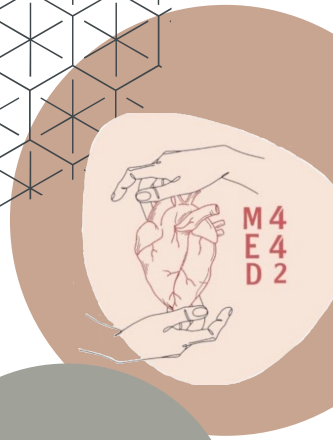
Foundation block

KSU



Hypersensitivity

W7
L5

Color index :

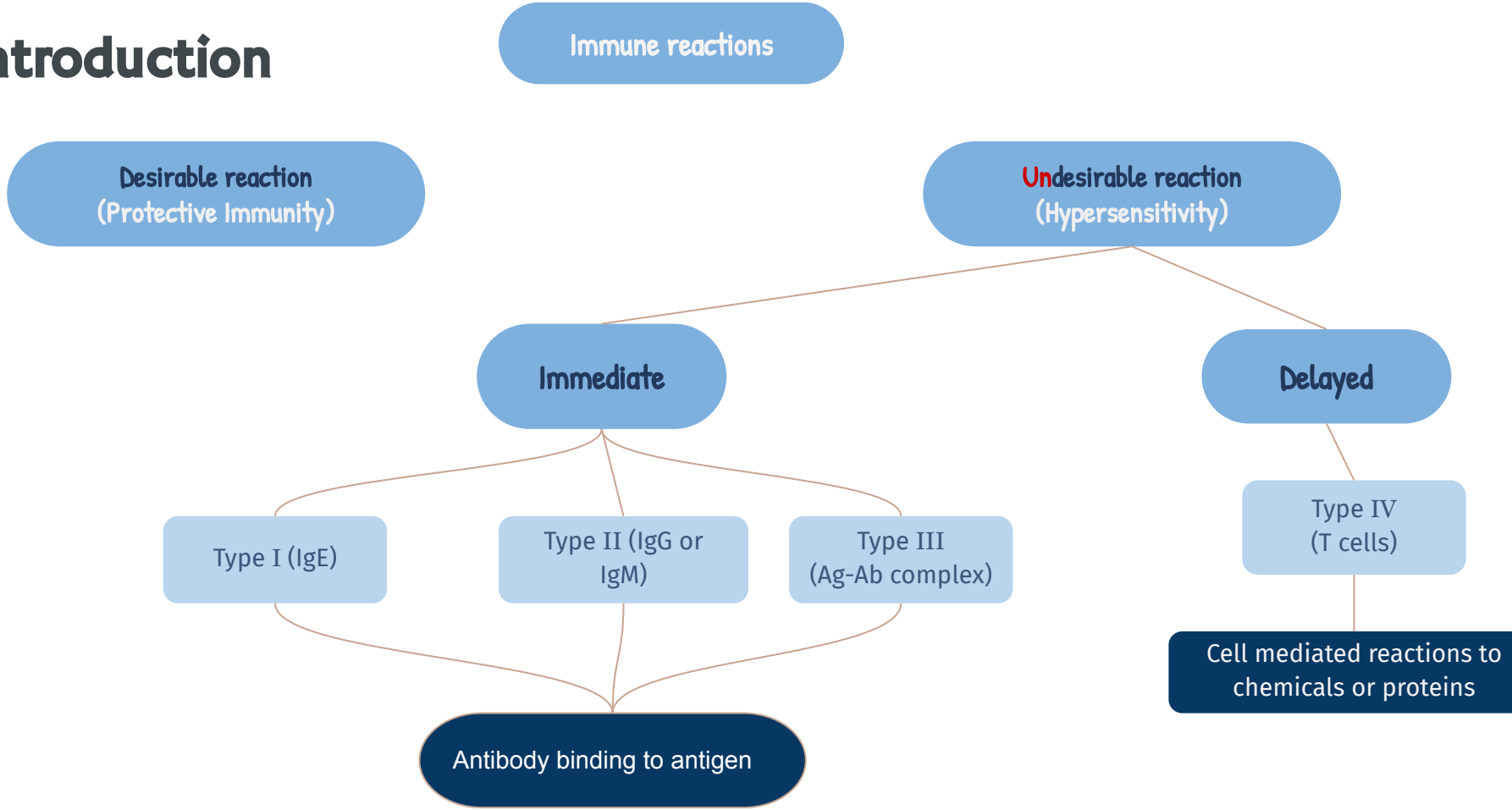
- Main text
- Important
- Dr notes
- Females slides
- Male slides
- Extra

Editing File

Objectives

- To know that hypersensitivity reactions are over and excessive immune responses that can be harmful to body in four different ways
- To be familiar with inflammatory processes in Type I hypersensitivity reaction that mediates allergic inflammation
- To recognize that Type II hypersensitivity deals with immune responses against antigens that are integral part of cell membrane and are usually associated with autoimmune disorders
- To know that Type III hypersensitivity reactions are mediated by immune complexes and cause vasculitis
- To describe Type IV hypersensitivity is a purely cell mediated immune response associated with chronic inflammation

Introduction



Type I Hypersensitivity

Also named as:

- Immediate Hypersensitivity
- Allergic reaction
- Anaphylactic reaction

Which is severe and rapidly progressing systemic form which can be quickly life threatening. It can occur within minutes to hours

- Bronchoconstriction and airway obstruction
- Blood vessel contraction

01 — **Antibody type:** IgE → Atopic individuals respond by producing large amounts of IgE in response to those otherwise harmless substances. In the other hand Non-allergic individuals respond to these allergens by producing IgG antibodies

02 — **Cellular components:** mast cells - basophils - eosinophils

03 — **Antigens (Allergens):** pollens - dust mites - animal dander - nuts - shellfish - various drugs

★ Low molecular weight
★ High solubility

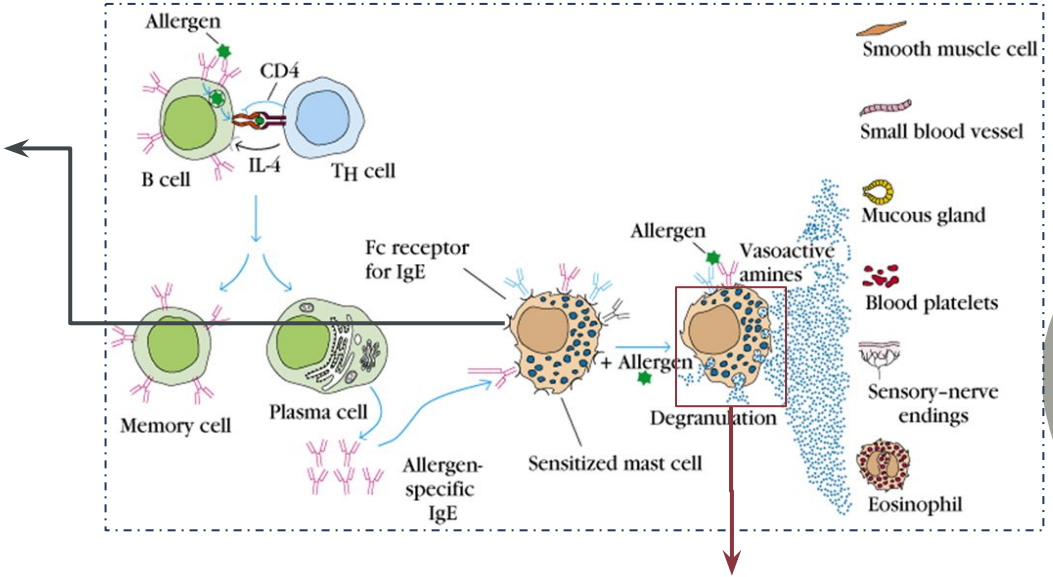
Dust mite

Type I Hypersensitivity - 2 phases

Sensitization phase

First contact with allergens

B cell displays antigen to TH2 cell activating plasma cells that will produce allergen specific IgE that binds to Fc receptor on mast cell surface

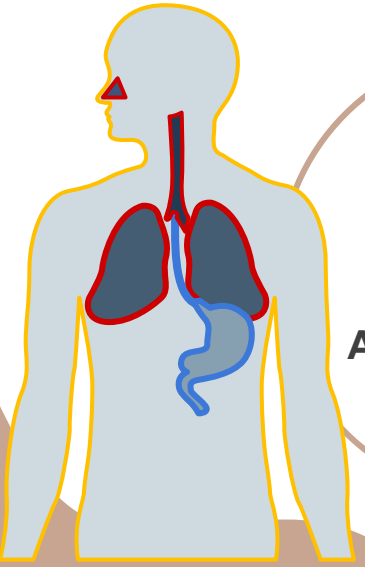


Challenge phase

Subsequent contact with allergens

- Allergen crosslinks with sensitized mast cell stimulating degranulation and release of vasoactive amines
- Symptoms appear in this phase

Allergy is a Systemic Disorder



Allergies can be divided into:

Ingested allergies

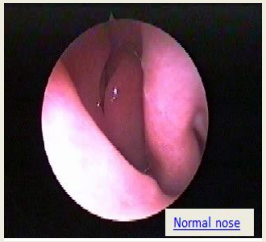
Food allergy:
- Esophagus
- Stomach

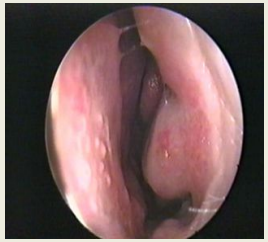
Contact allergies

Eczema
Urticaria
Allergic dermatitis
- Skin

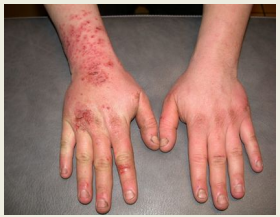
Inhaled allergies

Allergic rhinitis
Asthma
- Nose
- Pharynx
- Lungs

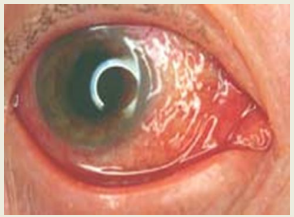




Rhinitis (inflammation of mucous membranes inside the nose)



Eczema



Conjunctivitis (inflammation of the outer layer of the eye and inner surface of the eyelid)

Injected Allergens

- Hymenoptera (bees, wasps, ants) sting venom enters the bloodstream

  Can cause:

  - ➢ Systemic inflammation
  - ➢ Anaphylactic shock (life threatening)

Venom: poisonous substance secreted by animals

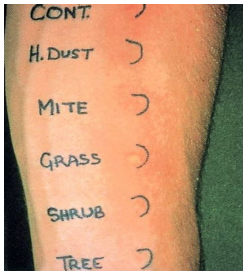
- Anaphylactoid reactions:
  - Are non - IgE mediated
  - may result from contrast media (injected to improve scan reading) or local anesthetics

Non-IgE mediated is like an Anaphylaxis but has similar effects (Non Immunological: mast cells are directly activated without antibodies)

Diagnosis of Allergy

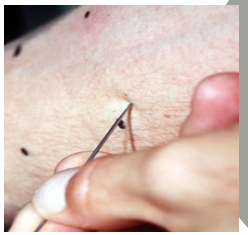
1. Skin prick test (SPT)

putting a small amount of allergen on skin then pricking it and waiting 15-20 mins to see if there is any reaction



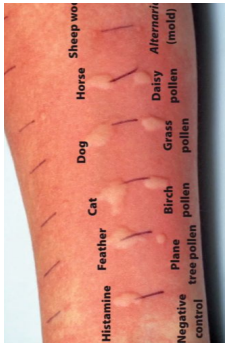
2. Specific IgE measurement (RAST)

testing IgE in serum



3. Elimination /Provocation test (Food allergy)

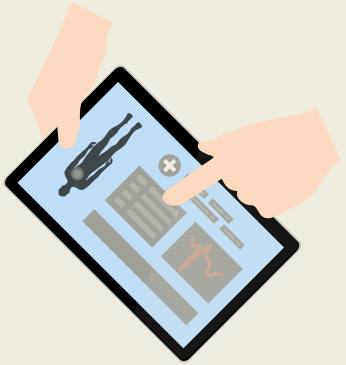
avoiding certain types of food until the allergy causing one is found



Primary and Secondary Mediators

Mediator	Effects
	PRIMARY
Histamine, heparin	Increased vascular permeability; smooth-muscle contraction
Serotonin	Increased vascular permeability; smooth-muscle contraction
Eosinophil chemotactic factor (ECF-A)	Eosinophil chemotaxis
Neutrophil chemotactic factor (NCF-A)	Neutrophil chemotaxis
Proteases	Bronchial mucus secretion; degradation of blood-vessel basement membrane; generation of complement split products
	SECONDARY
Platelet-activating factor	Platelet aggregation and degranulation; contraction of pulmonary smooth muscles
Leukotrienes (slow reactive substance of anaphylaxis, SRS-A)	Increased vascular permeability; contraction of pulmonary smooth muscles
Prostaglandins	Vasodilation; contraction of pulmonary smooth muscles; platelet aggregation
Bradykinin	Increased vascular permeability; smooth-muscle contraction
Cytokines	
IL-1 and TNF-α	Systemic anaphylaxis; increased expression of CAMs on venular endothelial cells
IL-2, IL-3, IL-4, IL-5, IL-6, TGF-β, and GM-CSF	Various effects (see Table 12-1)

Environmental and genetic basis for type I hypersensitivity



01 Environmental factors

Environmental factors include air pollution through to diet,and genetics both influence susceptibility to allergies

02 The hygiene hypothesis

The hygiene hypothesis has been advanced to explain increase in allergy incidence

- It proposes that exposure to some pathogens early in life provides a better T-cell balance. Avoids dominance of Th2 subset, which promotes IgE production by B cells (stimulating allergic response)

May explain why countries with improved hygiene are experiencing, increases in asthma and allergy rates

Type II hypersensitivity Features

Antibodies

IgG or IgM

It's Ab dependent process : in which specific Ab bind to Ag -> tissue damage or destruction.

For tissue antigen, not free antigen (autoimmunity)

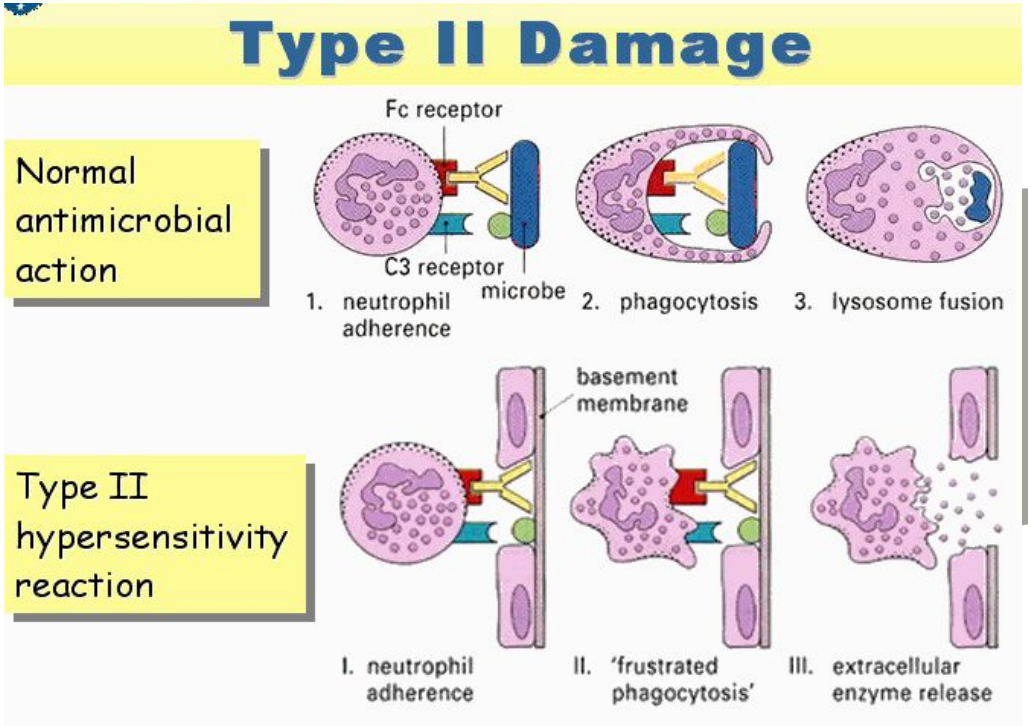
Antigens (Allergens)

-Exogenous antigens (microbial)

-Self antigens bound to cell membranes

Complement system

Activated (Invariable)



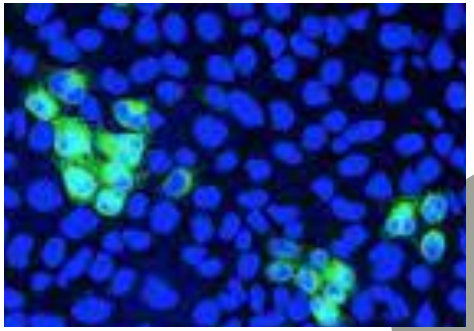
Type II hypersensitivity

Clinical examples

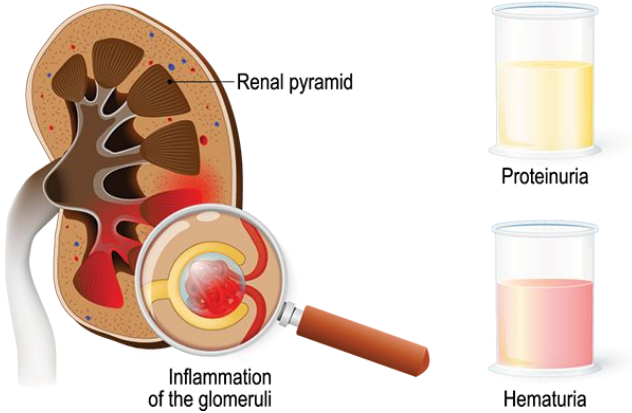
1. Mismatched blood transfusion (RBCs of donor will be attacked by the immune response of the Recipient)
2. Glomerulonephritis (anti-glomerular basement membrane) -> Ab against glomerular basement -> renal failure

Diagnosis of allergy

Detection of Ab & Ag by immunofluorescence (IF) in tissue biopsy specimens e.g. kidney & skin.



GLOMERULONEPHRITIS



Type III hypersensitivity Features

Antibodies

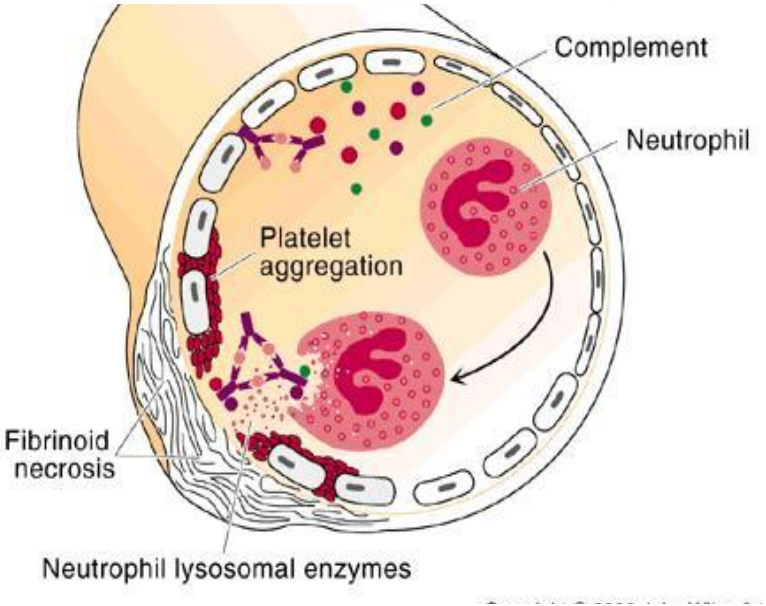
IgG IgM

It's Ab dependent process : in which specific Ab bind to Ag -> tissue damage or destruction.

For tissue antigen, not free antigen (autoimmunity)

Antigens

Free Soluble antigen



Complement system

It is activated after formation of immune-complex (antigen react with antibody) which is capable of inducing an inflammatory response

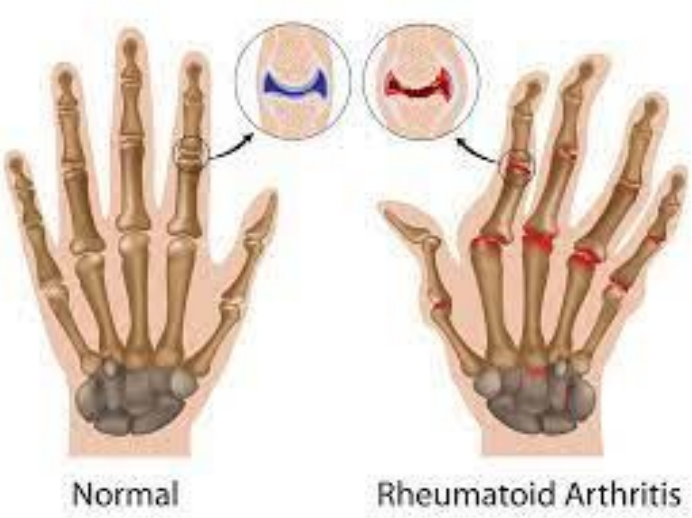
Type III hypersensitivity

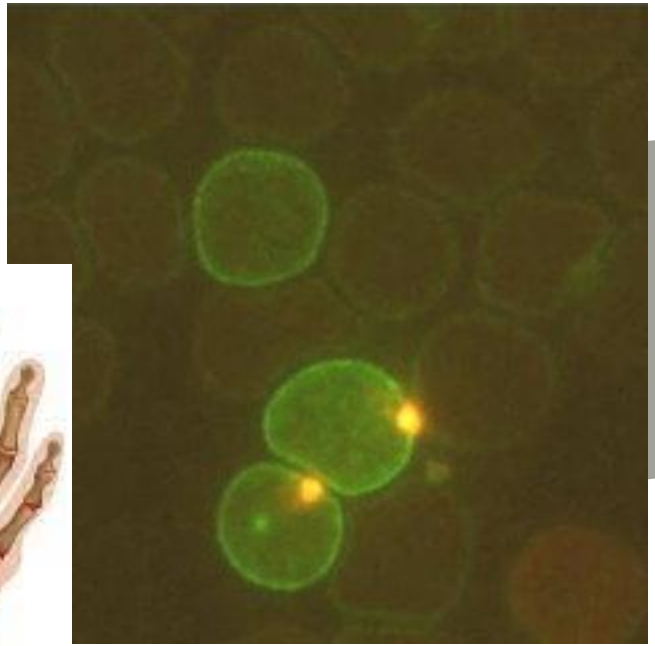
Clinical examples

1. Glomerulonephritis
2. Rheumatoid Arthritis
3. Systemic Lupus Erythematosus (SLE)

Diagnosis

Immuno-complexes detection in blood/tissue using Immunofluorescence





Type IV hypersensitivity Features

Cells

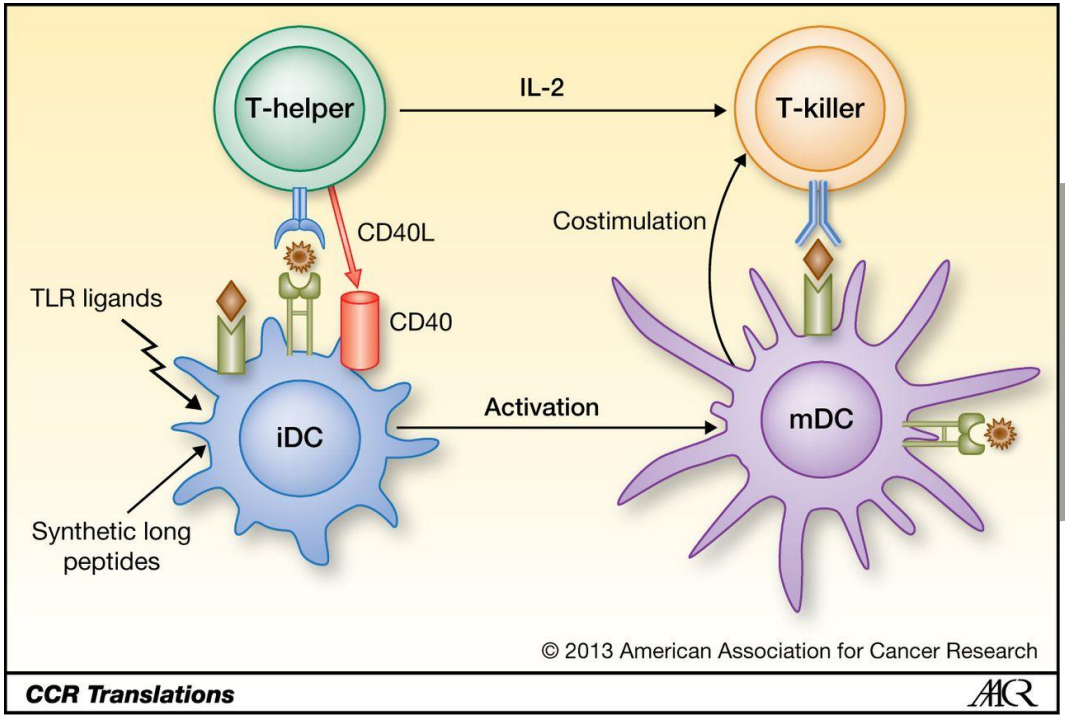
No Ab are included!! Generally CD4 and occasionally CD8 - CD activates macrophages via Th1

Antigens

Presented to T cells by APCs (involving both MHC classes)

Some info.

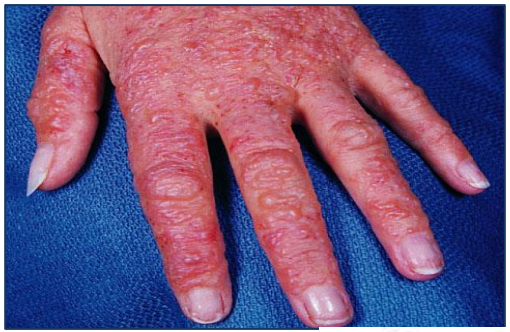
Known as “delayed type hypersensitivity”(DTH) (2-4 days ; 48h-72h) or “cell-mediated hypersensitivity”

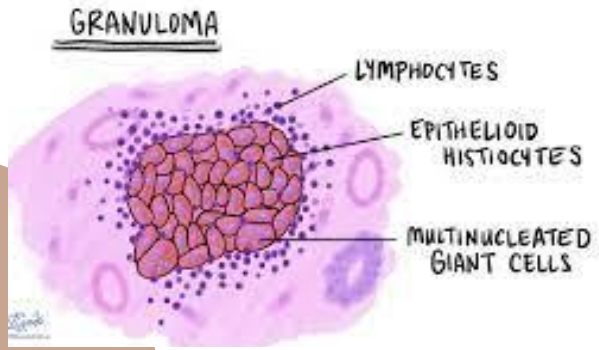


Type IV hypersensitivity

Clinical examples

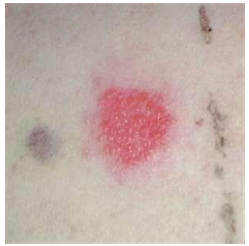
1. Contact dermatitis 2. Granuloma formation





Diagnosis

1. **Delayed skin test (Mantoux/Tuberculin test) :** consists of an intradermal injection of 0.1 ml of PPD tuberculin (Tuberculin Purified Protein Derivative) for 24-72 hours then the diameter of the reaction is measured.
2. **Patch test :** used for contact dermatitis, It's done to see if a particular substance is causing allergic reaction or not. Allergens are applied to patches then placed on your skin for 48-72 hours. "During this time you should avoid bathing or sweating".
3. **Lymphocyte transformation test :** blood smear then add Ag & wait to see if, the blood will recognize that Ag or not.



<- Skin patch test

Type IV hypersensitivity (Pathophysiology of Contact dermatitis)

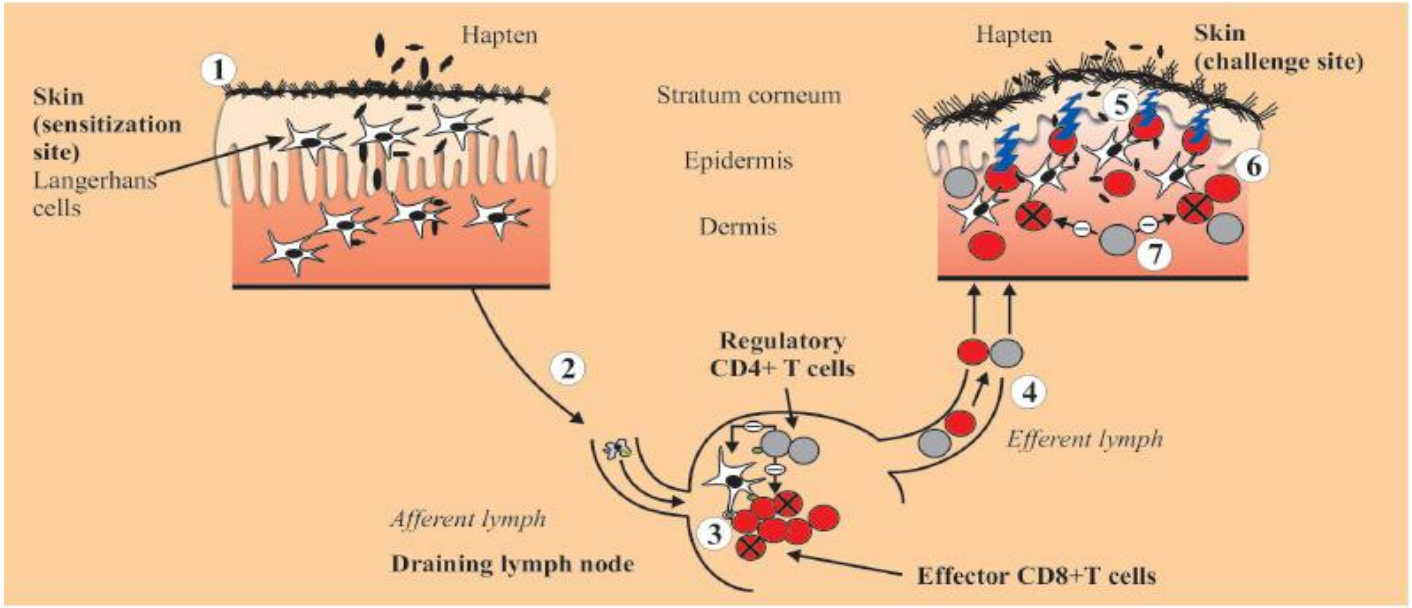


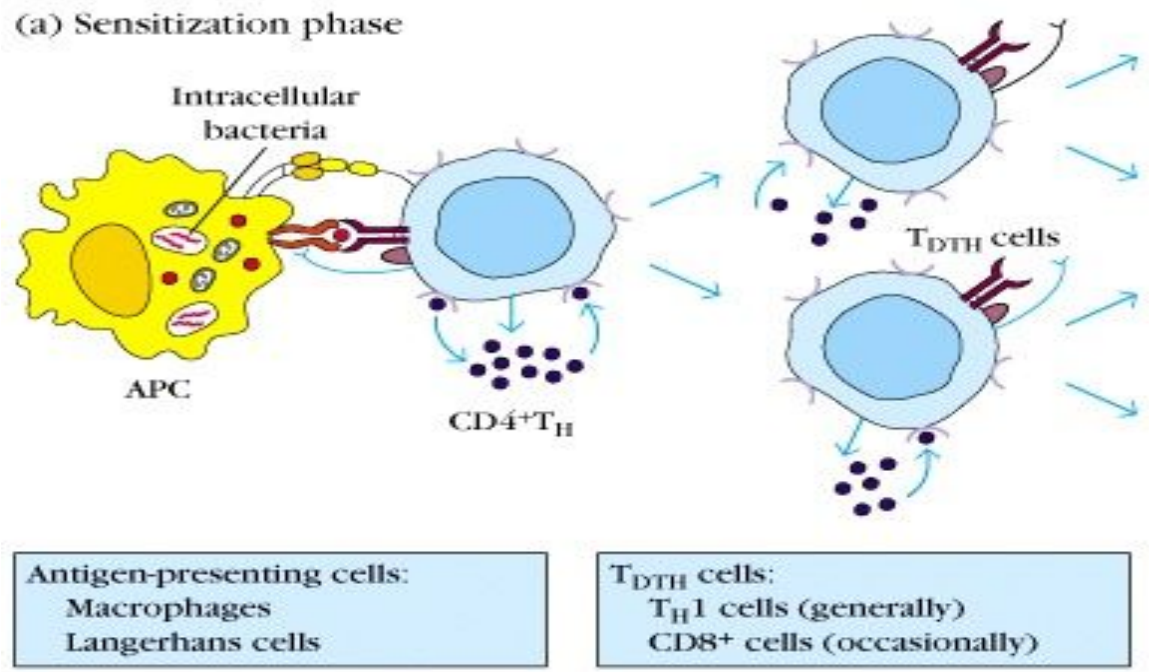
FIGURE 1: Pathophysiology of allergic contact dermatitis

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).

Development of type IV hypersensitivity response

CD4+ Th1 (generally) or CD8+ (occasionally) are activated by APCs like (macrophages and langerhans) via MHC Class I or II and become T-DTH (delayed type T cell)

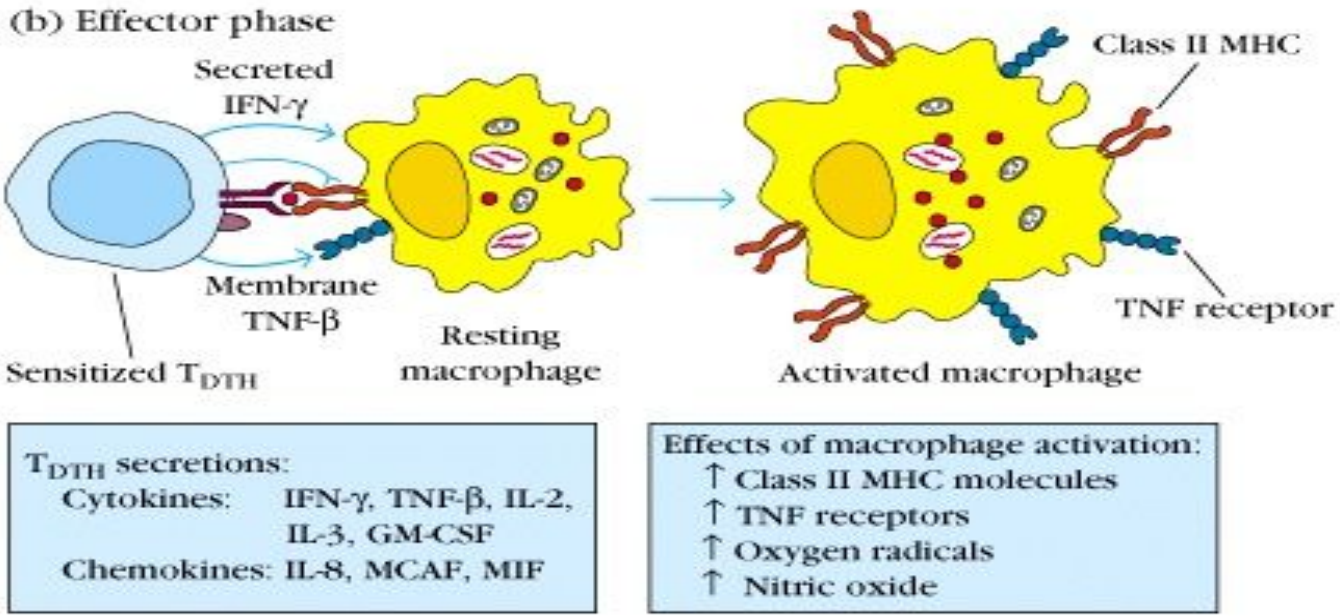


Development of type IV hypersensitivity response

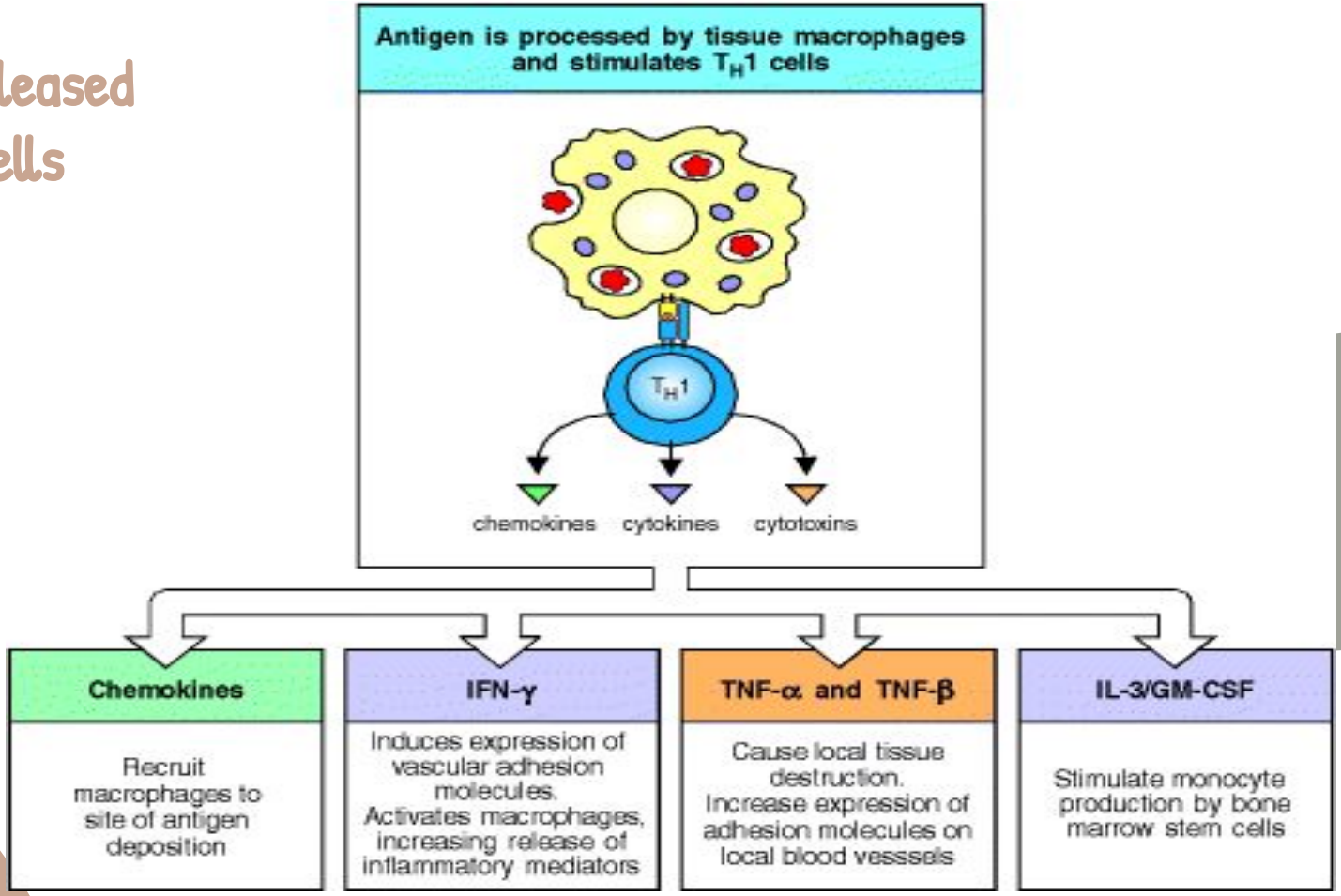
Sensitized T-DTH secretes chemical mediators to (activate macrophages) that act non-specifically.

Chemical mediators :
-Chemokine
-IFN-γ
-TNF α & β
-IL-3/GM-CSF

Macrophage activation increases the following :
-MHC Class II
-TNF receptors
-ROS
-Nitric Oxide



Mediators released by TDTH cells



Take Home massages

1

Type I (IgE), II (IgG) and III (IgG) hypersensitivity reactions are mediated by antibodies whereas Type IV hypersensitivity reaction is a cell mediated immune response.

2

Hypersensitivity reactions are undesirable, excessive, and aberrant immune responses associated with disorders such as allergy, autoimmunity and chronic inflammation.

MCQs

Q1: In immediate hypersensitivity, normal people produce which antibodies?			
A- IgG	B- IgM	C- IgE	D- IgD
Q2:Type I hypersensitivity is diagnosed by all of the following except:			
A- Skin prick test (SPT)	B- Specific IgE measurement (RAST)	C- Patch test	D- Provocation test
Q3: Mismatched blood transfusion results in which type of hypersensitivity?			
A- Type I	B- Type II	C- Type III	D- Type IV
Q4: Cell mediated hypersensitivity is:			
A- Type I	B- Type II	C- Type III	D- Type IV

1:A
2:C
3:B
4:D

MCQs

Q5: how we can diagnose type III hypersensitivity			
A- Skin prick test	B- Lymphocyte	C- transformation	D- Immunofluorescence
Q6: Food allergies is example of			
A- Type I	B-Type II	C- Type III	D- Type IV
Q7: Which one is secondary mediator			
A- Serotonin	B- Histamine	C- Cytokines	D- Heparin
Q8: Complex-mediated Hypersensitivity			
A- Type I	B- Type II	C- Type III	D- Type IV

5:D
6:A
7:C
8:C

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