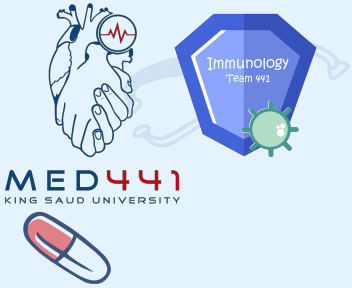
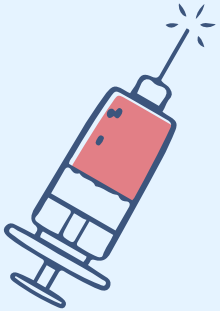
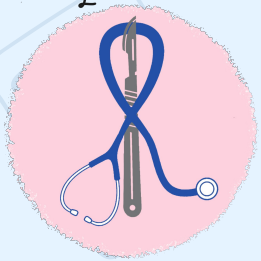


Hypersensitivity



Revised & Reviewed by:
Abdulaziz & Bahammam
Faye Wael Sendi



Colour index:

Main text

IMPORTANT

Drs notes

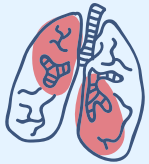
Females slides

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

Everything will be explained in detail

Type I Hypersensitivity

Helpful video
Helpful video

- 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

Atopic >> has allergy
Non-Atopic (non-allergic) >> has NO allergy

Antibody type	IgE
Cellular components	mast cells - basophils - eosinophils
Antigens (Allergens)	pollens - dust mites - animal dander - nuts - shellfish - various drugs

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

★ Low molecular weight
★ High solubility

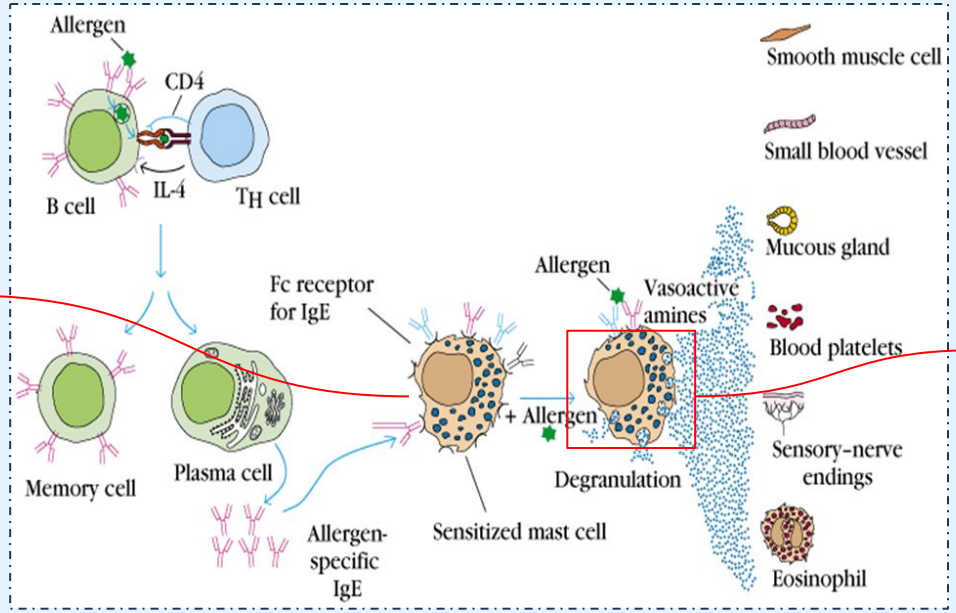
Dust mite

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

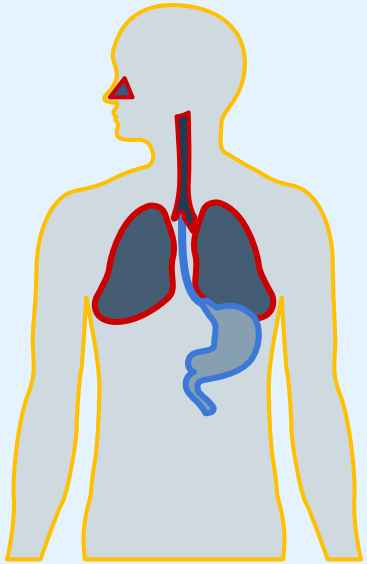
- Allergies can be divided into:

1. Ingested allergies

Food allergy
- Esophagus
- Stomach

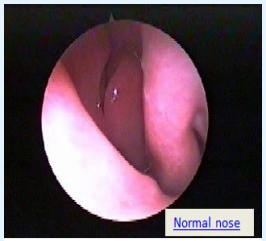
2. Contact allergies

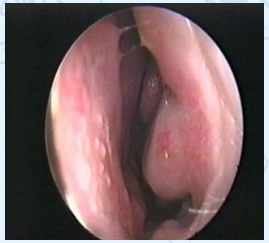
Eczema
Urticaria
Allergic dermatitis
- Skin



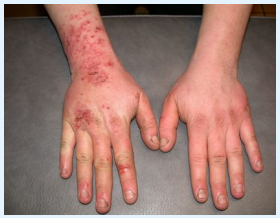
3. Inhaled allergies

Allergic rhinitis
Asthma
- Nose
- Pharynx
- Lungs

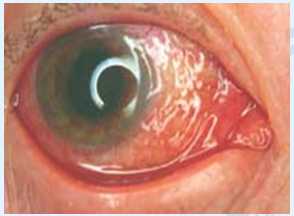




Rhinitis (inflammation of mucous membranes inside the nose)



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)

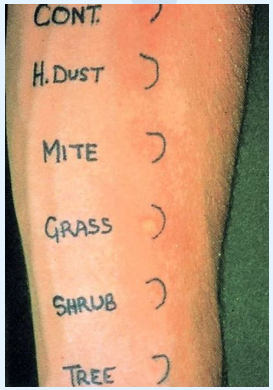
  Venom: poisonous substance secreted by animals

- 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)

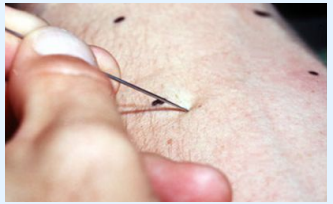
Diagnosis of Allergy

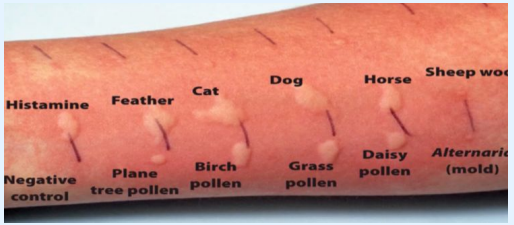
1. Skin prick test (SPT) putting a small amount of allergen on skin then pricking it and waiting 15-20 mins to see if there is any reaction



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





مو موجودة بالسلايدز ولكن شرحها دكتور الأولاد

Primary and Secondary Mediators

Mediator	Effects
	PRIMARY Pre-formed and immediately released
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 Newly synthesized
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

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

Helpful video

Helpful video

Antibody type — IgG (or IgM)

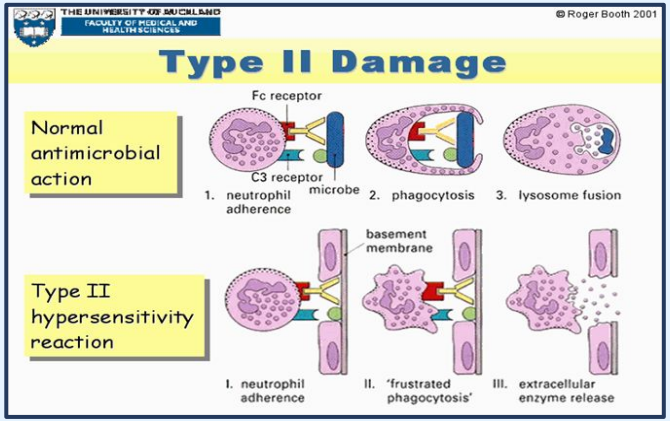
Antigens — bound to cell membranes

- **Self** antigens (autoimmunity)
- **Exogenous** antigens (microbial)

Diagnosis — Detection of antibodies and antigens by Immunofluorescence in tissue biopsy specimens

e.g. kidney, skin etc

★ Special for it's invariable complement activation (constant)

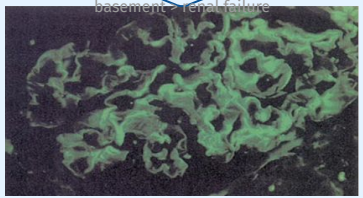


In the normal condition, neutrophils attack microbes as antimicrobial action
But in type II, neutrophils attack the basement membrane like blood vessels

Clinical Examples

Glomerulonephritis (anti-glomerular basement membrane)

Producing antibodies against glomerular basement > renal failure



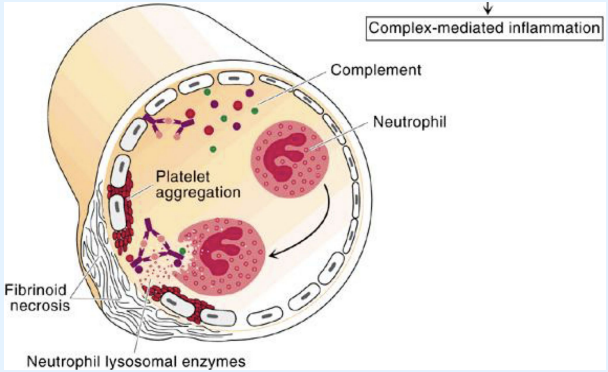
Mismatched blood transfusion

RBCs of donor will be attacked by the immune response of The recipient)

Type III Hypersensitivity (immune-complex mediated)

Helpful video

Antibody type	IgG (or IgM)
Antigen	Free soluble Antigens



439: in the normal state, phagocytes (neutrophils/macrophages) will clear out the immune-complexes after the immune reaction. But in type III reaction, the immune-complexed will be bigger in size so it will be hard for phagocytosis the complexes

Antibody (IgG/IgM) + Free Antigen (soluble)

↓

Immune - complex formation

↓

Complement activation (classical pathway)

↓

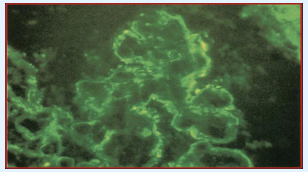
Attraction of inflammatory cells

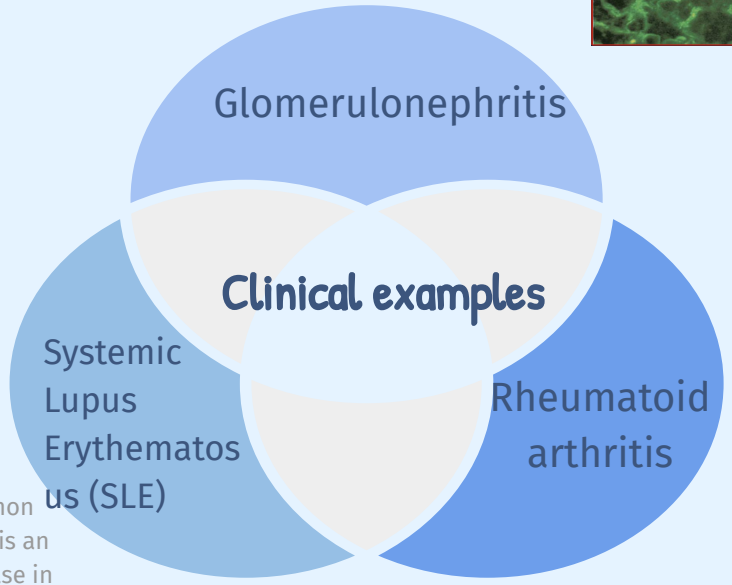
Immune complexes are deposited in tissues like:

- kidneys (nephritis)
- joints (arthritis)
- blood vessels (vasculitis)

Type III Hypersensitivity (immune-complex mediated)

inflammation of the part of the kidneys that filters blood (called glomeruli)





It's the most common type of lupus, SLE is an autoimmune disease in which the immune system attacks its own tissues, causing widespread inflammation and tissue damage in the affected organs

long-term autoimmune disorder that primarily affects joints

Diagnosis

- Demonstration of specific immune complexes in the blood or tissues by: Immunofluorescence

Type IV (Delayed Type Hypersensitivity) DTH

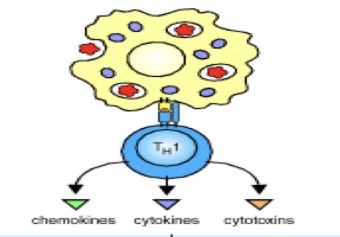
Helpful video

Antibody type	No antibodies (Cell-mediated)
Cellular components	**CD4** generally and **CD8** occasionally
Antigens	Presented to **T** cells by APCs (involving both MHC classes"I or II")

CD activates macrophages via Th1

Wil be mentioned next slide

Mediators release by T_{DTH} cells



Chemokines

Recruit macrophages to site of Antigen deposition

IFN-γ

- Induces expression of vascular adhesion molecules
- Activates macrophages
- Increasing release of inflammatory mediators

TNF-α , TNF-β

- Cause local tissue destruction
- Increase expression of adhesion molecules on local blood vessels

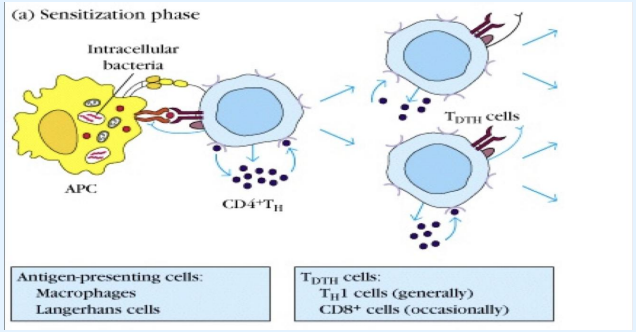
IL-3/GM-CSF

Stimulate monocytes production by bone marrow stem cells

Type IV (Delayed Type Hypersensitivity) DTH

- **Phase I (Sensitization phase)** **1-2 weeks**

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)

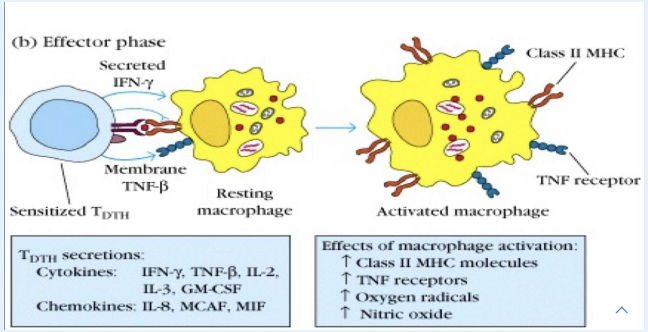


DIFFERENT THAN TYPE I CHALLENGE PHASE !

- **Phase II (Effector phase)** **24-72 hours**

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

Please see previous slide

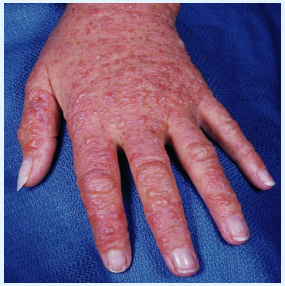


Type IV (Delayed Type Hypersensitivity) DTH

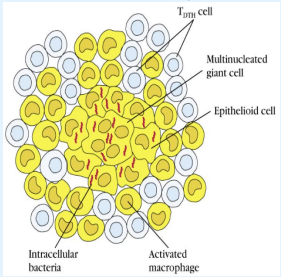
Clinical examples

DIFFERENT THAN TYPE I ALLERGIC DERMATITIS !

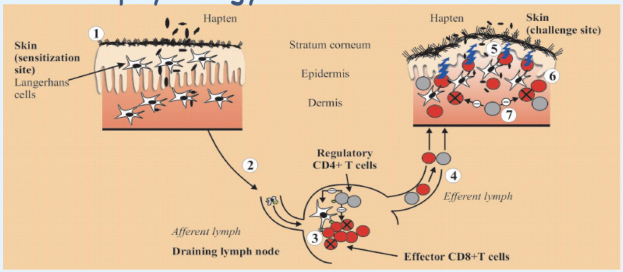
Contact dermatitis



TB granuloma formation (persistent antigen)

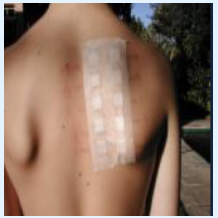


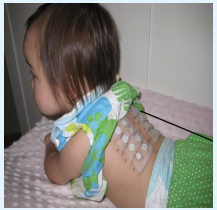
Pathophysiology of Contact dermatitis



Diagnosis

- **Delayed skin test (Mantoux test)**
  The Mantoux skin test consists of an intradermal injection of 0.1 ml of PPD tuberculin (Tuberculin Purified Protein Derivative) for 24-72 hours then measure the diameter of the reaction
- **Lymphocyte transformation test**
  Take Sample of blood on slide, add the antigen and wait to see if, the blood will recognize that antigen or not
- **Patch test (Contact dermatitis)**
  It's done to see if a particular substance is causing allergic reaction or not. In this test, allergens are applied to patches (as seen in picture below) then placed on your skin for 48-72 hours. During this time you should avoid bathing or sweating.





Skin patch Test

Summary video

Summary

	Type I	Type II	Type III	Type IV
Alternative name	Immediate Hypersensitivity; Allergy	Cytotoxic Hypersensitivity	Complex-mediated Hypersensitivity	Cell-mediated Hypersensitivity
Antibody	IgE	IgG (or IgM)	Ag-Ab Complex	N/A (Mediated by T cells)
Mechanism	Allergen causes IgE binding to mast cells and basophils (sensitization) followed by crosslinking and release of vasoactive amines (challenge)	Ab directed against cell surface antigens which mediates cell destruction by complement activation	Ag-Ab complexes deposited in various tissues induce complement activation creating an inflammatory response mediated by neutrophils	"Sensitized" TH1 cells release cytokines that activate macrophages or Tc cells which mediate direct cellular damage (effector)
Examples	-Anaphylaxis -Eczema -asthma -Rhinitis -Urticaria -Food allergies	-Mismatched Blood transfusion -Glomerulonephritis (anti-glomerular basement membrane)	-Necrotizing vasculitis -Glomerulonephritis (Rheumatoid Arthritis) -SLE	-Contact Dermatitis -Tb granuloma
Diagnosis	-Skin prick test (SKT) -Specific IgE measurement (RAST) -Elimination/ Provocation test	-Immunofluorescence	-Immunofluorescence	-Delayed skin test -Patch test -Lymphocyte transformation

Take Home Messages

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

Q1-A , Q2-C , Q3-B , Q4-D

MCQs

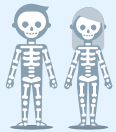
Q5: how we can diagnose type III hypersensitivity			
A- Skin prick test	B- Lymphocyte	C- transformation	D- Immunofluorescence
Q6: Food allergies is example of			
A- Type I	B-Type II	C- Type III	D- Type IV
Q7: Which one is secondary mediator			
A- Serotonin	B- Histamine	C- Cytokines	D- Heparin
Q8: Complex-mediated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

Q5-D, Q6-A, Q7-C, Q8-C

Special thanks and gratitude to
Immunology Team (439)

Team leaders:

Yara Almufleh - Ibrahim Alahmadi



Team members:

- Sarah Alhamlan
- Sahar Hakami
- Maram Alenazi
- Lama Bin Salamh
- Rahaf Alrayes
- Areej Altamimi
- **Leen Alhadlaq**
- Shaimaa Alqaoud
- Rahmah Alzahrani
- Aisha Alhamed
- Abdulaziz Annab
- Firas Alqahtani
- **Mohammed Alfaris**
- Turki Alkhalifa
- Abdulaziz Ayman

Immunology441@gmail.com