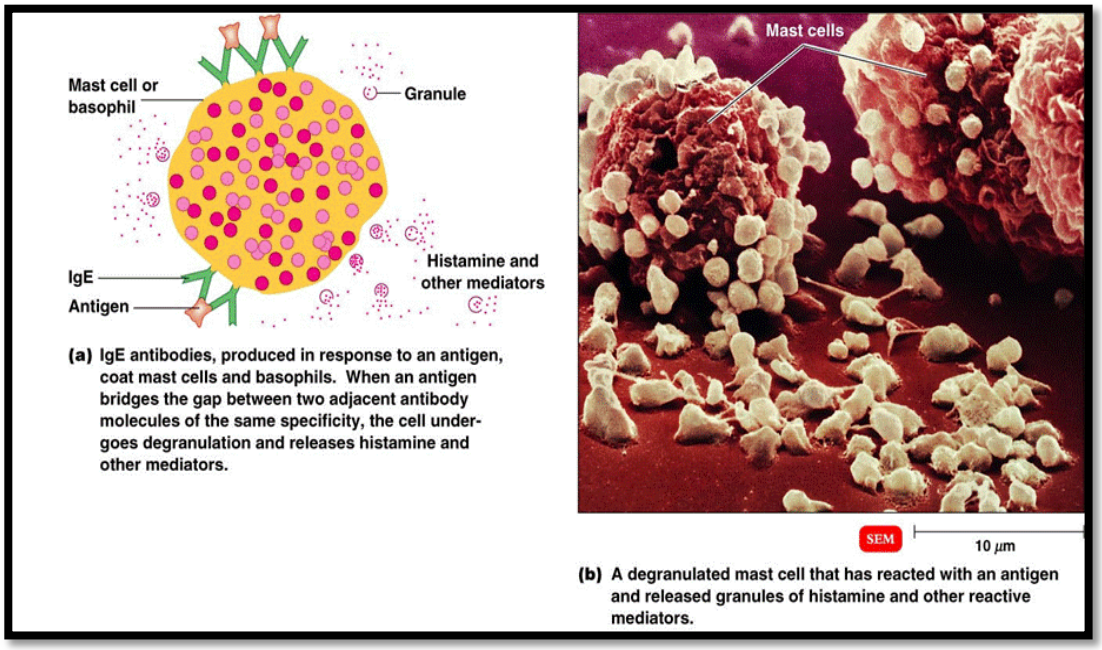


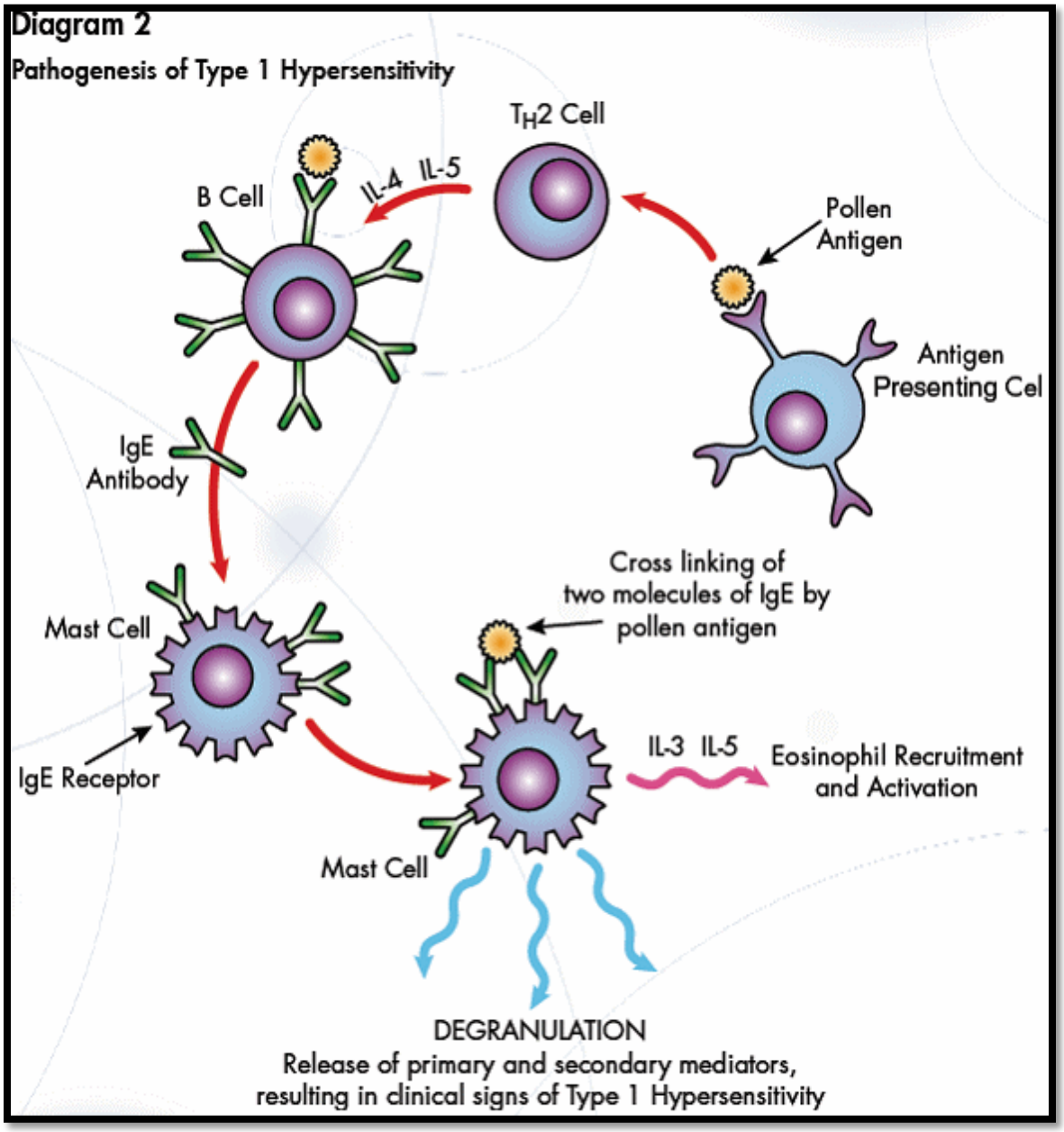
Illustration showing phase 1 and phase 2 of type 1 hypersensitivity reaction



How degranulation and release of histamine occurs



Second Illustration showing Phase 1 and Phase 2 in Type 1 hypersensitivity reactions



Type1 reactions result in :

- Vasodilatation and increased capillary permeability .
- Edema
- Vasoconstriction (arteries and arterioles).
- Bronchoconstriction.
- Increased mucus secretion.

*The site of allergen entry →Determine the symptoms

Sites of entry

Inhaled	Ingested (oral rout)	Injected
• deposits in: nasopharyngeal & bronchial tissues • Result in: • 1- allergic rhinitis • 2- allergic asthma	• Food allergy(GIT symptoms)	• e.g bee sting venom enters the Blood: • 1- systemic inflammation • 2- anaphylactic shock

Anaphylactoid reaction:

- **Non** IgE mediated.
- May result from contrast media or local anesthetic.

To help you understand
Some drugs (polymyxin, morphine, x-ray contrast and others) may cause an "anaphylactoid" reaction (anaphylactic-like reaction) on the first exposure. This is usually due to a toxic reaction, rather than the immune system mechanism that occurs with "true" anaphylaxis

Diagnosis:-

- Skin pick test (SPT)
- Intradermal test.
- (RAST) → To measure IgE
- Elimination / provocation test →Used to check for food allergies

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Type II hypersensitivity

(Cytotoxic H/S)

Features:

- Antibody → IgG. or IgM
- Antigens →(Bound to cell membranes).

source of antigens :

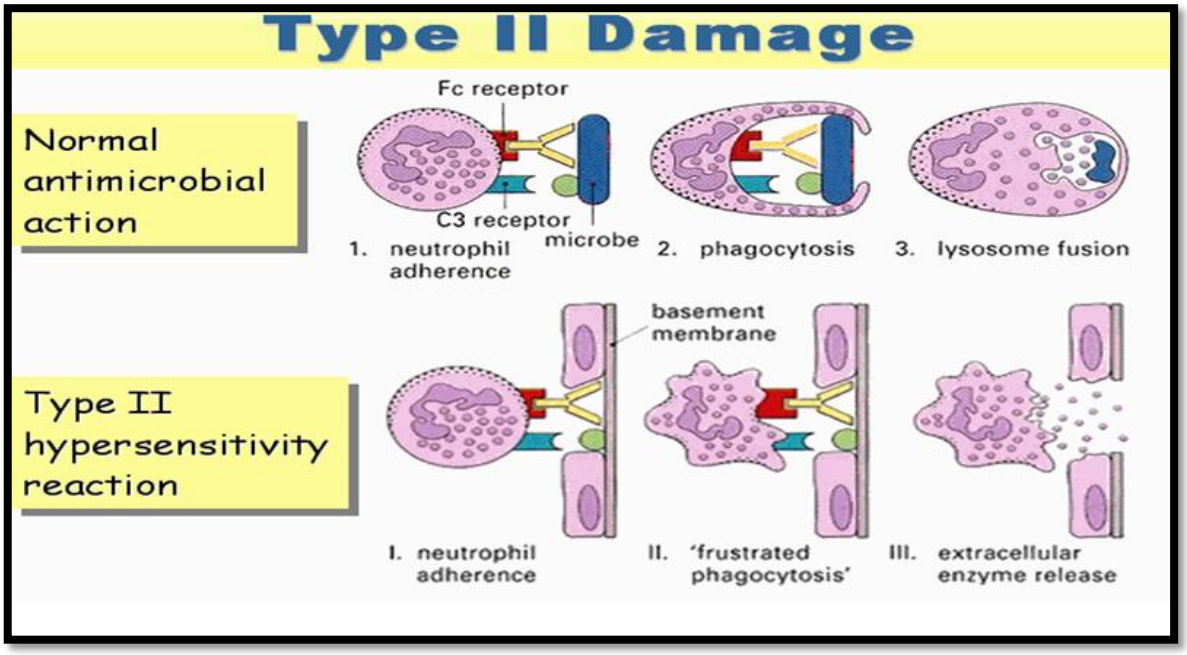
- Endogenous (Self – antigens).
- Exogenous (microbial antigens).
- Complement activation (Invariable).

Mechanism of Damage :

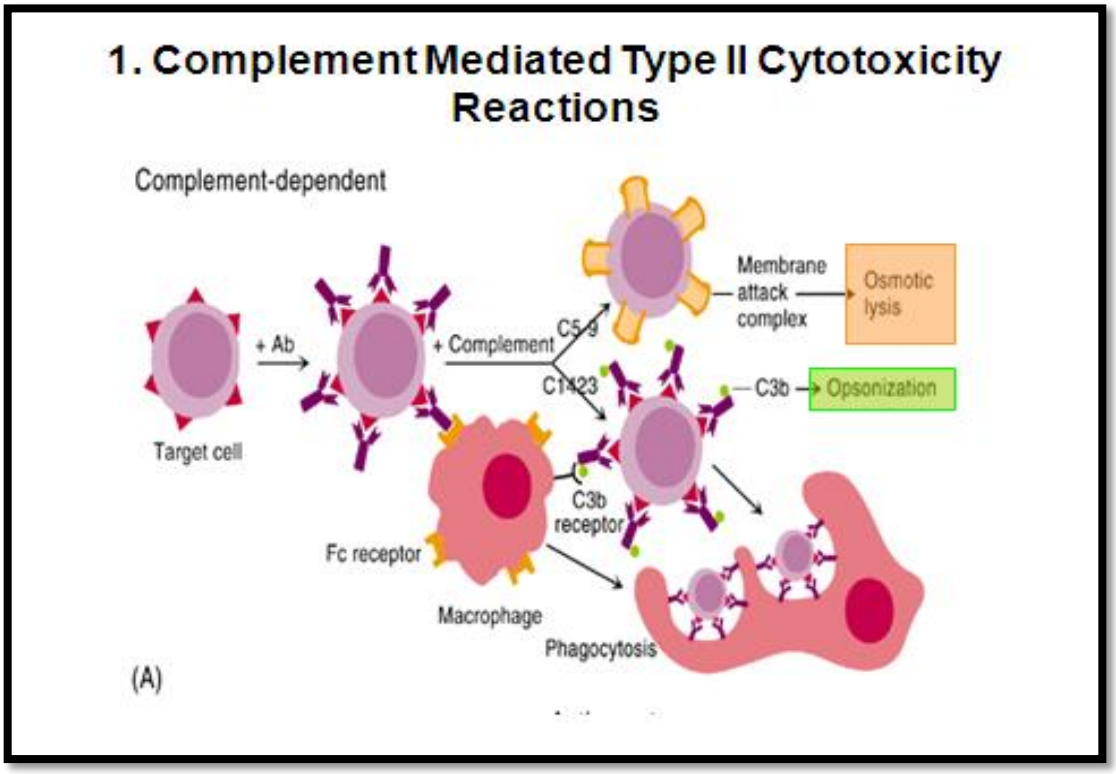
Two ways :

- Neutrophil-mediated damage
- Complement mediated damage

Neutrophil-mediated damage



Complement mediated damage



Clinical examples : (what the damage results in)

- Glomerulonephritis (anti-GBM). * Anti-glomerular basement membrane antibody* → Type 2 H/S
- Mis-matched blood transfusion → Type 2 H/S

Diagnosis:-

Detection of antibodies and antigens by Immunofluoresence in tissue biopsy specimens e.g. kidney , skin etc.

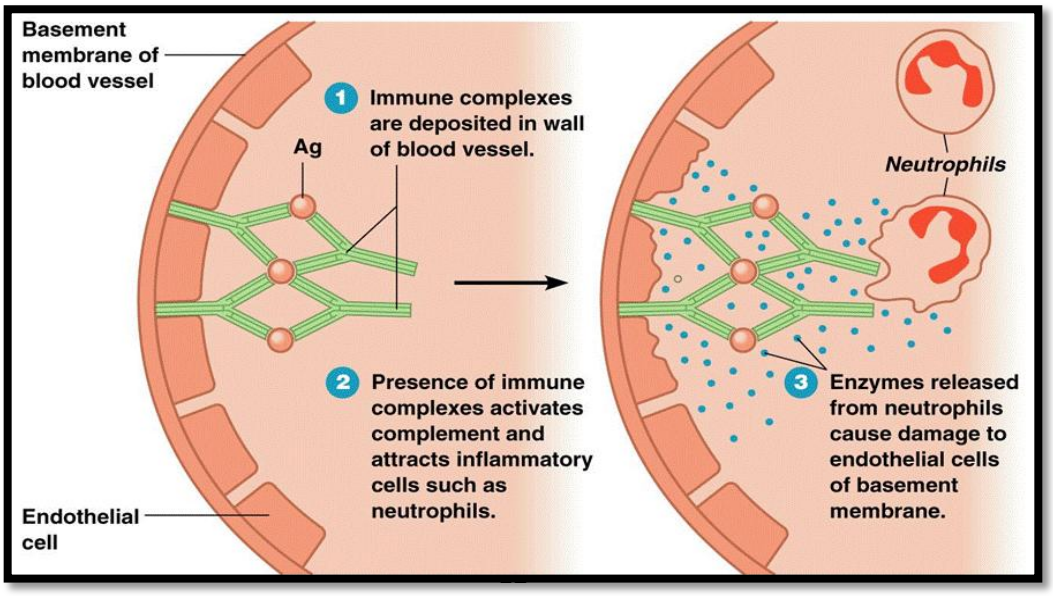
Type III Hypersensitivity

(immune – complex H/S .)

Features:-

- Antibody → IgG
- Antigens → Soluble.
- Immune – Complex formation→Complement activation. attraction of inflammatory cells .

Pathophysiology of type III reactions



Type III reactions occur in two forms :

- Complexes with antibody excess →are termed Arthus – type reactions →**.(localized).**
- Complexes with antigen excess →are termed serum – sickness reactions →**(systemic).**

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Type III H/S, clinical examples :

- Glomerulonephritis *Different from the one caused by type2 H/S*

- Drug eruptions → some drug can cause it

Diagnosis (type III) :

Demonstration of specific immune complexes in the blood or tissues by → Immunofluoresence .

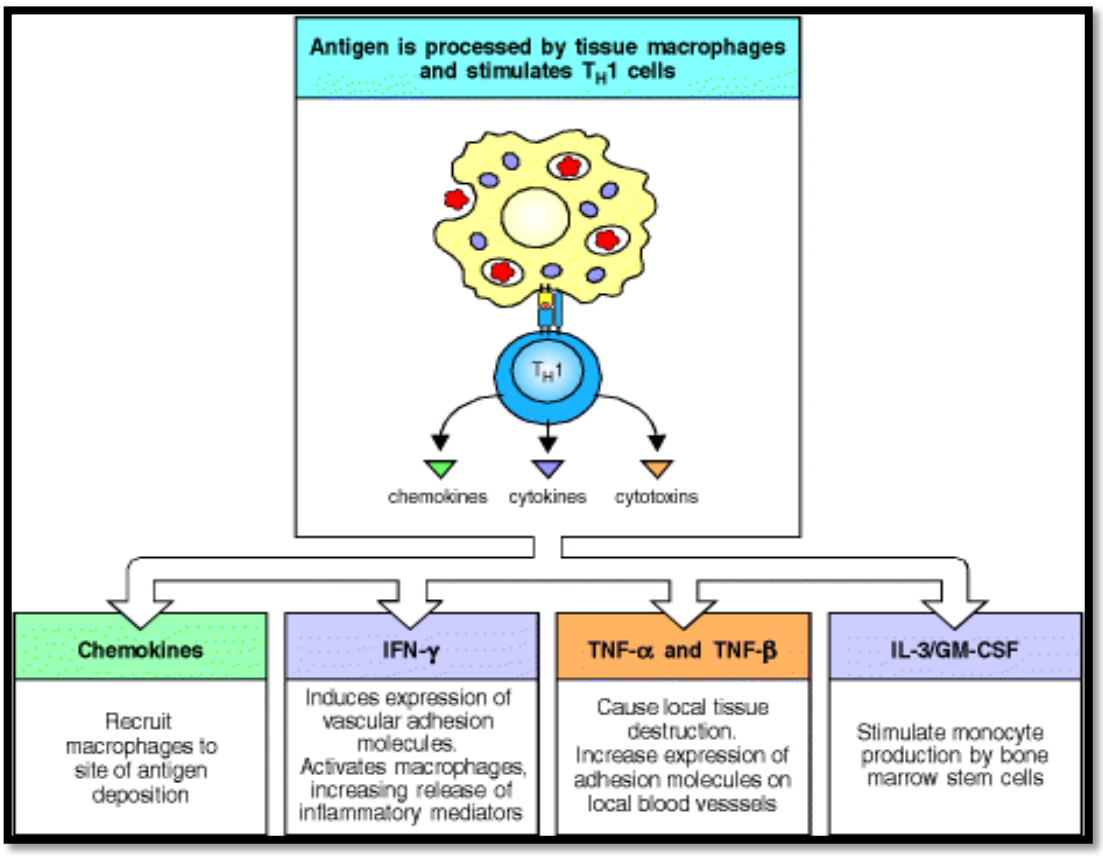
To help you understand
Immunofluoresence → this technique uses the specificity of antibodies to their antigen to target fluorescent dyes to specific biomolecule targets within a cell, and therefore allows visualisation of the distribution of the target molecule through the sample

Type IV hypersensitivity

(delayed H/S):

- cell-mediated-T(DTH)cells.(delyed type hypersensivity T cells
- activated macrophages .
- delayed- onset (2 – 4 days).
- secondary abnormal cellular responses .
- granuloma formation .

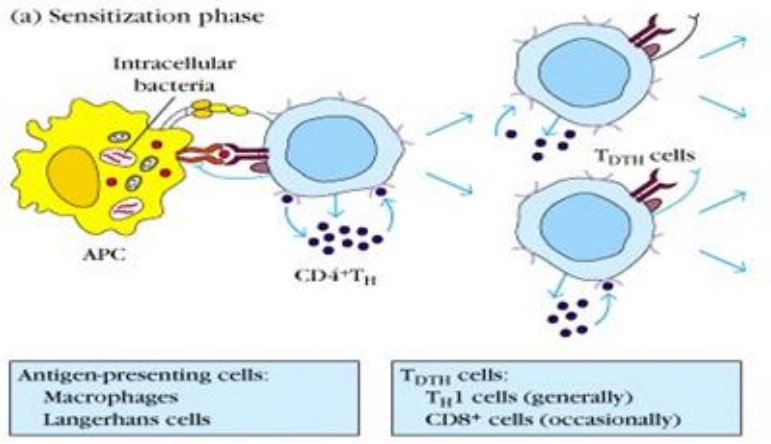
Mediators released by TDTH cells.



Development of DTH Response

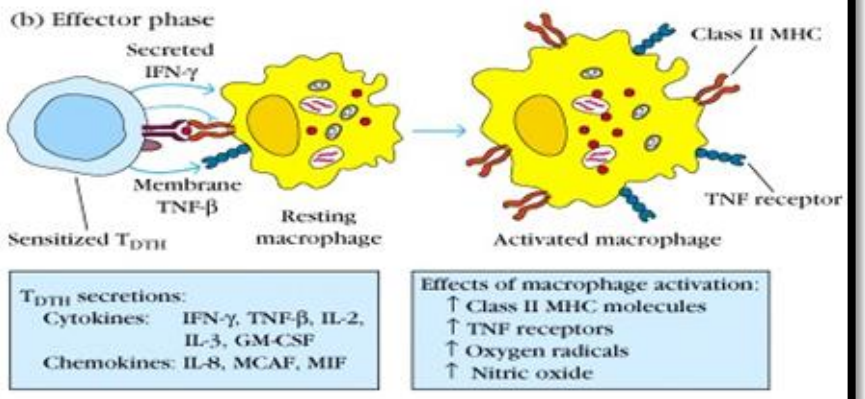
Development of DTH Response

Sensitization phase:
1-2 week period



Effector phase:
24-72 hours

Effector cells (activated macs) act non-specifically



Pathophysiology of allergic contact dermatitis.

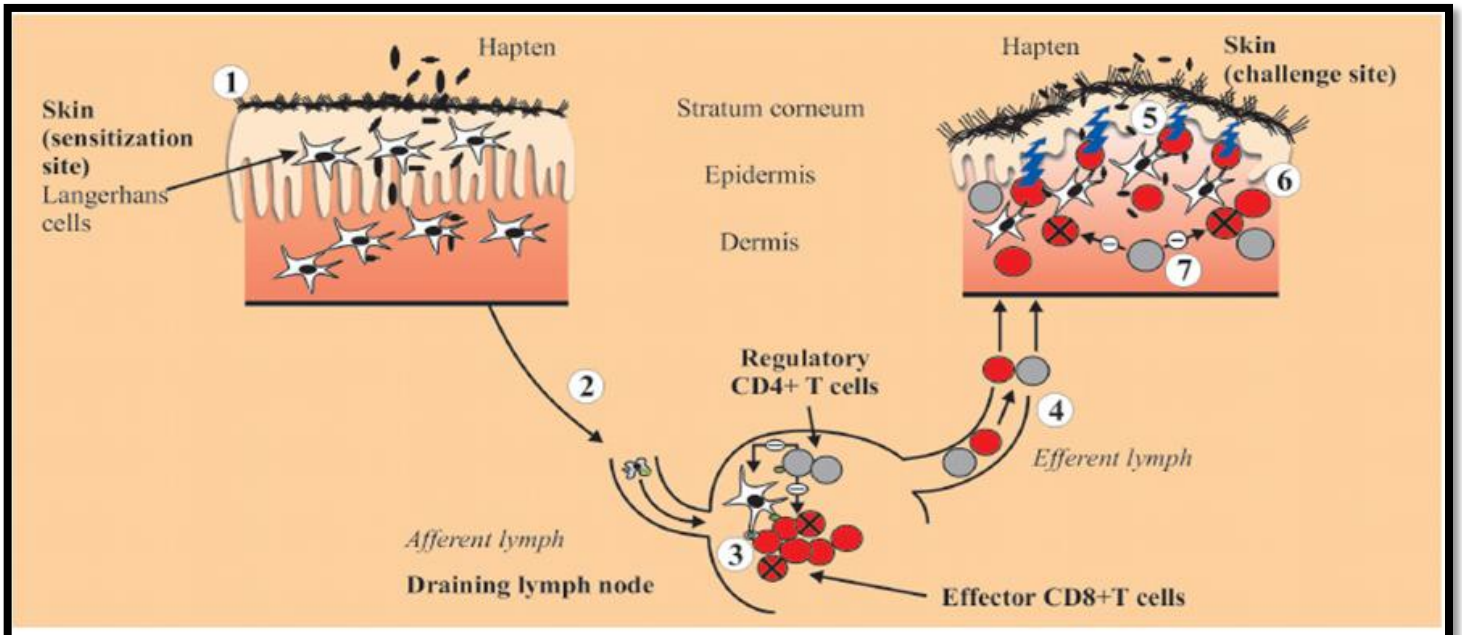


FIGURE 1: **Pathophysiology of allergic contact dermatitis**
Sensitization phase (afferent phase). Haptens penetrate the epidermis (step 1) and are uptaken by epidermal cells including skin DC which migrate to the draining lymph nodes (step 2) where they present haptenated peptides to both CD8+ effector T cells and down-regulatory CD4+ T cells (step 3). Specific T cell precursors clonally expand in draining lymph nodes, recirculate via the blood and migrate to tissues including the skin (step 4).
Elicitation phase (challenge phase, efferent phase). When the same hapten is applied on the skin, it is uptaken by epidermal cells, including skin DC and keratinocytes (step 5) which present haptenated peptides to specific T cells. Activation of CD8+ CTLs induces apoptosis of keratinocytes and production of cytokines and chemokines by skin resident cells (step 6). This leads to the recruitment of leucocytes from the blood to the skin. CD4+ T cells may block activation/expansion of CD8+ effectors in lymph nodes during sensitization and in the skin during the elicitation phase of CHS (step 3 and 7).

Type IV clinical examples;

- Allergic contact dermatitis
- T.B. granuloma (persistent antigen).

Diagnosis (type IV):

- Delayed skin test → Mantoux test .
- Patch test →Used for contact dermatitis →Patch is left on skin for at least 48 hour
- Lymphocyte transformation test (detection of activation markers by flow cytometry).

To help you understand
Flow cytometry is a technique for counting and examining microscopic particles, such as cells and chromosomes