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Submitted to:

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Subject:

PATHOLOGY & MICROBIOLOGY

Hypersensitivity reactions:
immunopathology

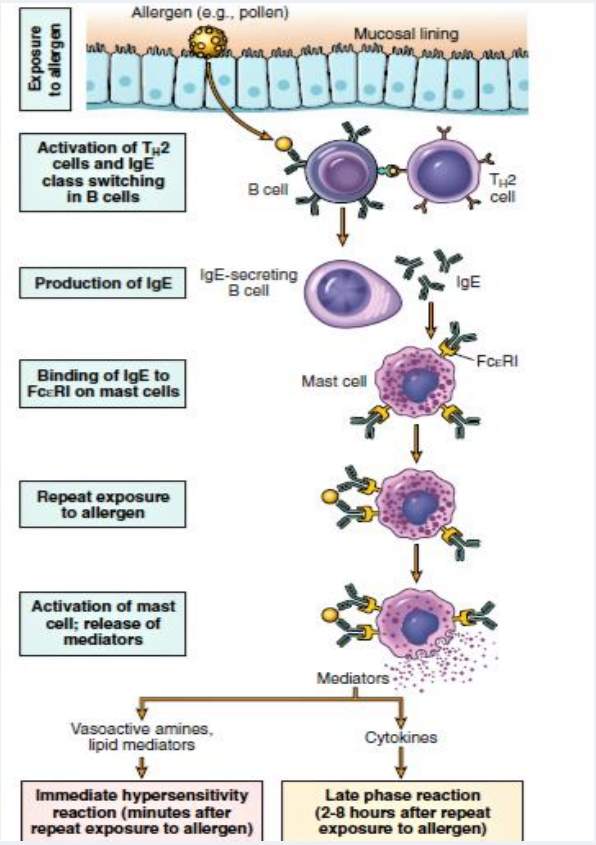
INTRODUCTION

Hypersensitivity reactions (HR) are immune responses that are exaggerated against any antigen or foreign harm full particle or allergen.
These are classified into four types according to the response.

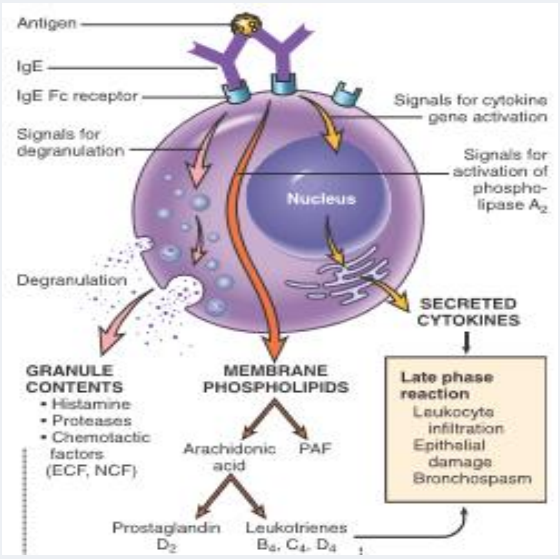
- HR type I or Anaphylactic Response.
- HR type II or cytotoxic-Mediated Response.
- HR type III or immune-Complex Reactions.
- HR type IV or Cell Mediated Response.

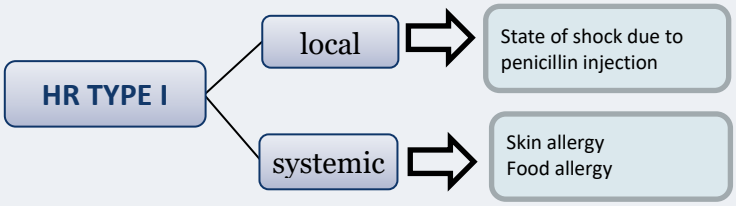
HR TYPE I (ANAPHYLATIC RESPONSE)

- This reaction is immediate (within minutes)
- Antigen and antibody (IgE) bound to mast cells
- Different chemical mediators are release that will cause reactions (histamine, enzymes as proteases, cytokines as TNF)
- The release substance has potential to cause tissue damage.
- HR type I can be systemic or local.



Action	Mediators
Vasodilation, Inc. permeability	Histamine, PAF Histamine PAF, Leukotrienes C_4, D_4, E_4 Neutral proteases that activate complement and kinins Prostaglandin D_2
Smoot muscle spasm	Leukotrienes C_4, D_4, E_4 Histamine Prostaglandins PAF
Cellular infiltration	Cytokines, e.g., TNF Leukotriene B_4 Eosinophil and neutrophil chemotactic factors





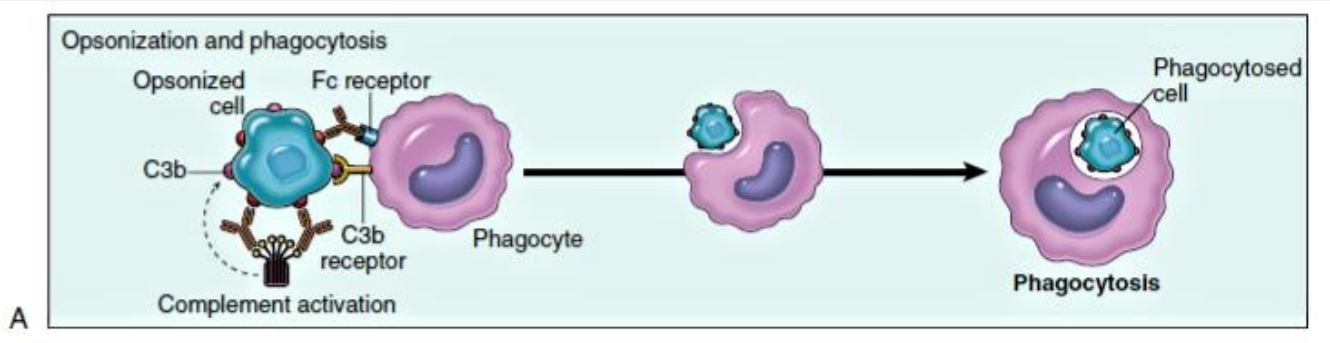
HR Type II (CYTOTOXIC-MEDIATED RESPONSE)

- The antibody reacts directly with the antigen that is bounded to the cell membrane to induce lysis
- This occur by three mechanisms
  A) Antibody-dependent cellular cytotoxicity (ADCC)
  B) Complement- and Fc Receptor-Mediated Inflammation
  C) Antibody-Mediated Cellular Dysfunction

- **Antibody-dependent cellular cytotoxicity (ADCC)**
  - opsonization and phagocytosis
  - It requires the cooperation of leukocytes, and cell lysis occur without phagocytosis

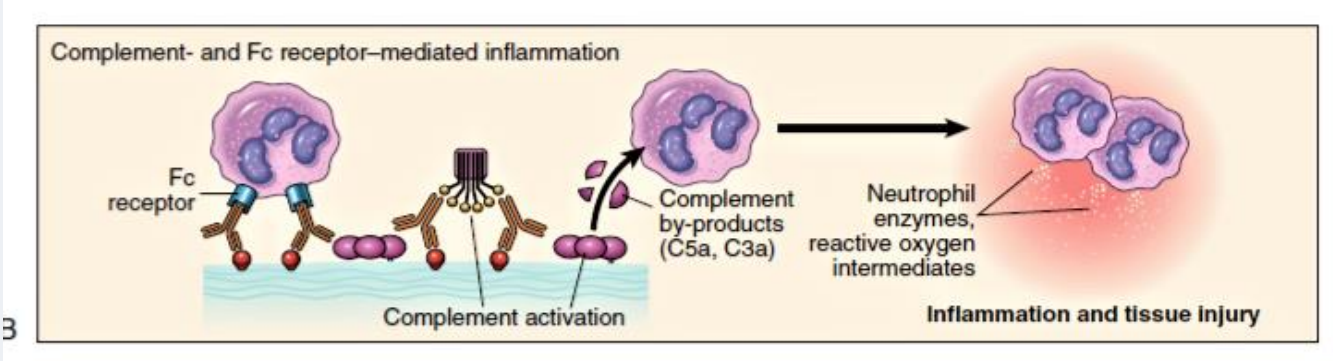
Occur in following situations:

- Transfusion reactions.
- Erythroblastosis fetalis.
- Autoimmune hemolytic anemia, agranulocytosis, and thrombocytopenia.
- Certain drug reactions.



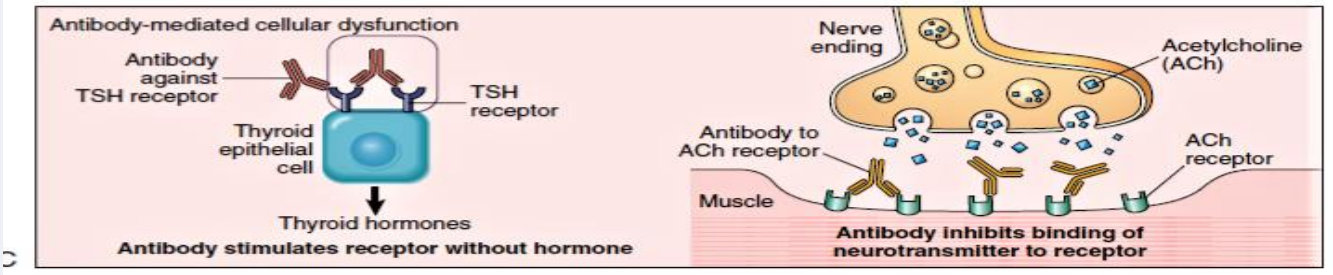
- **Complement- and Fc Receptor-Mediated Inflammation**

  The deposited antibodies activate complement, such as C5a (and to lesser extent C3a and C4a), that recruit neutrophils and monocytes



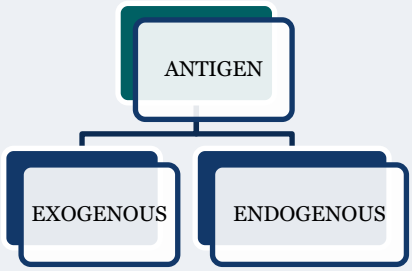
- **Antibody-Mediated Cellular Dysfunction**

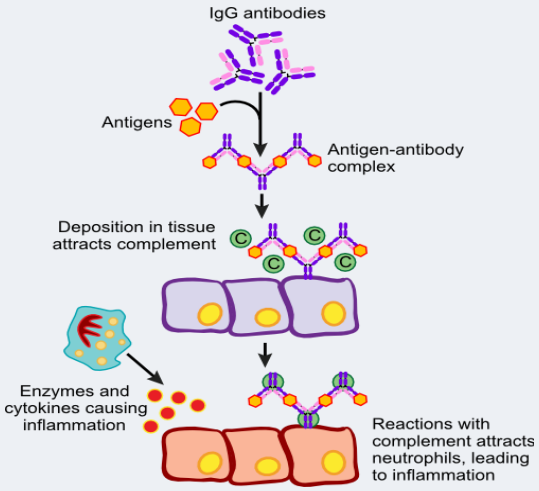
Antibodies directed against cell-surface receptors either impair (Ach receptor in myasthenia gravis), or stimulate (TSH receptor in Graves' disease – thyrotoxicosis) without causing cell injury or inflammation.



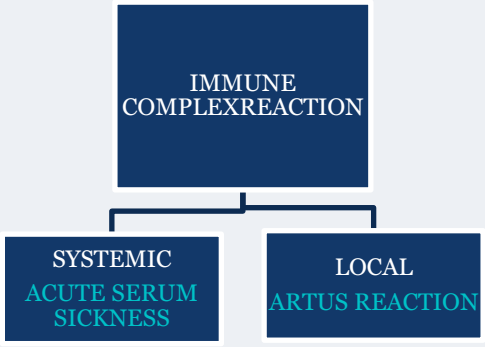
HR Type III (IMMUNE -COMPLEX REACTION)

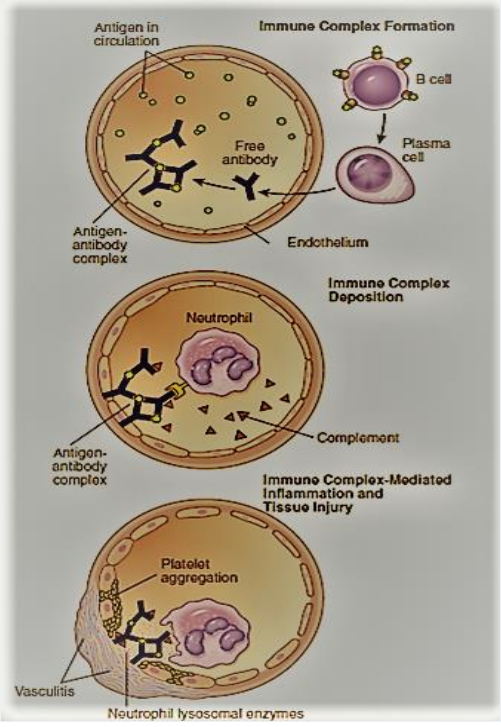
- Antigen combines with antibody within the circulation and deposits.
- At the site of deposit, they elicit inflammation reactions.





ACUTE SERUM SICKNESS	ARTUS REACTION
complexes are deposited in tissues, they initiate an acute inflammatory reaction. Approximately 10 days after antigen administration), clinical features such as fever, urticaria, arthralgia, lymph node enlargement, and proteinuria appear.	A localized area of tissue necrosis resulting from acute immune complex vasculitis, usually elicited in skin.



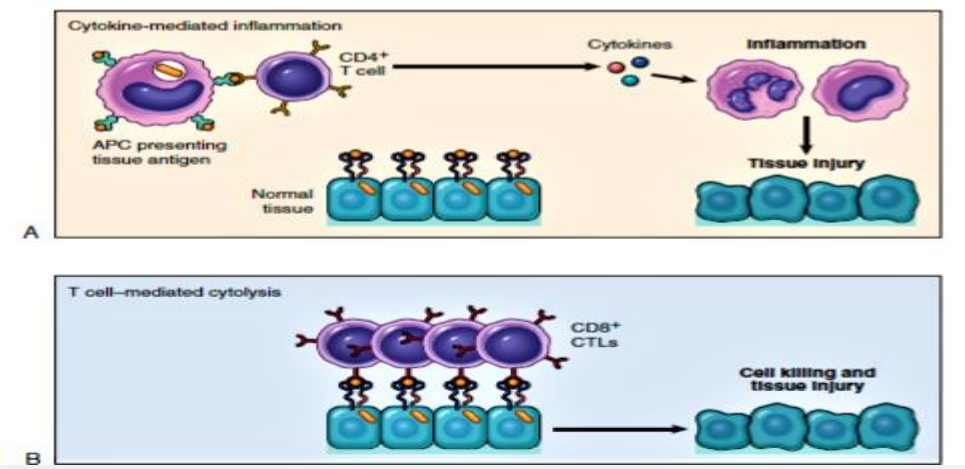


HR Type IV (CELL MEDIATED RESPONSE)

- Is initiated by antigen-activated (sensitized) T-lymphocytes.
- It includes:
  A) Delayed type hypersensitivity (mediated by CD4+ (helper) T-lymphocytes)
  B) Direct cell cytotoxicity (mediated by CD8+ (cytotoxic) T-lymphocyte.

- It is the principal pattern of immunologic response to a variety of intracellular microbiologic agents such as
- Mycobacterium tuberculosis, also to many viruses, fungi, protozoa, and parasites.
- Graft rejection is another instance of cell-mediated reaction.
- Also involved in tumor immunity.

Delayed type hypersensitivity	Direct cell cytotoxicity
Tuberculin reaction: Produced by intracutaneous injection of tuberculin (a protein-lipopolysaccharide component of tubercle bacillus). In previously sensitized individual, reddening and induration appear in 8 to 12 hours, reach a peak in 24 to 72 hours and thereafter slowly subside	Sensitized CD8+ T cells kill antigen-bearing target cells. Such effector cells are called cytotoxic T- lymphocytes (CTLs). Two principal mechanisms of T cell-mediated damage: 1. Perforin- granzyme -dependent killing. 2. Fas-ligand-dependent killing



Mnemonic: "ACID"

Hypersensitivity Reaction	*Description*
Type I **IgE-mediated; quick onset after exposure** **A**llergic	Bee stings Latex Certain medications (e.g. Penicillin)
Type II **Cytotoxic/antibody-mediated** **C**ytotoxic	Hemolytic reactions Goodpasture syndrome Hyperacute graft rejection
Type III **Immune complex/IgG/IgM mediated** **I**mmune complex deposition	Hypersensitivity pneumonitis Systemic lupus erythematosus Polyarteritis nodosa Serum sickness
Type IV **Delayed or cell-mediated** **D**elayed	Chronic graft rejections PPD test Latex Nickel Poison ivy

Reference

- Lecture
- Robin pathology
- https://www.dentalcare.com/en-us/professional-education/ce-courses/ce1/types-of-hypersensitivity-reactions