LECTURE IV

Antigens, their types. Human immune system, organs and tissues, immunocompetent cells. Immune response, cooperation of immunocompetent cells in the immune response. Immune response. Antibodies. Serological reactions. Immunopathology, immunodeficiency, autoimmune diseases, hypersensitivity reactions.

Immunoprevention, immunotherapy

Antigens

- Genetically foreign substances stimulating specific immune responses(synthesis of antibodies, specific cellular immune response) are called antigens.
- Antigens may be both chemically pure (plasma albumin, egg albumin, purified microbial toxin) as well as complex drugs, cells, and tissues.

Antigens

- Antigens are commonly proteins.
- However, complex polysaccharides, lipopolysaccharides, polypeptides, some artificial polymeric compounds have antigenic properties as well.

Properties of antigen:

- **Foreigness**– the main feature of antigen. An antigen must be a foreign substance for organism.
- However, antigenic determinants of genetically nonrelated animals or biopolymers may have similarities. They are called ***cross antigens***.
- The antigens of some microorganisms are not recognized by immune factors because they are similar to the antigens of the human body. This phenomenon known as antigenic mimicry.

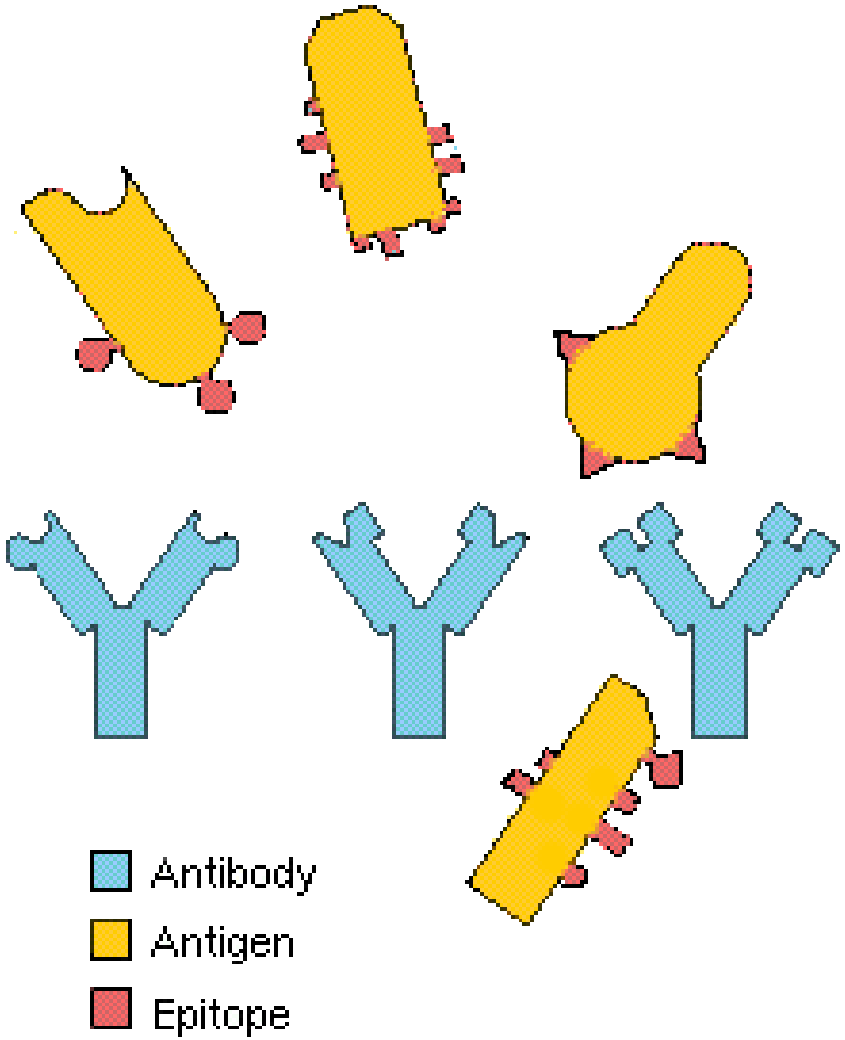
Xeno-, allo-, izoantigens

- ***Xenoantigens*, or *heterophil antigens*** – are the same for organisms of same genera, species.
- ***Allogens*, or *group antigens*** are the same for genetically different same species. Based on alloantigens the population of organisms can be grouped to different groups. Exp., blood group antigens.
- ***Isogenous*, or *species antigens*** are the same only for genetically identical organisms, exp. Siamese twins, inbreeding animals, genetic clones.

Properties of antigen:

- **Antigenicity**– ability to induce antibody production.
- Only specific sites of antigen molecule called antigen determinants or epitopes provide antigenicity by inducing antibody production and binding with them.
- Each antigen has one or more antigenic determinants. The majority of antigens have many epitopes in other words they are multivalent.

Epitopes



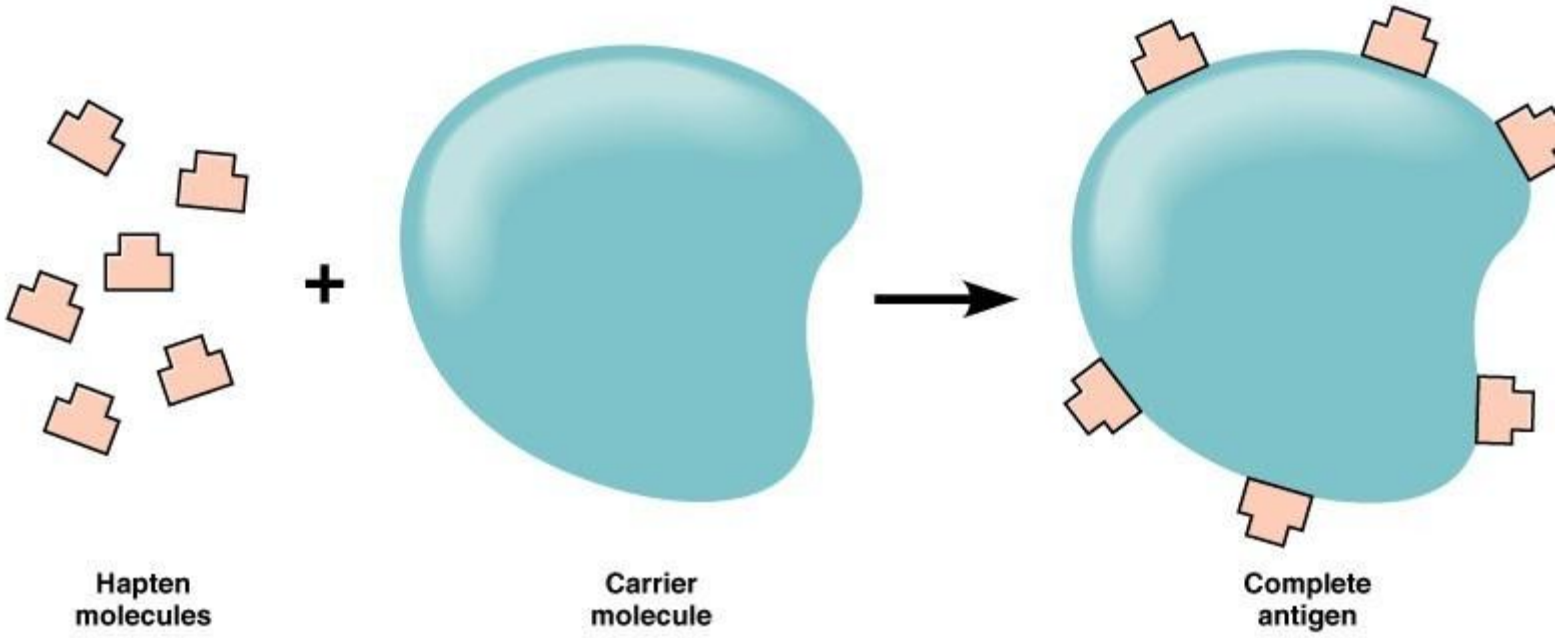
Properties of antigens:

- **Immunogenicity** –ability of antigen to form immunity.
- Immunogenicity depends on molecular structure of antigen and reactivity of macroorganism.
- Despite similarities antigenicity and immunogenicity they are different phenomenons. For example, bacterial dysentery agents have high antigenicity, however they do not form strong immunity, ie they have weak immunogenicity.

Haptens

- ***Haptens***, or inncomplete antigens have antigenicity and weak immunogenicity.
- They are small nonproteinic molecules that elicit an immune response only when attached to a large carrier such as a protein

Haptens



Properties of antigens

- **Specificity**– ability of antigen to elicitspecific immune response.
- Interactions between antigens and antibodies have high specificity. This feature is used in diagnosis of microorganisms in diagnostic laboratories.
- Strength of antibody-antigen connection– affinity vary in proportion with the similarity of their binding sites. Antigens differ in their affinity.

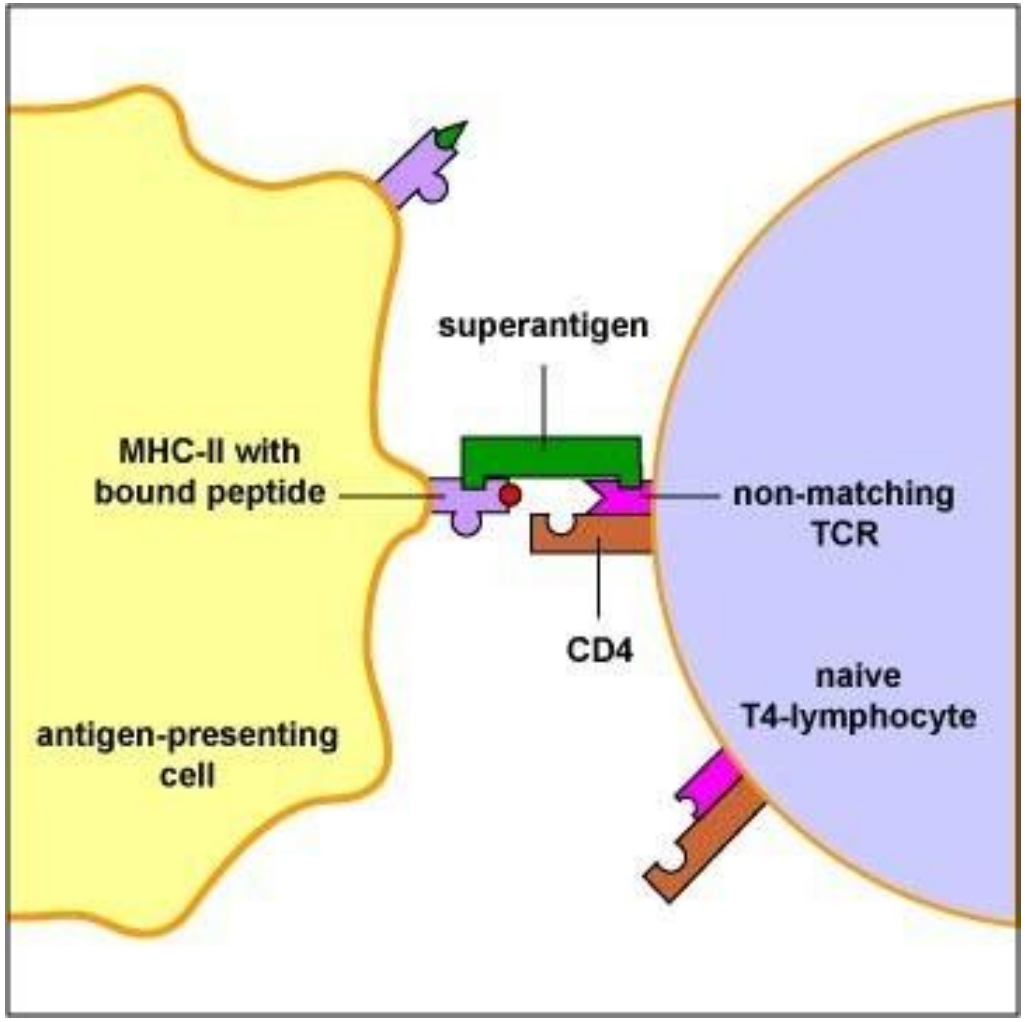
Immunogens, tolerogens and allergens

- ***Immunogens*** cause productive infection accompanied with release of immunity factors (antibodies, antigen reactive lymphocyte clones).
- - *T-dependent antigens*
  - *T-independent antigens*
- ***Tolerogens*** – induce tolerancy or areactivity in macroorganism. Tolerogenic molecules are characterized by high dispersion due to their monomerism, small molecular weight, high density of epitopes.
- ***Allergens*** do not differ from immunogens and cause immediate or delayed hipersensitivity reactions.

Superantigens

- Some antigens can activate T-helpers without APC and T-helper cooperation.
- These molecules called s***uperantigen***s can bind to MHC II-TCR complex and form false signal.

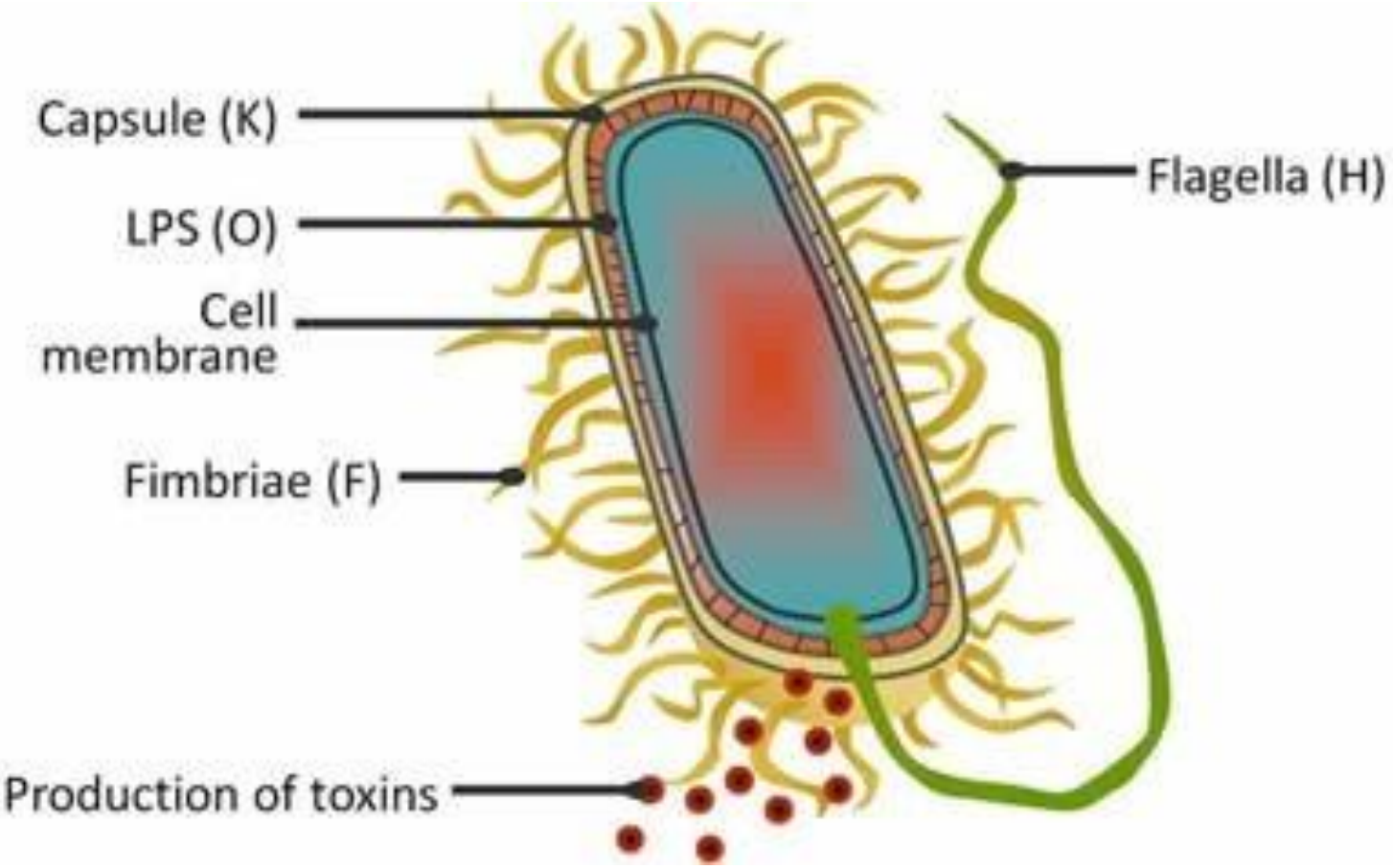
Superantigens



Microorganism antigens

- Bacterial antigens
- *Flagella antigen, or H-antigen*
- *Somatic, or O-antigen*
- *Capsule*, or *K-antigen*
- *virulency antigen*, or *Vi-antigen*
- *Exotoxins, enzymes*
- Viral antigens
- *Virus specific antigens*

Bacterial antigens



Human organism antigens

- *Erythrocyte antigens*
- *ABO system antigens*
- *rhezus-antigens*
- *Major Hystocompatibility Complex –MHC (Human Leukocyte Antigen* - HLA) antigens
- 2 types of MHC antigens.
- I.class MHC exist in all nucleated cells,
- II.class MHC exist commonly in immune competent cells.

Hystocompatibility antigens

- Tissue compatibility antigens are found on the membranes of all cells in the body.
- Most of them belong to the *Main Hystocompatibility Complex* (*MHC*) antigens.

MHC

- Human MHC abtigen is called HLA as it first was described in leucocytes(*Human Leuкocyte Antigen*).
- HLA synthesis is provided by genes located in the short arm of the 6th human chromosome. Three of these genes - HLA-A, HLA-B and HLA-C - encode MHC class I proteins.
- Some HLA-D loci encode class II MHC proteins (DP, DQ, and DR).
- Locus III is located between I and II loci. The genes that encode the two components of the complement (C2 and C4 are located in this locus.

MHC

- Thus, there are two main classes of MHC molecules. Class I MHC is expressed in all nuclear cells, and Class II MHC is mainly expressed on the surface of immunocompetent cells.
- There are no individuals with the same MHC antigen in the entire human population, in other words, all people differ in these antigens. However, the exception is single-egg twins, as well as genetic clones. Therefore, the compatibility of these antigens in tissue transplantation(relative compatibility), is taken into account.

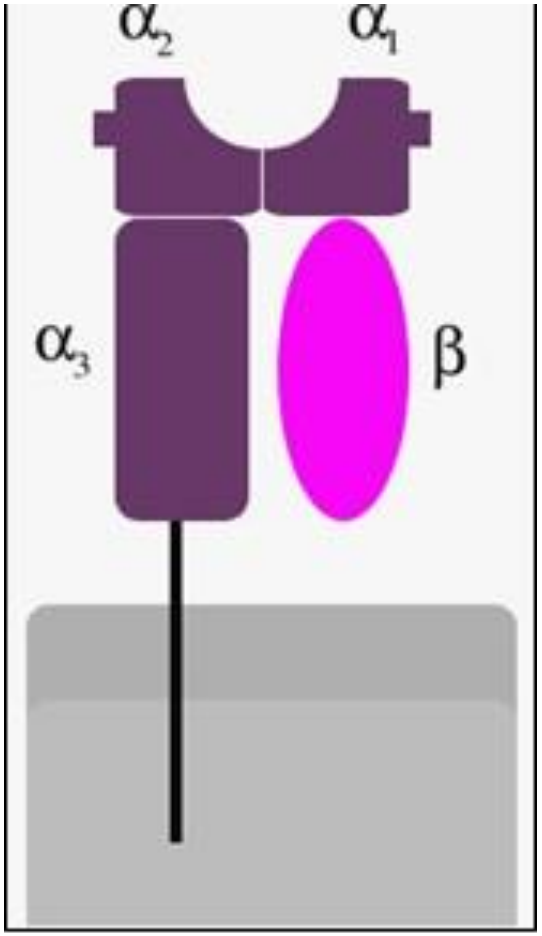
IIclass MHC participate in immune response induction

- This process has several steps:
- Fragments of the antigen molecule are expressed on the surface of APC (dendritic cell, macrophage, etc.) in the form of a complex "class II MHC + antigen".
- This complex is recognized and analyzed by T-helpers (CD4 + lymphocytes).
- When the peptide in a Class II MHC is detected, the T-helper begins to synthesize the appropriate cytokines and the specific immune response mechanism begins to work.

MHC structure and fumctions

- MHC antigens are glycoproteins located on cell membrane
- Some MHC fragments have homologous with immunoglobulins structure

I class MHC proteinləri **glycoproteins located in all nucleated cells**



I class MHC are unique for each individual, biological passport of organism and a "native" markers of immune competent cells.

Viral infections and mutations alter the structure of MHC class I.

- Modified MHC I are cause activation of T-killers($CD8^+$ lymphocytes).
- Thus, cells with altered MHC I are recognized as foreign cells and destroyed.

IIclass MHC

- IIclass MHC proteins are glycoproteins and located on macrophage, T-helper, B-lymphocytes, spleen dendritic cells surface

IIclass MHC differ structurally and functionally from Iclass MHC.

- IIclass MHC are expressed only in specific cell(especially immune competent cells) surfaces.
- IIclass MHC contain peptides obtained by endocytosis and not synthesized in cells, for exp. Viral antigens.

CD-antigens

- Cell membranes have morfofunctionally identical group antigens called markers.
- Markers of immune competent cells are well studied.
- These antigens are called ***CD-antigens (cell differentiation antigen)***. They are structurally glycoproteins and some have immunoglobuline nature.

Specific immunity

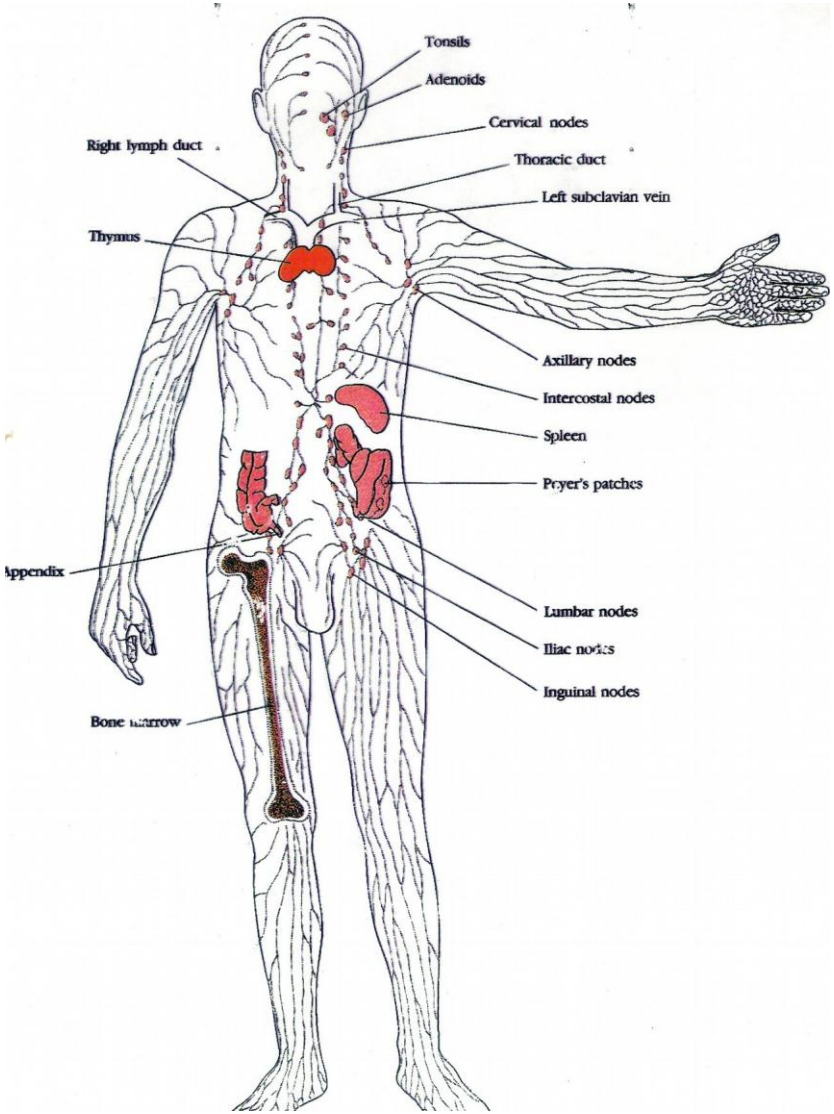
- Depends on type of antigen entering organism with help of special factors.
- Defense factor created for any antigen cannot act on other antigens. Thus, this defense factor is specific

Immune system of organism

- Cells, tissues and organs developing response to genetically foreign substances –immune system of organism. Immune system has three main features:

- It is spread throughout the body;
- It has cells circulating in blood, lymphatic system;
- The immune system has a unique ability to produce antibody molecules, immunoglobulins, which have a very high specificity against various antigens that are genetically foreign.

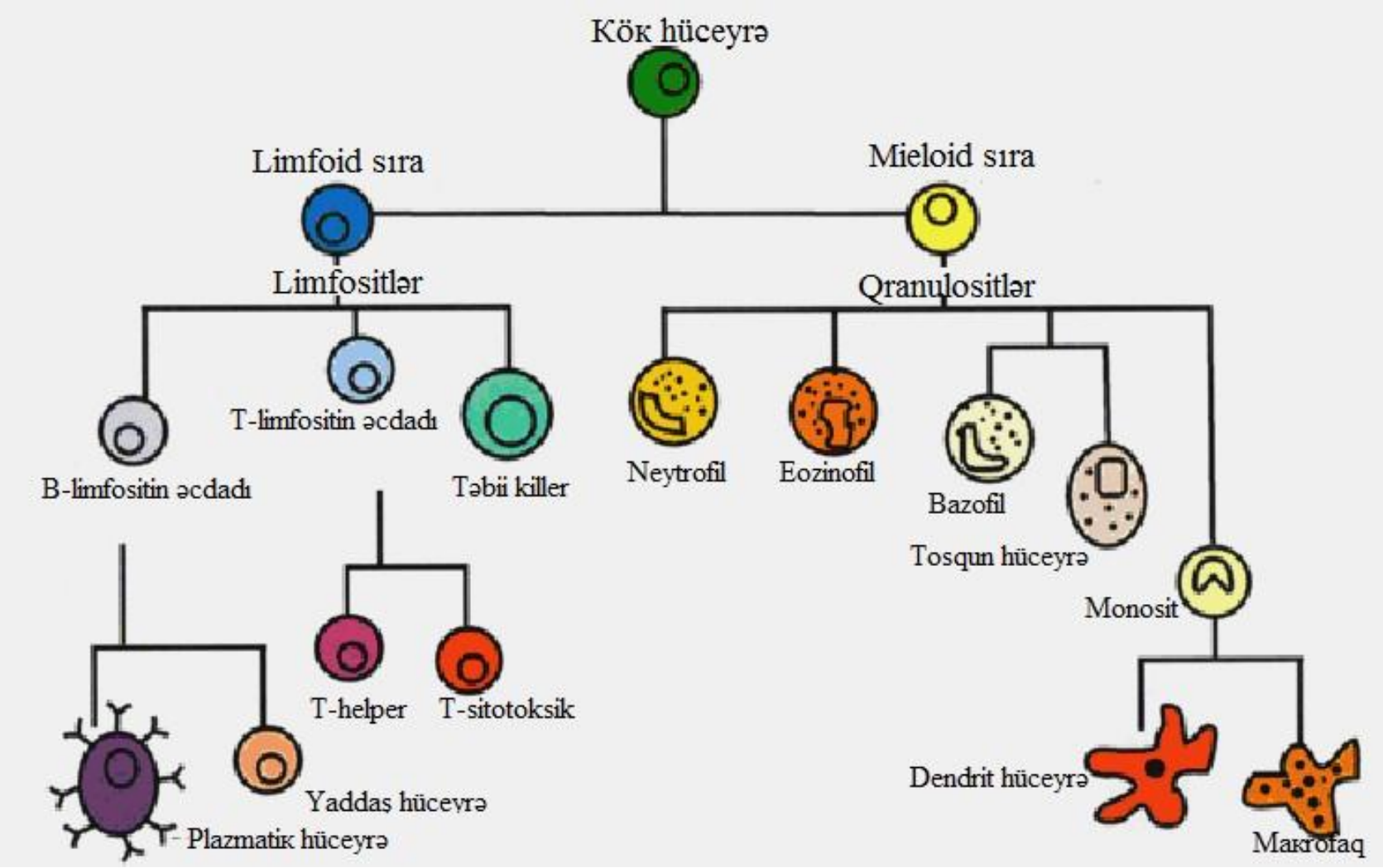
Immune system



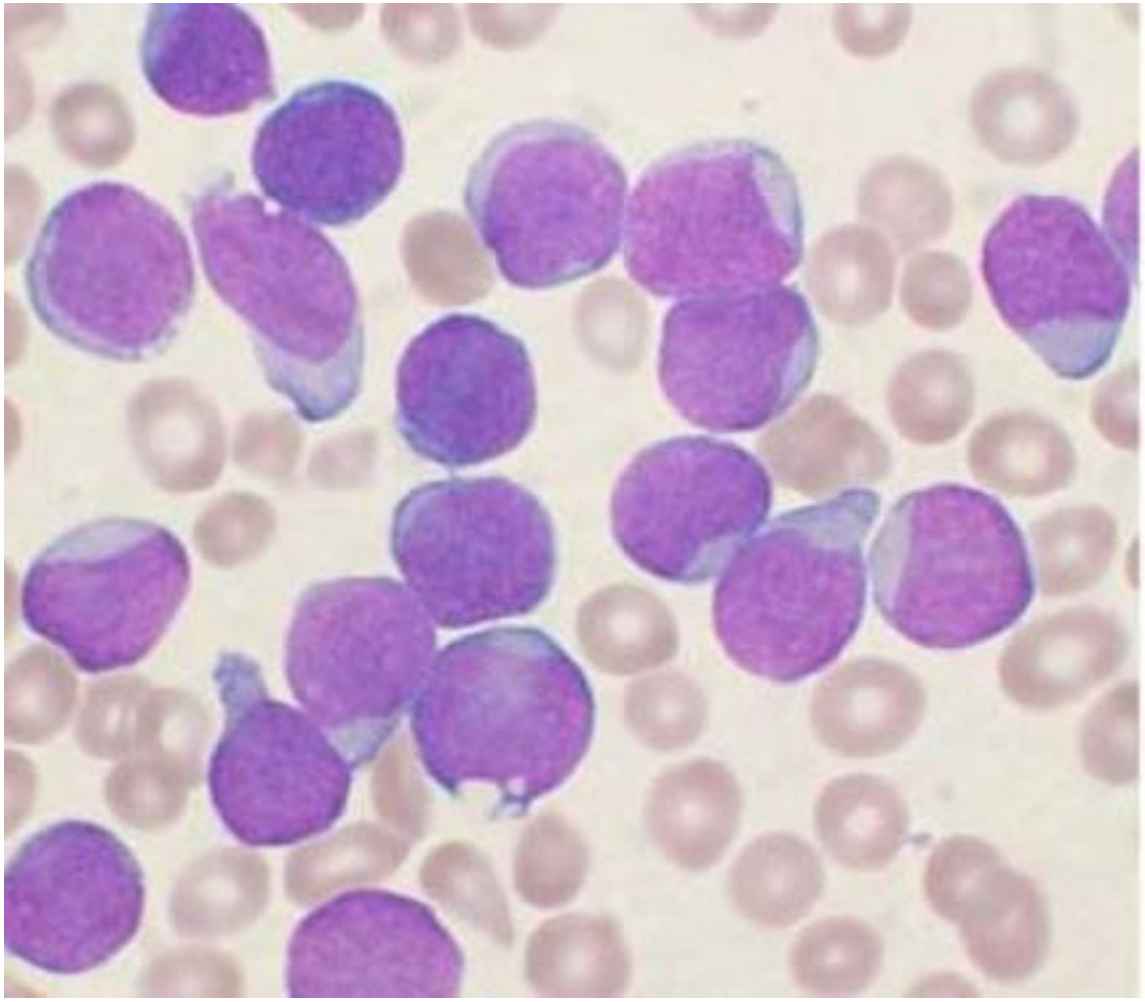
Organs of immune system

- **Central organs of immune system-** support creation and selection of immune cells
- bone marrow, thymus
- **Periferic organs** – control genetic stability of organism
- spleen, lymphatic nodes and follicles

Development of immune system cells



Immune system cells- lymphocytes



Lymphocytes

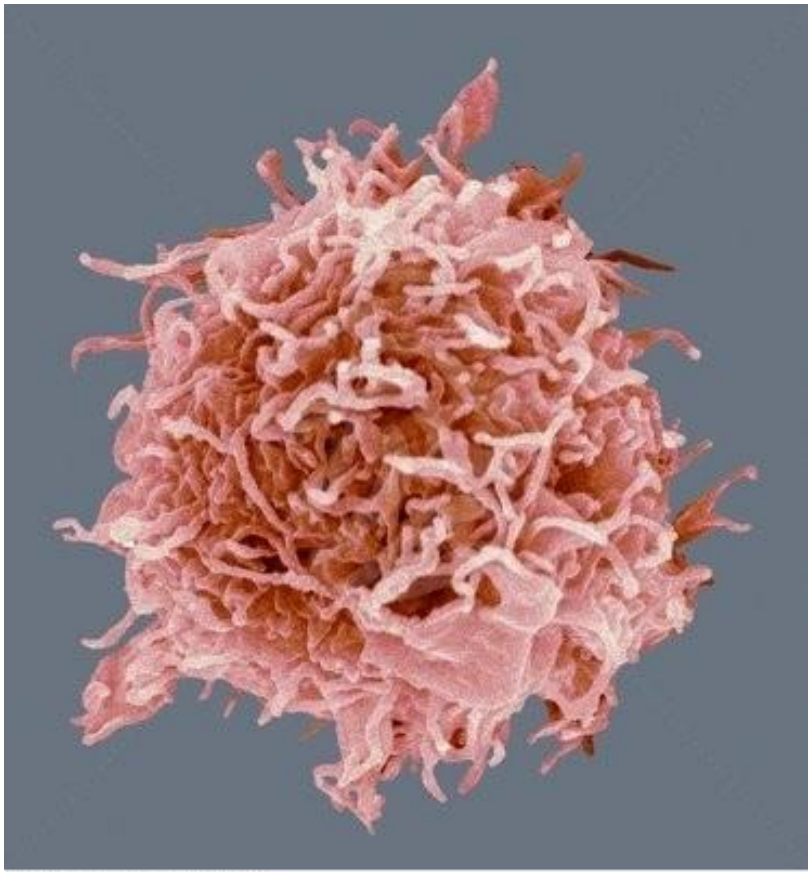
Mature lymphocytes have two subpopulations.

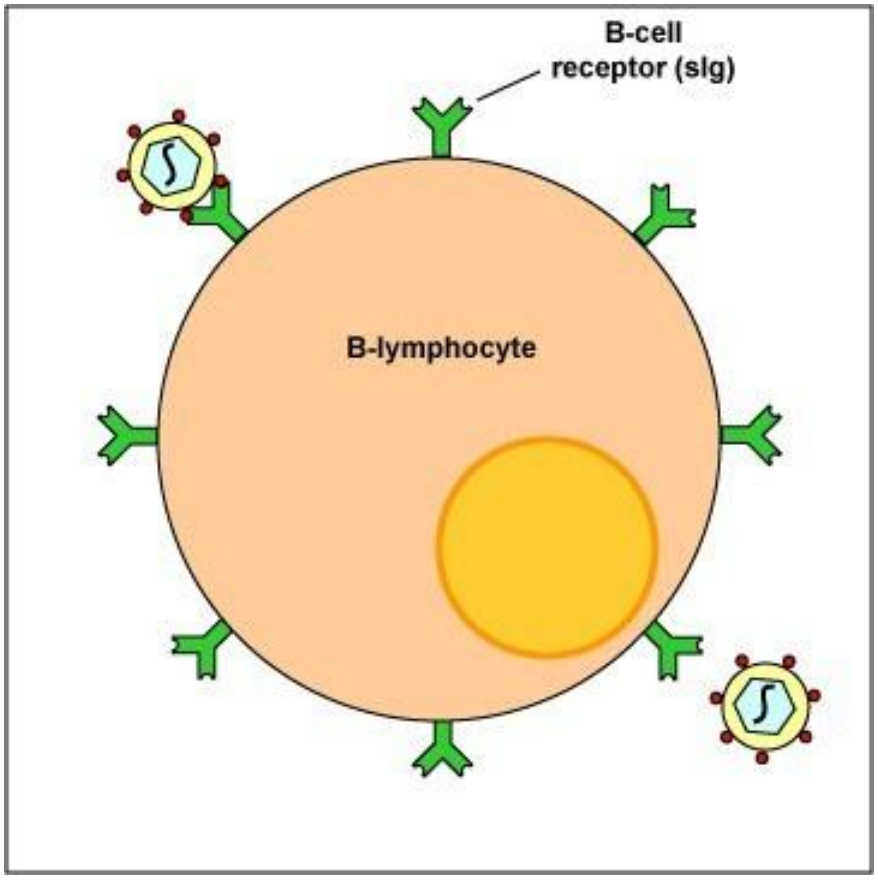
- B **-** lymphocytes
- **T –** lymphocytes
- **O –** lymphocytes

B-lymphocytes and plasmocytes

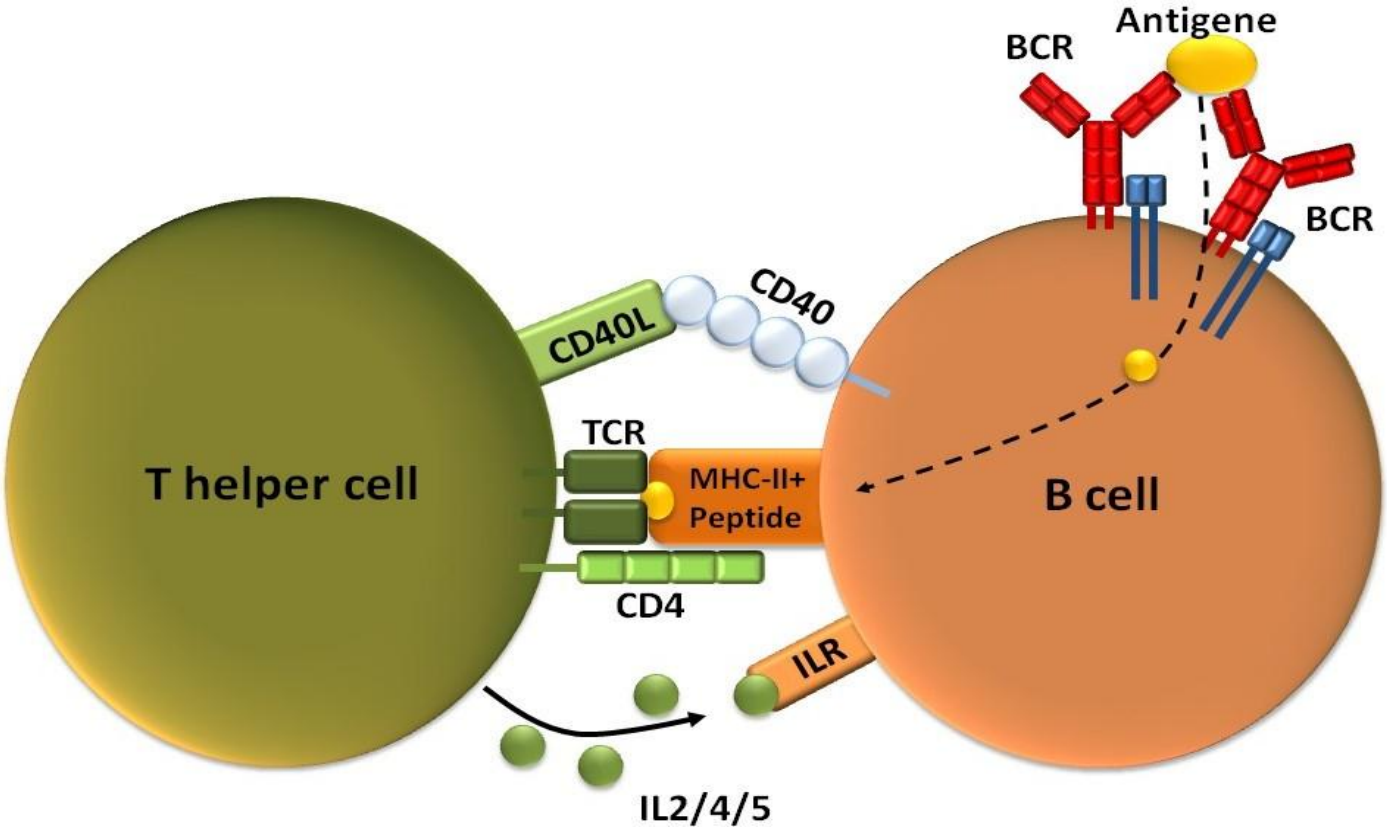
- Create humoral immunity by synthesis of antibodies
- Participate in development of immunological memory
- Participate in immediate type immune responses

B-lymphocytes

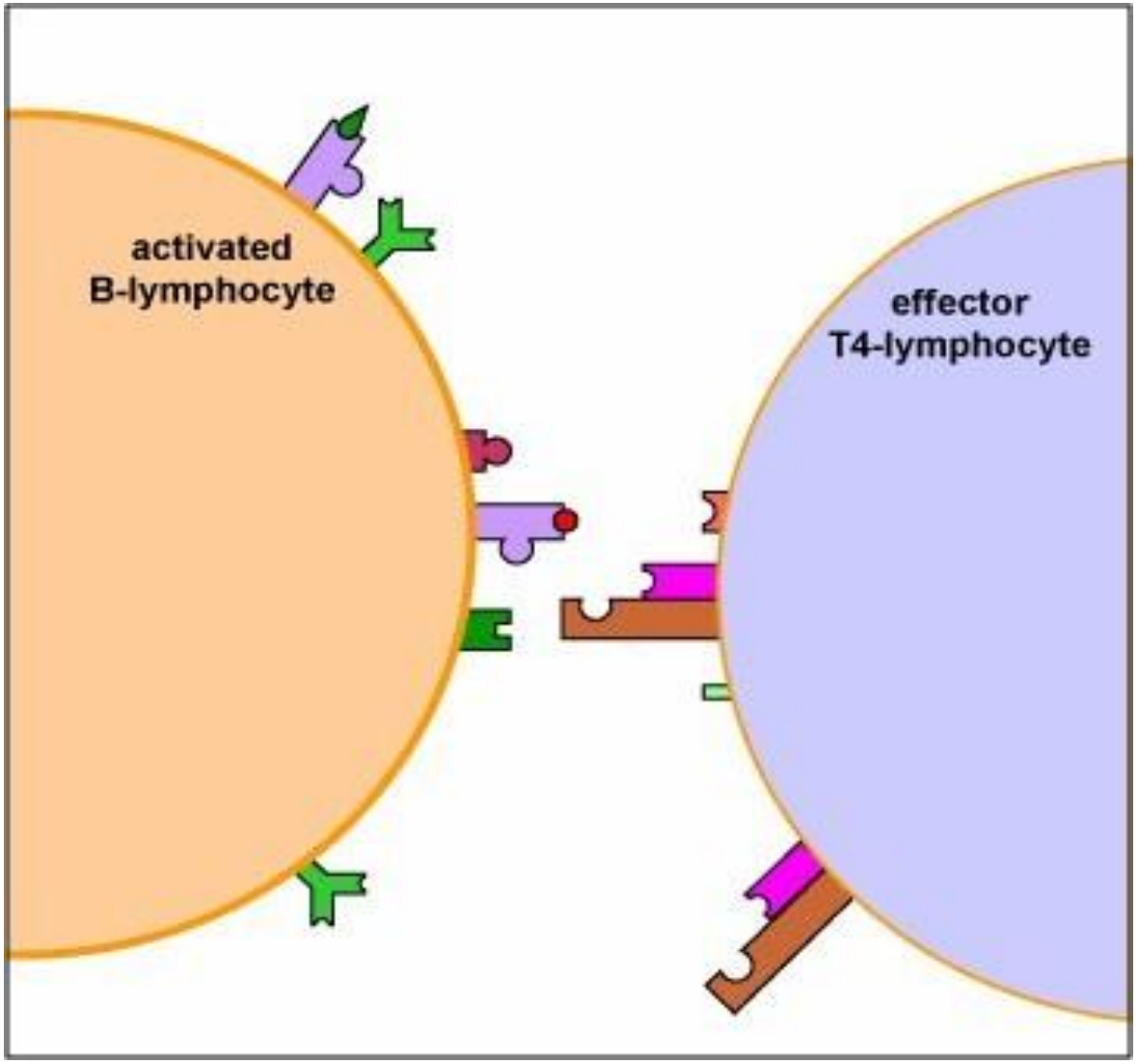




B-lymphocytes recognize antigen in cooperation with T-helpers



B-lymphocytes recognize antigen in cooperation with T-helpers



T-lymphocytes

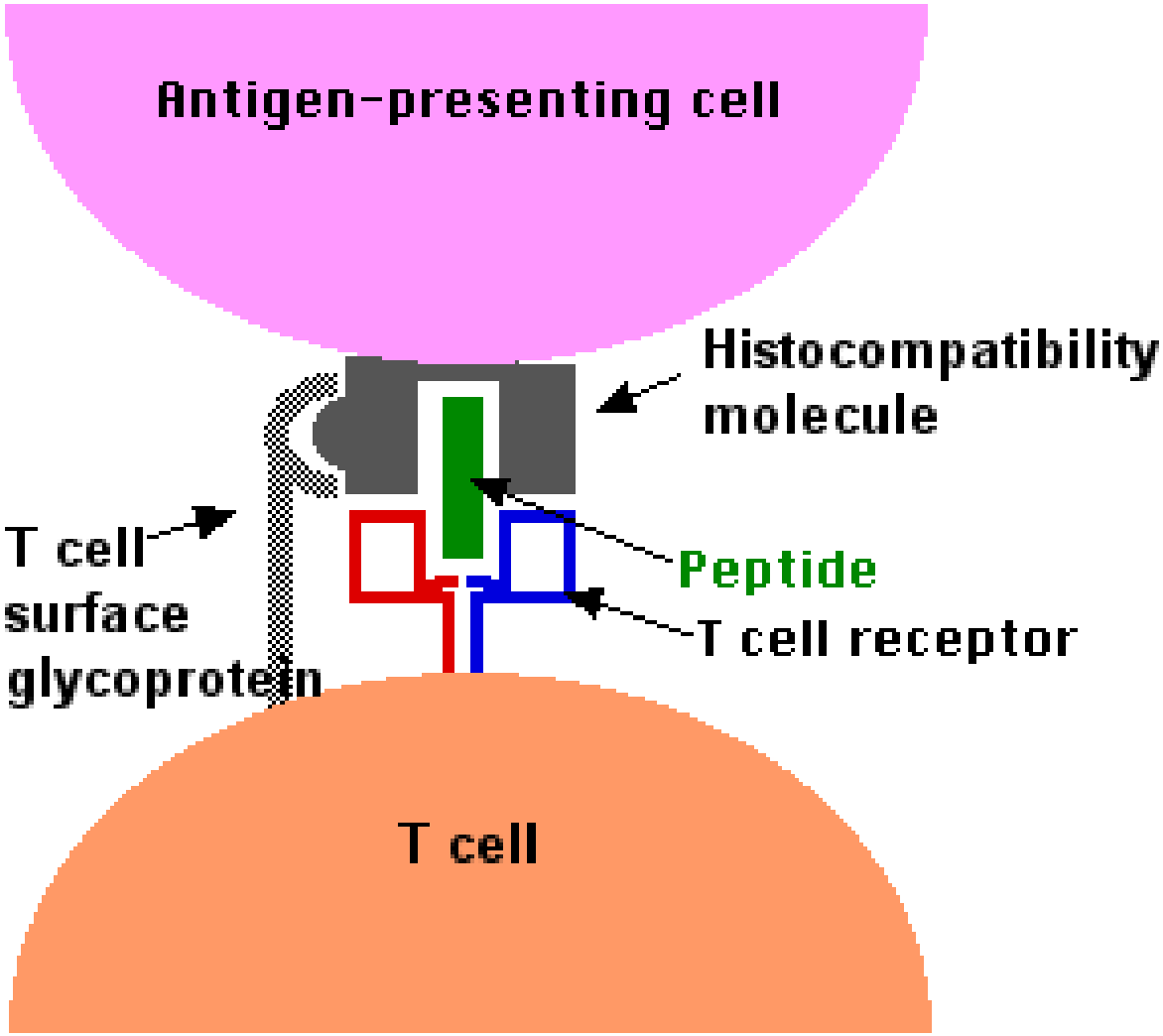
- **T-helpers(CD4)**
- Recognize antigens with help of antigen presenting cells and activate other immune cells
- **T-killers (CD8)**

kill target cells by antibody independent cytotoxicity r

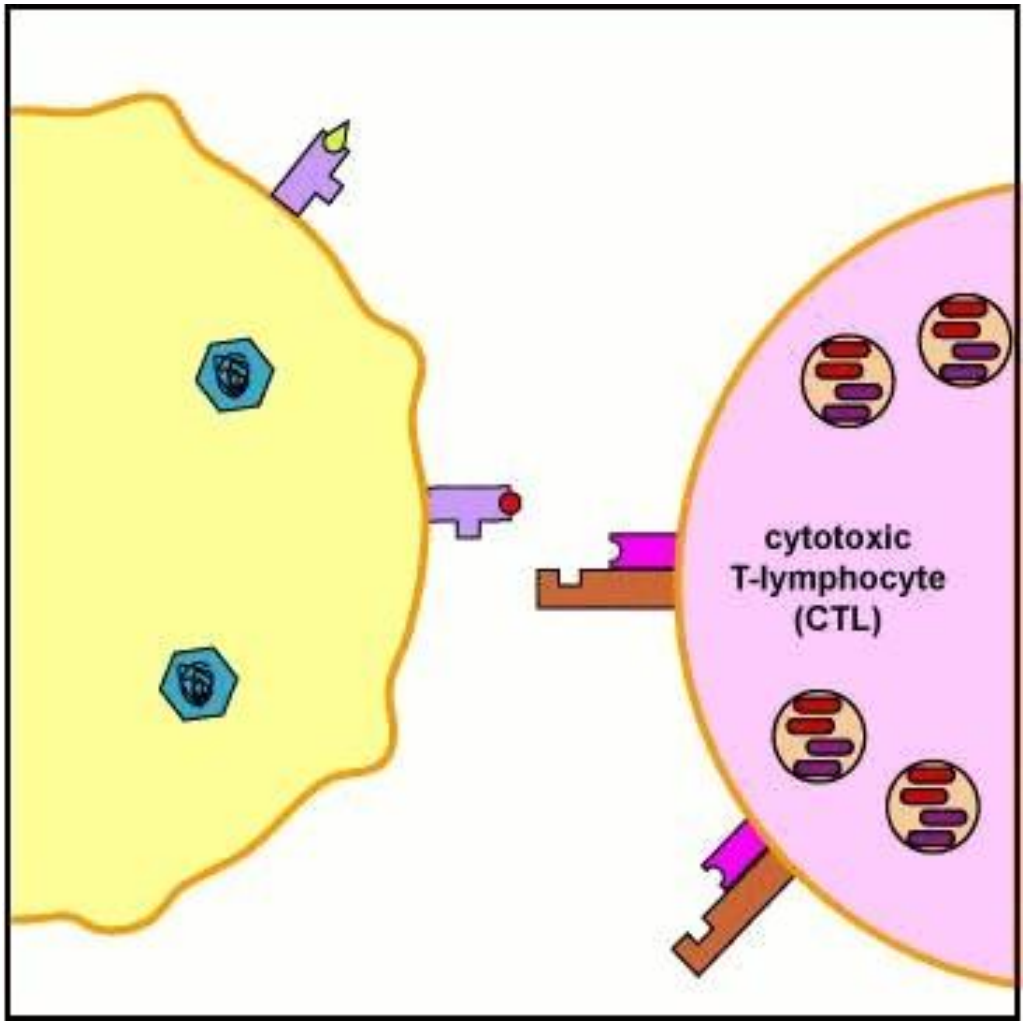
- **T-supressors**

weaken immune response, thus playing immune regulatory role by

T-lymphocytes recognize antigens presented by macrophages



T-lymphocytes (T-killers) destroy target cells by antibody independent citotoxicity



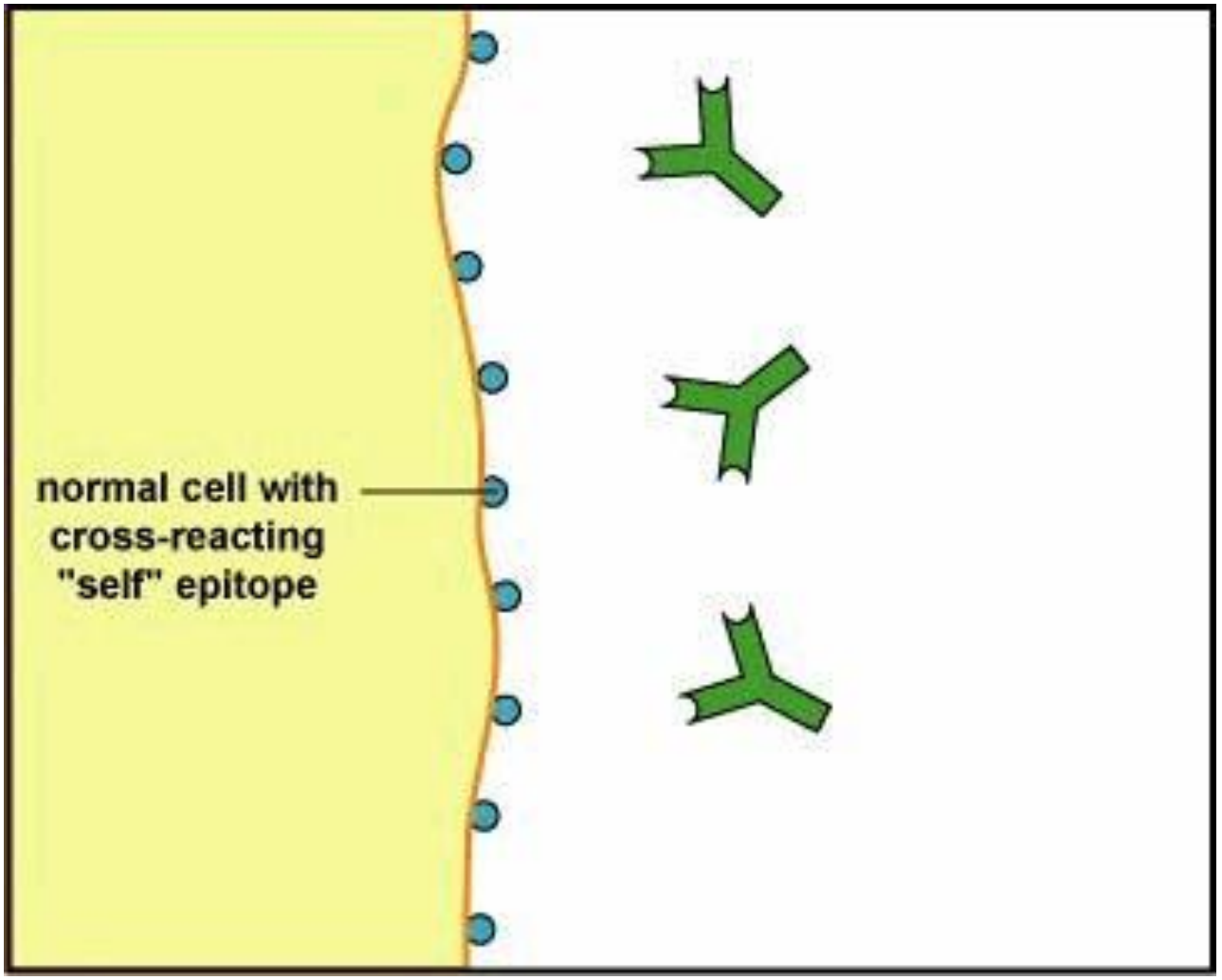
NK-cells

(eng. «natural killer»)

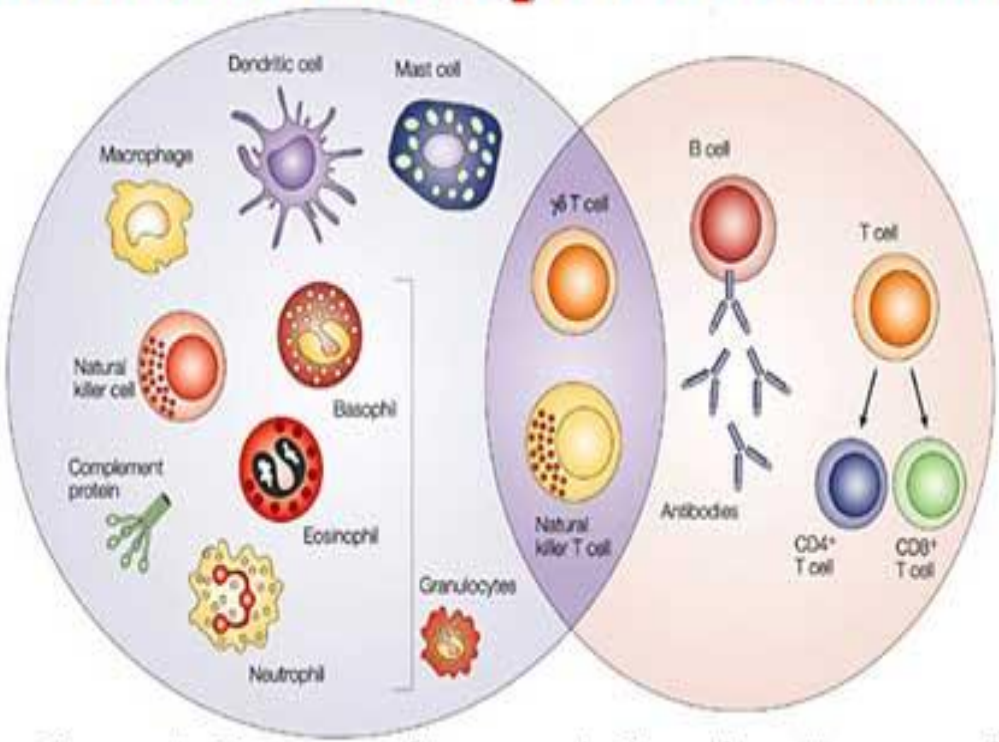
- The main defensive cells against intracellular parazites and genetically foreign cells(tumour cells)
- Act independently from specific immunity
- Destroy target cells by antibody dependent and independent cell citotoxicity

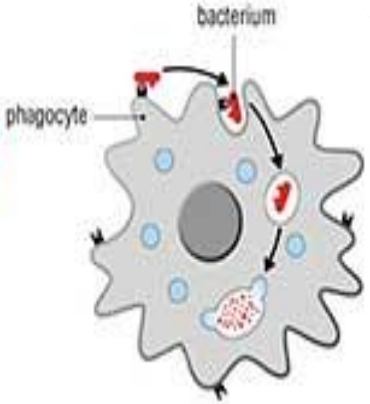
NK-cells attack tumour cells

NK-cells action on target cell



Difference between
Innate and Adaptive Immunity





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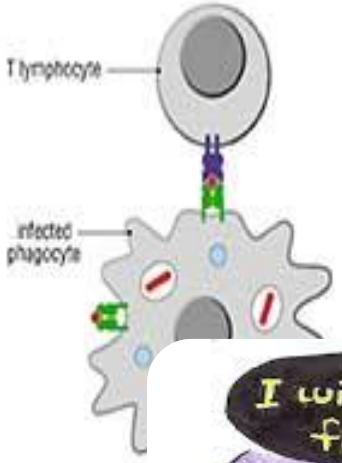
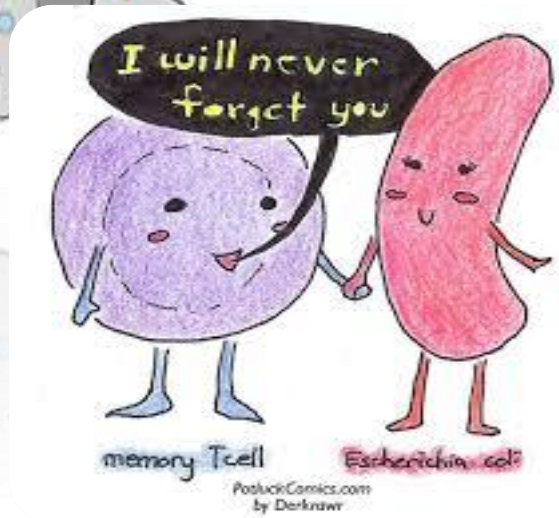
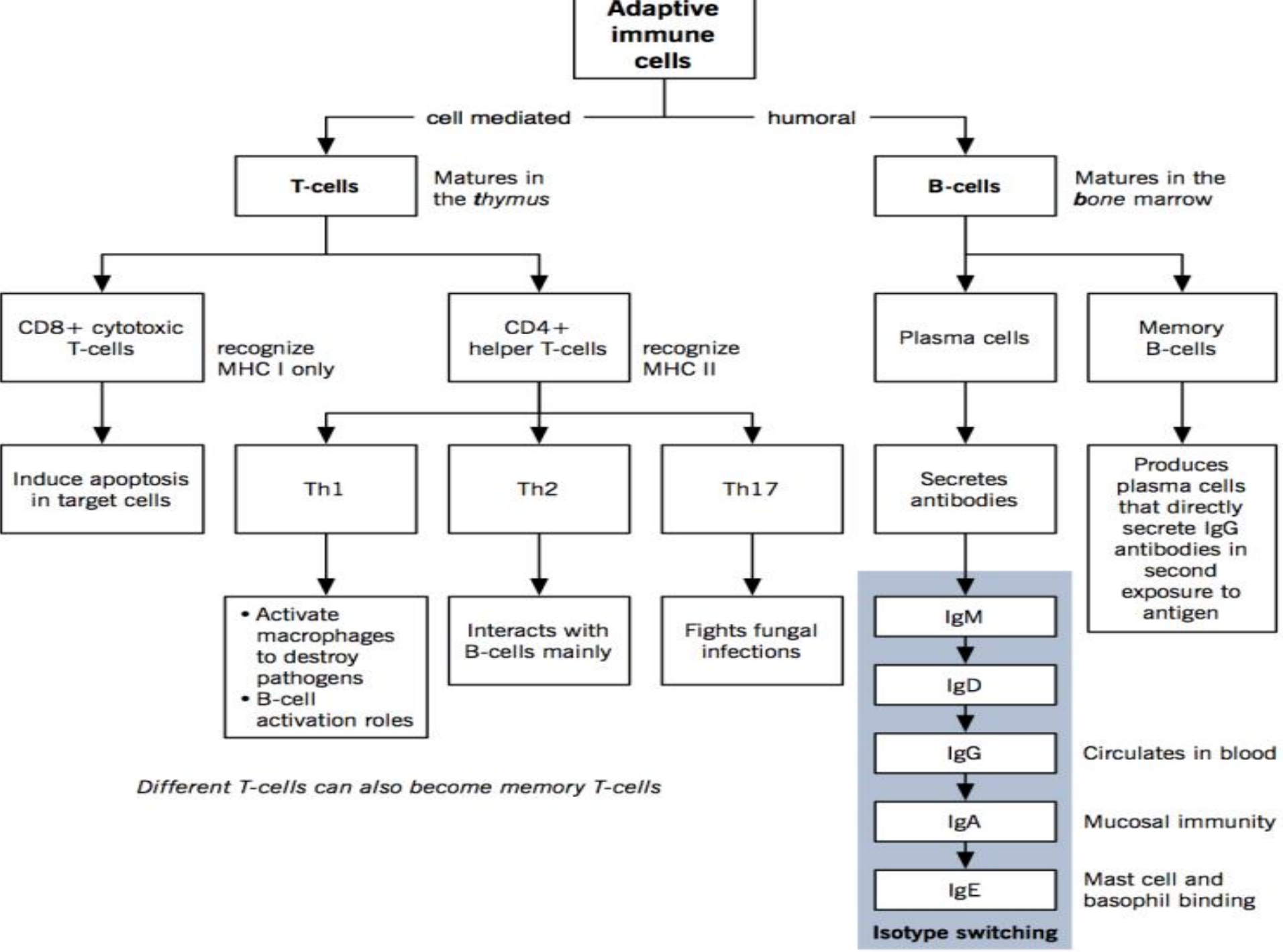


Innate Immunity **Adaptive Immunity**

Nature Reviews | Cancer




Adaptive immune cells
cell mediated
humoral
T-cells
Matures in the thymus
B-cells
Matures in the bone marrow
CD8+ cytotoxic T-cells
recognize MHC I only
CD4+ helper T-cells
recognize MHC II
Plasma cells
Memory B-cells
Induce apoptosis in target cells
Th1
Th2
Th17
Secretes antibodies
Produces plasma cells that directly secrete IgG antibodies in second exposure to antigen
• Activate macrophages to destroy pathogens
• B-cell activation roles
Interacts with B-cells mainly
Fights fungal infections
IgM
IgD
IgG
Circulates in blood
IgA
Mucosal immunity
IgE
Mast cell and basophil binding
Isotype switching
Different T-cells can also become memory T-cells

What is an antibody?

- Produced by Plasma cell (B-lymphocytes producing Ab)
- Essential part of adaptive immunity
- Specifically bind a unique antigenic epitope (also called an antigenic determinant)
- Possesses antigen binding sites
- Members of the class of proteins called immunoglobulins

Immunogenicity

- **Immunogencity:** is the ability to induce a humoral (antibody) and/or cell-mediated immune response.

- Weak immunogens
- Strong immunogens

What determines immunogenicity ?

- **Foreignness:** essential for immunogenicity (self-responsive immune cells are eliminated during lymphocyte development)
- **Size:** Bigger>Smaller
- **Chemical composition:** Proteins > nucleic acids / polysaccharides / lipids
- **Structure:** Primary /secondary /tertiary structures play a role
- **Physical form:** Particulate> Soluble

Host factors affecting immunogencity

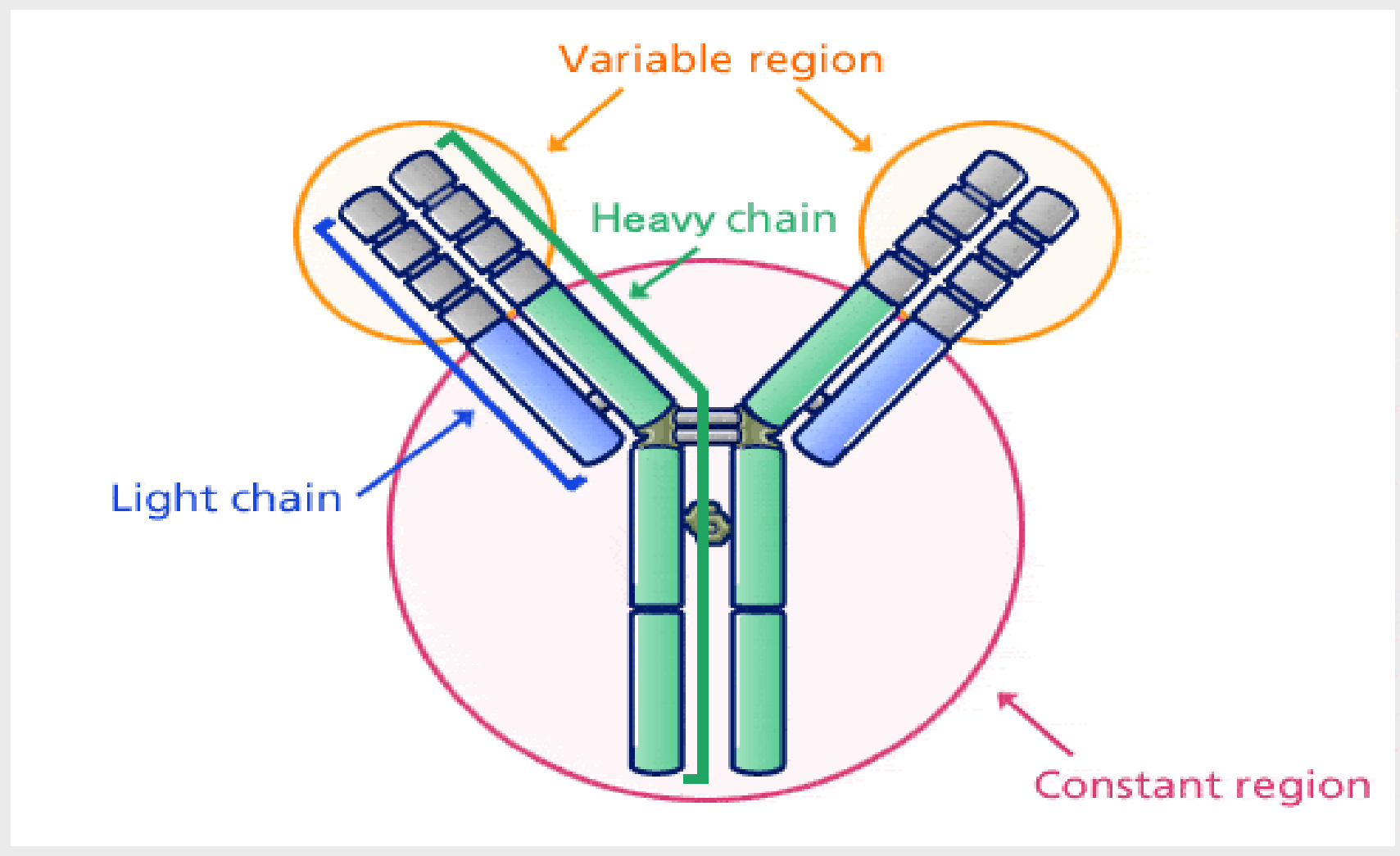
- Difference across species (interspecies)

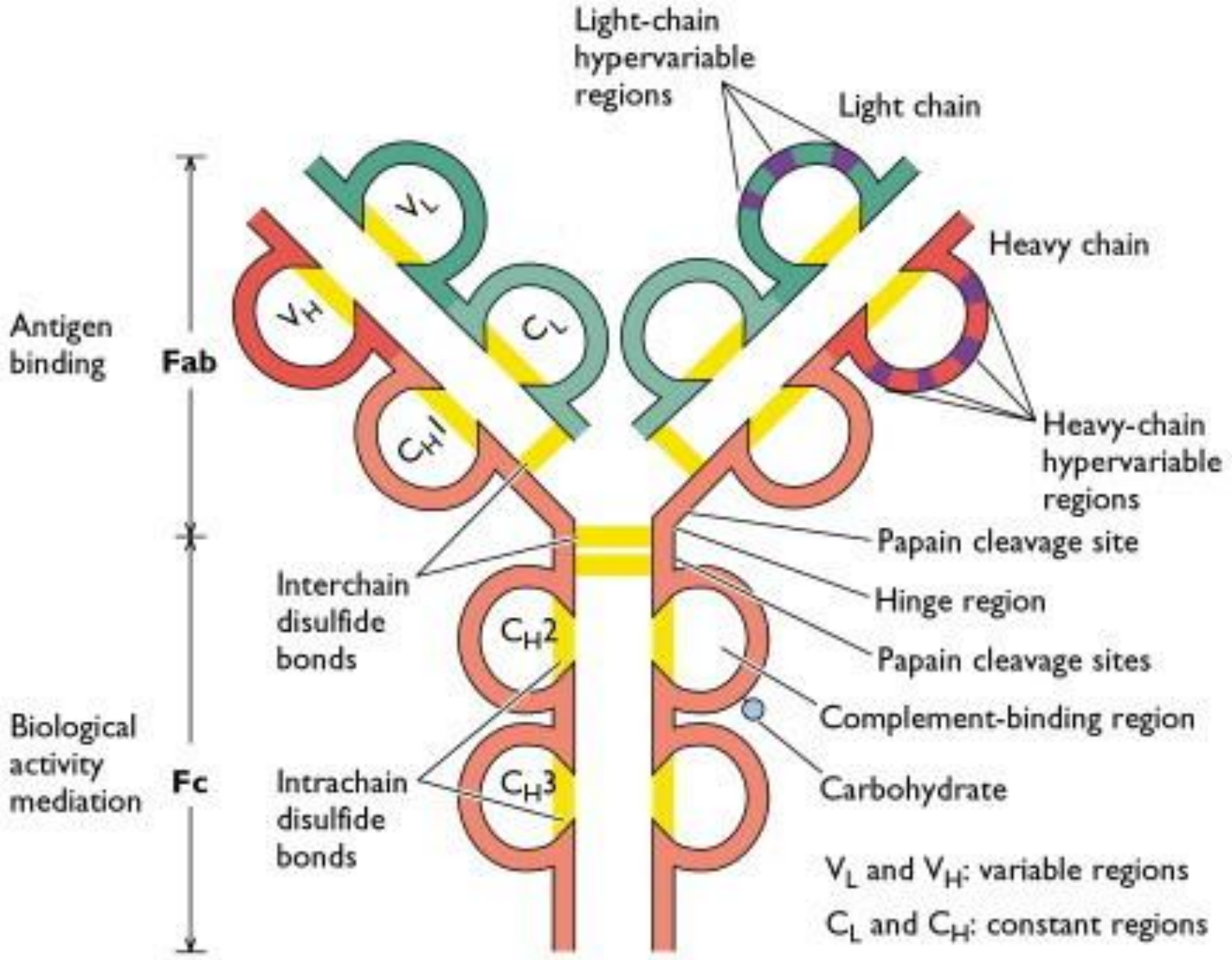
- Differences within a species (intraspecies)
  - Responders / non-responders to vaccine
  - differences in disease severity in epidemics

⇨ **Genetics**

⇨ **Age**

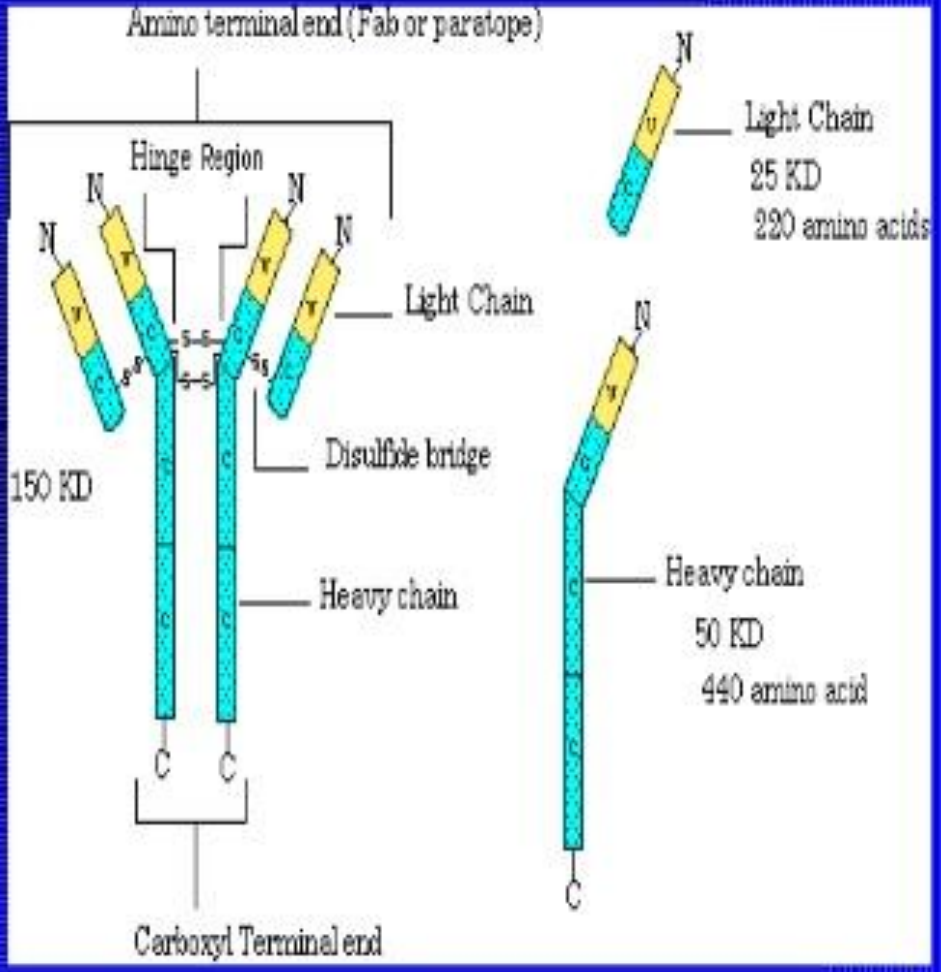
Structure of Antibody



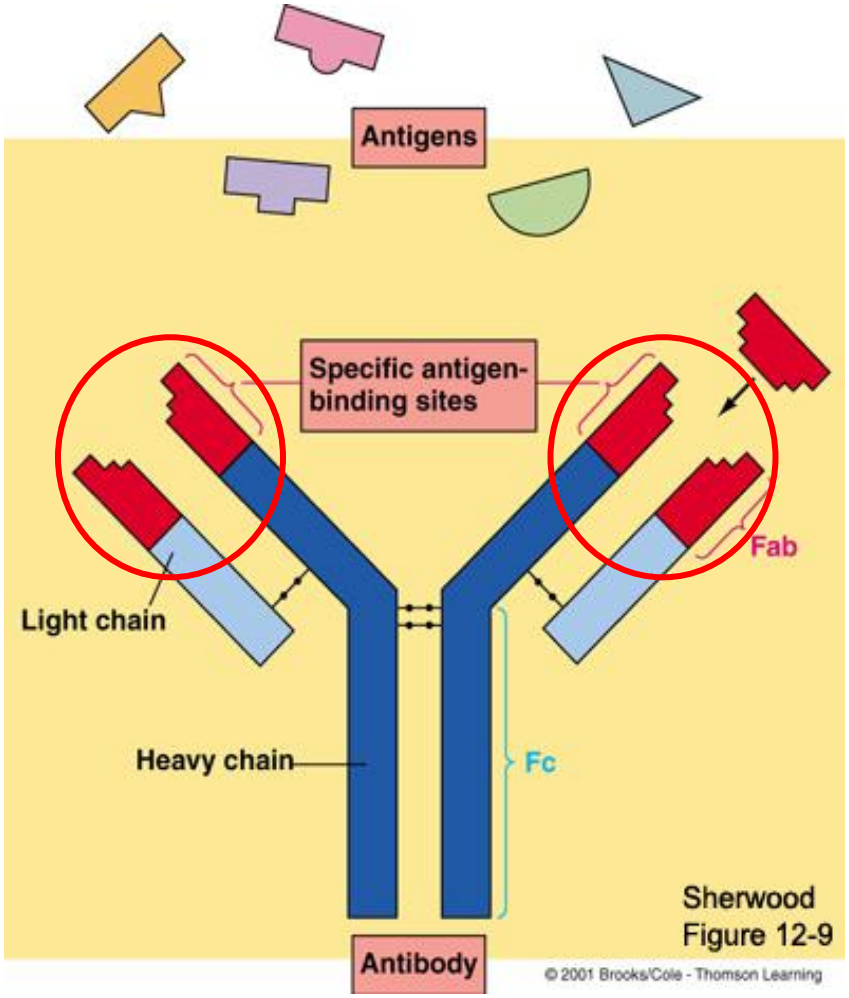

Light-chain hypervariable regions
Light chain
Heavy chain
Heavy-chain hypervariable regions
Papain cleavage site
Hinge region
Papain cleavage sites
Complement-binding region
Carbohydrate
Interchain disulfide bonds
Intrachain disulfide bonds
Antigen binding
Fab
Biological activity mediation
Fc
V_L
V_H
C_L
C_H1
C_H2
C_H3
V_L and V_H: variable regions
C_L and C_H: constant regions

Basic structure

- Composed of 4 polypeptide chains.
- 2 identical light and 2 identical heavy chains
- Linked by disulphide bonds
- Light chains similar in all immunoglobulins
- Light chains occur in 2 varieties kappa and lambda
- Light and Heavy chains are subdivided into variable and constant region.
- Each heavy and light chain contains amino terminal in variable region carboxy terminal in constant region



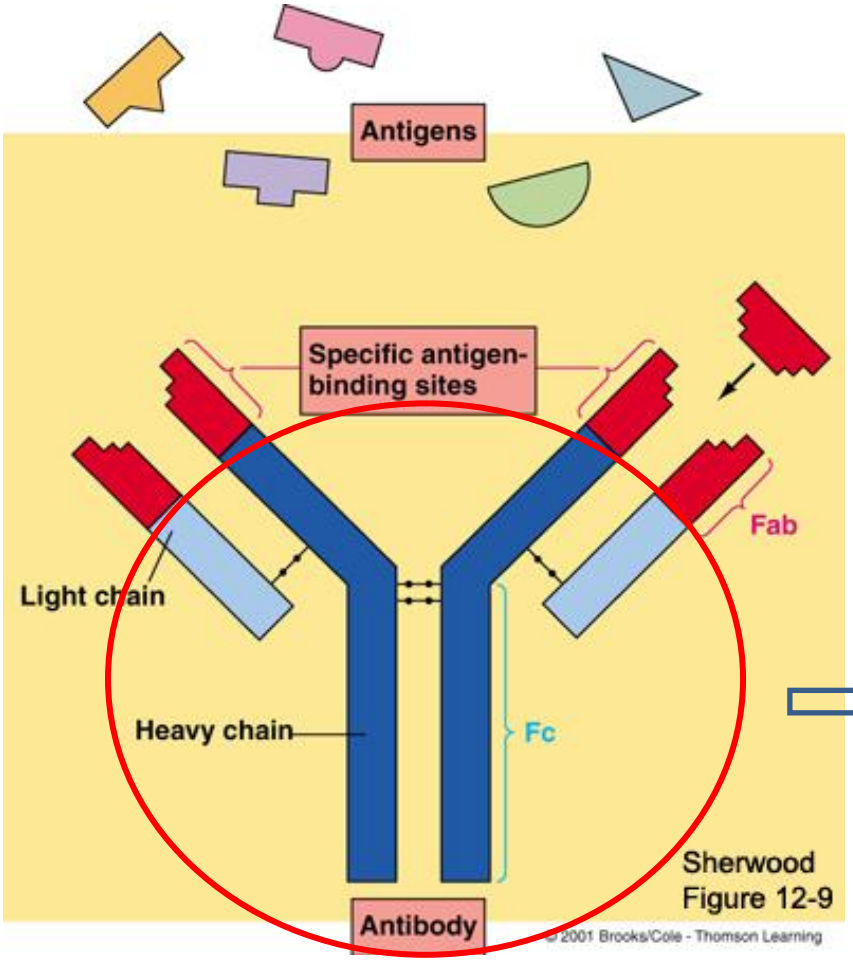
Antibody: Fab



Fab region

- Variable region of the antibody
- Tip of the antibody
- Binds the antigen
- Specificity of antigen binding determined by V_H and V_L

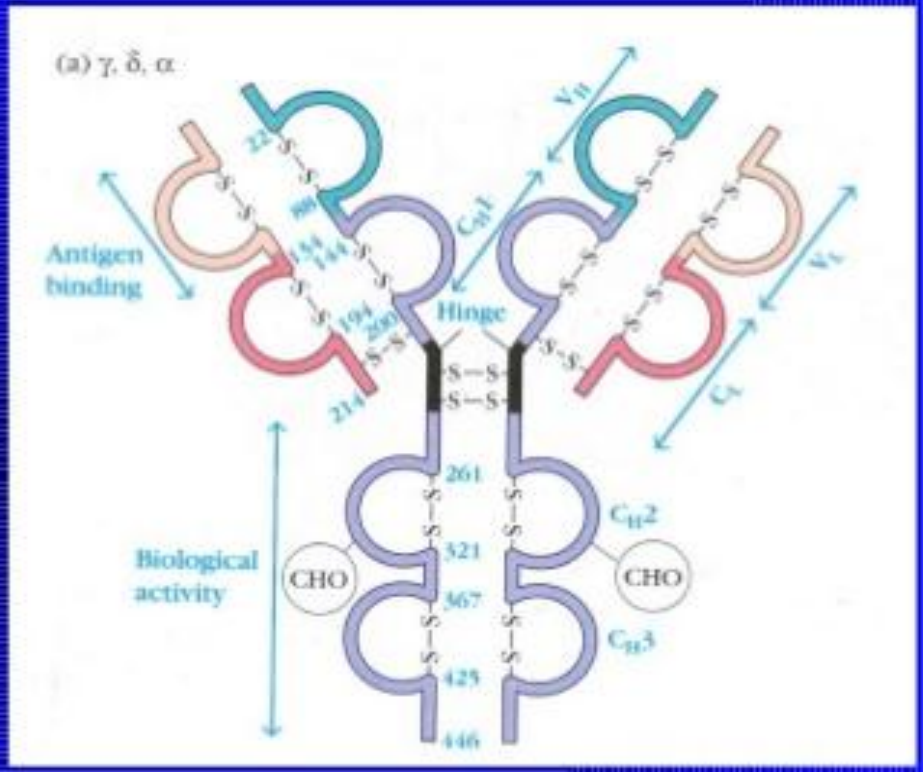
Antibody: Fc



Fc region

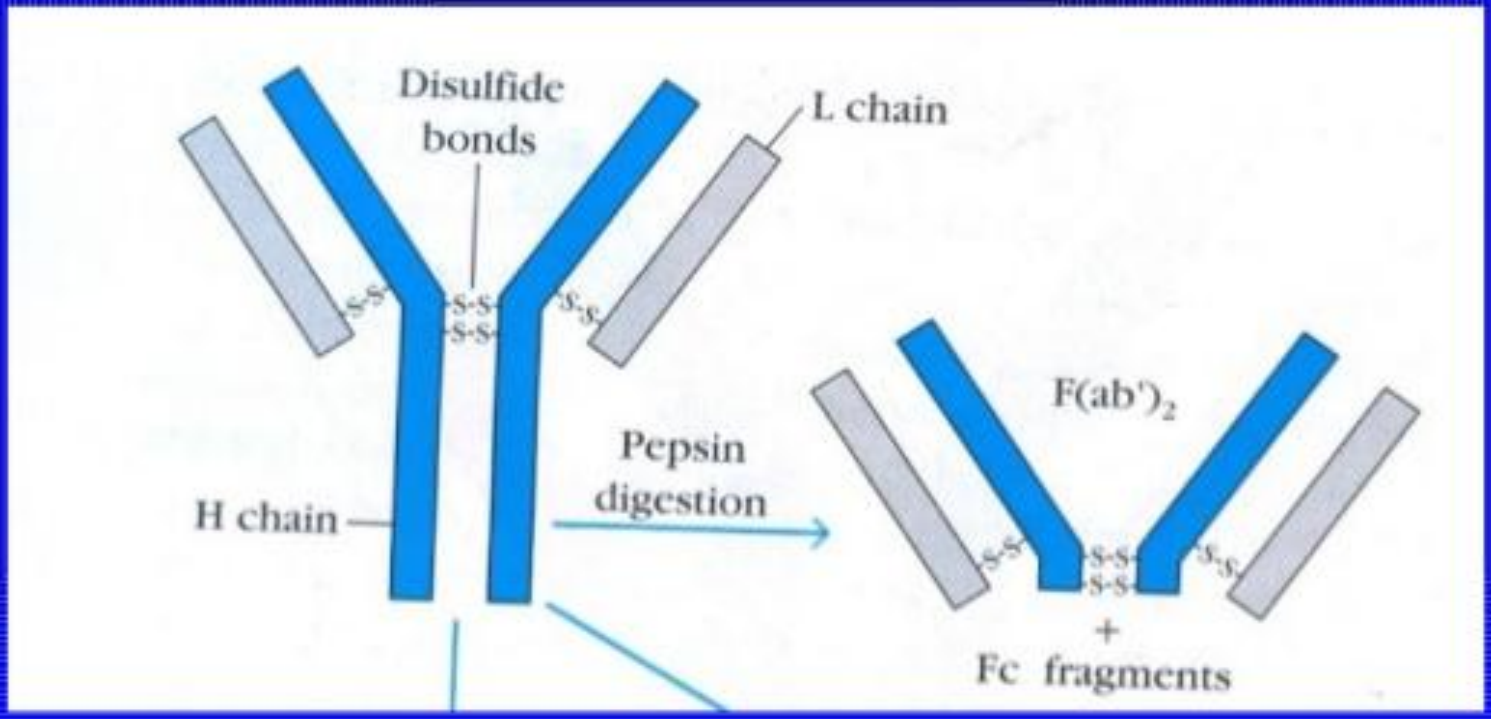
- Constant region
- Base of the antibody
- Can bind cell receptors and complement proteins

- Heavy chains are structurally and antigenically distinct for each class
- Each immunoglobulin peptide chain has intra chain disulphide bonds- form loops
- Each loop is compactly folded to form a globular structure- domain
- Light chain contains a single variable domain (VL) and a single constant domain (CL).
- Heavy chain contains one variable domain (VH) and 3 constant domains (CH1, CH2, CH3)
- Hinge region is the segment in heavy chain - between CH1, CH2



Pepsin digestion

- Produce a single fragment composed of two Fab like subunits F(ab)2 binds antigen
- Fc fragment is not recovered- digested to small numerous peptides.

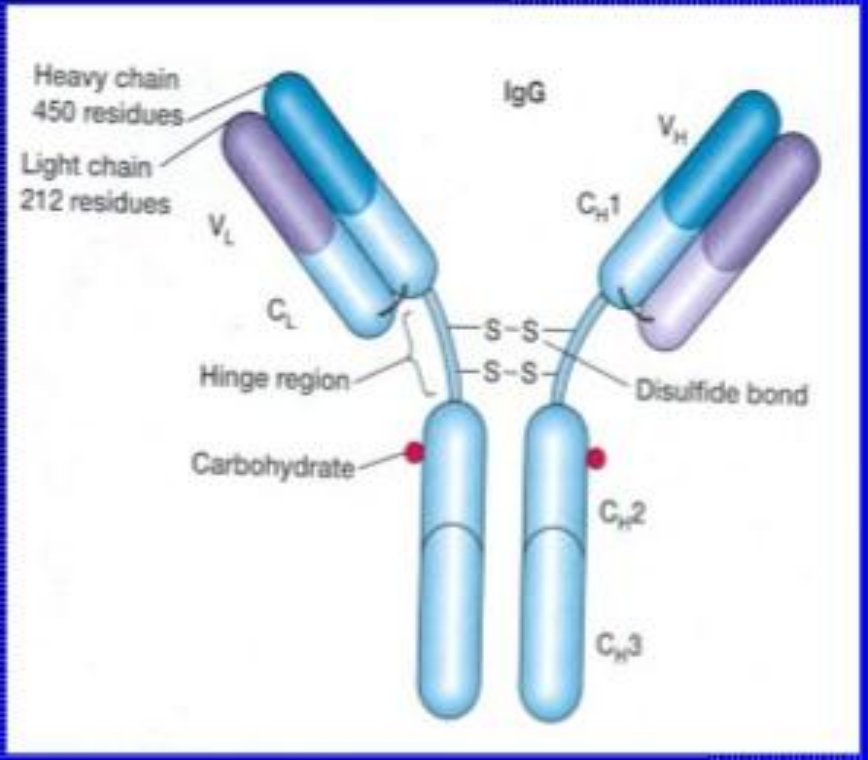


Classification

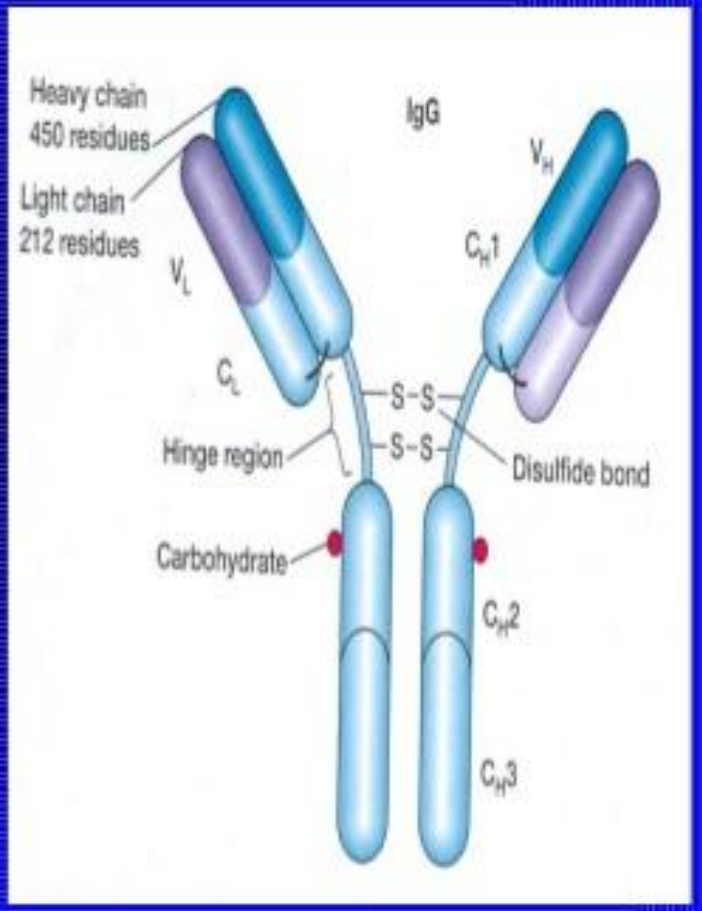
- Based on structure and antigenic nature of H chain the immunoglobulins are classified into 5 classes.
- Ig G- (gamma)
- Ig A- *(alpha)*
- *Ig M- (mu)*
- *Ig D- (delta)*
- *Ig E - (epsilon)*

Immunoglobulin G (Ig G)

- Most abundant class in serum
- Constitutes 80% total immunoglobulin
- Present in blood, plasma and tissue fluids
- Contains less carbohydrate than other immunoglobulins
- It has a half life of 23 days: the longest of all of the immunoglobulin isotypes

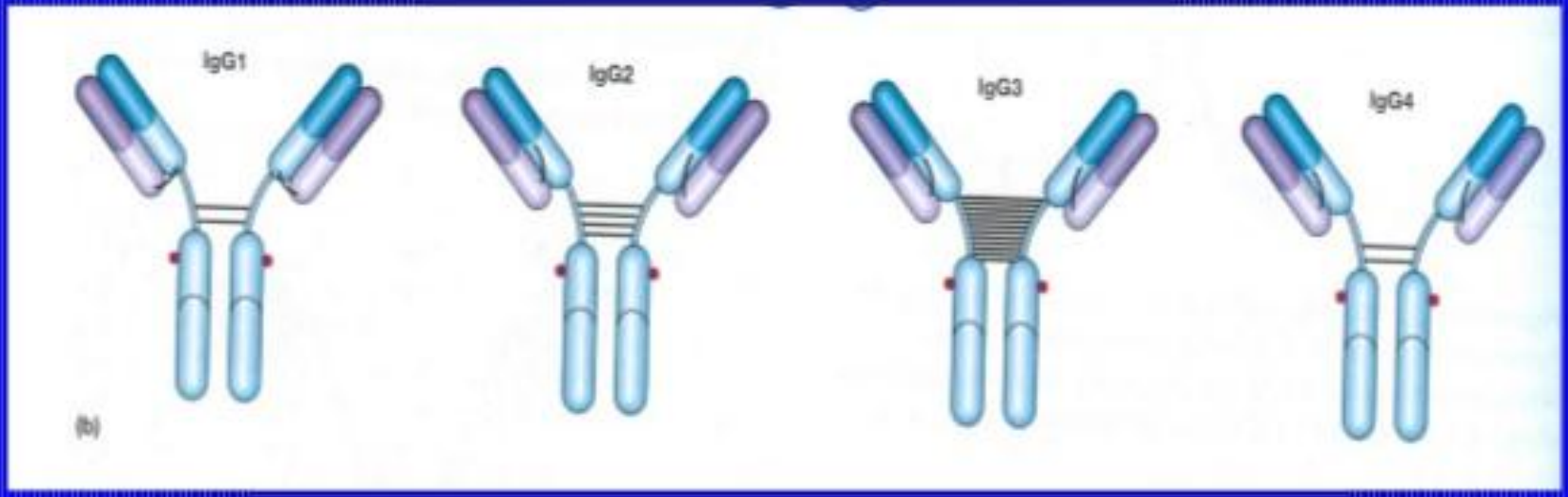


- Crosses placenta and provide natural immunity to foetus and neonate at birth
- Acts against bacteria and viruses by opsonizing
- Neutralize toxin
- Activate complement by classical pathway
- Catabolism of IgG is unique in that it varies with its serum concentration



Sub classes of Ig G

- Ig G1, Ig G2, Ig G3, Ig G4.

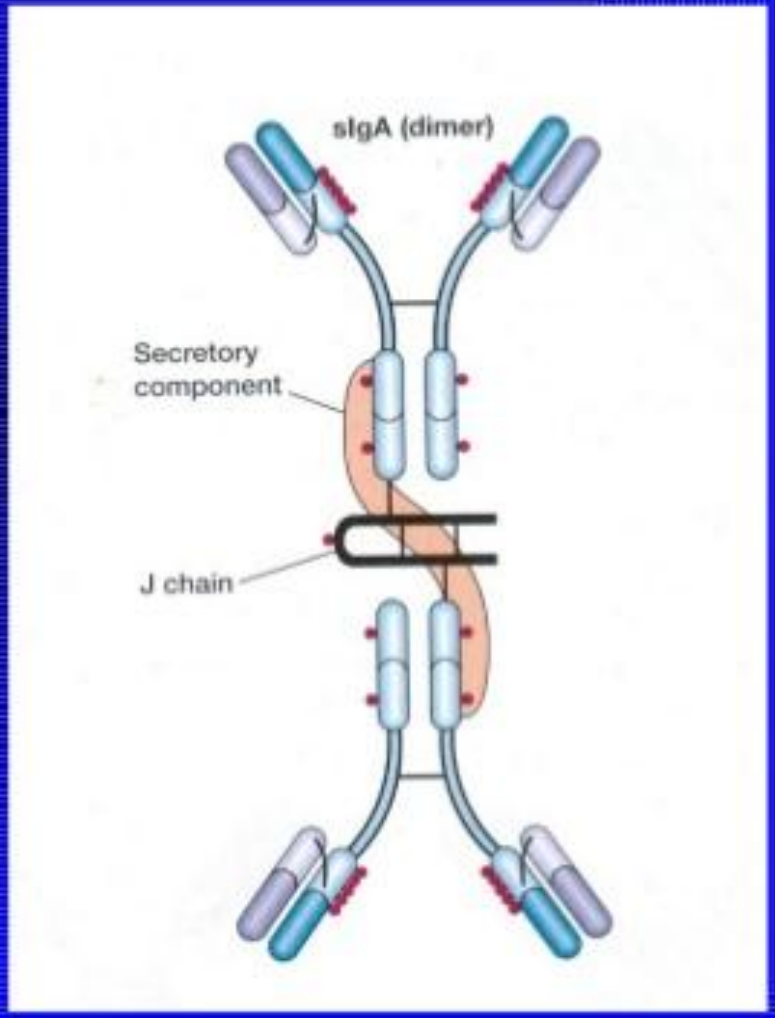


Biological function of subclasses

- IgG1, IgG3, IgG4 – cross placenta and protect foetus
- IgG3 activates complement
- IgG1 and IgG3 binds to Fc receptor on phagocytic cells, monocytes and macrophages and mediate opsinization.

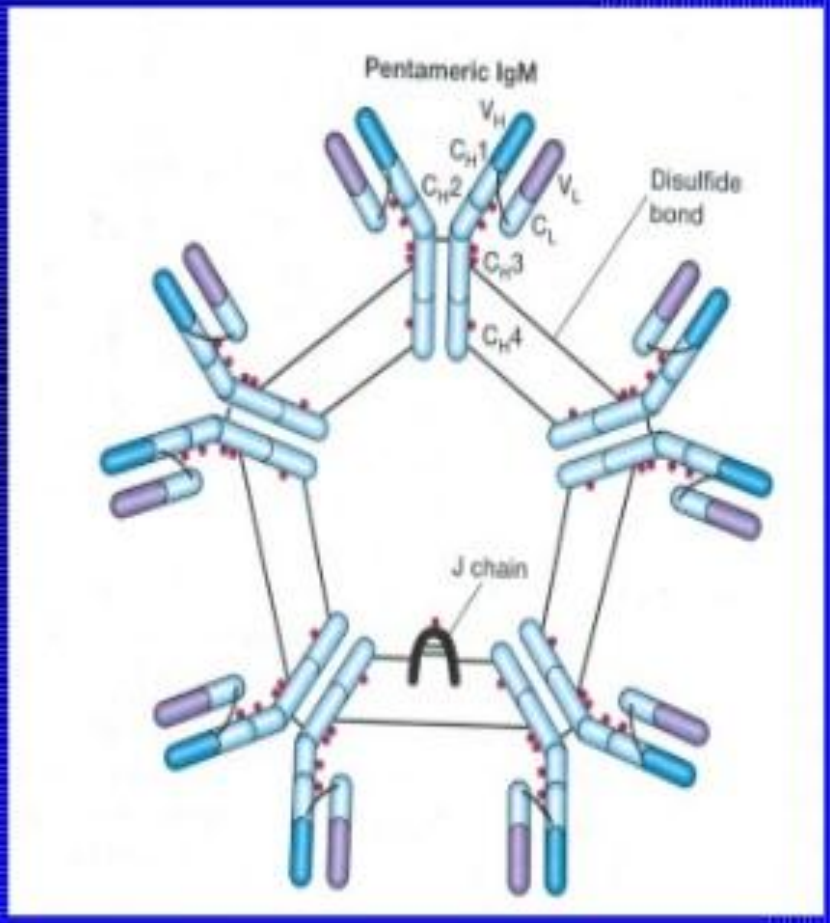
Immunoglobulin A (Ig A)

- Constitutes 10-15 % of total immunoglobulins
- Present in milk, saliva, tears, mucous of respiratory tract, digestive tract and genitourinary tract.
- In serum exist as monomer
- In external secretions exist as dimer called secretory Immunoglobulin.
- Has 'J' chain and secretory piece.
- Half life: 6-8 days



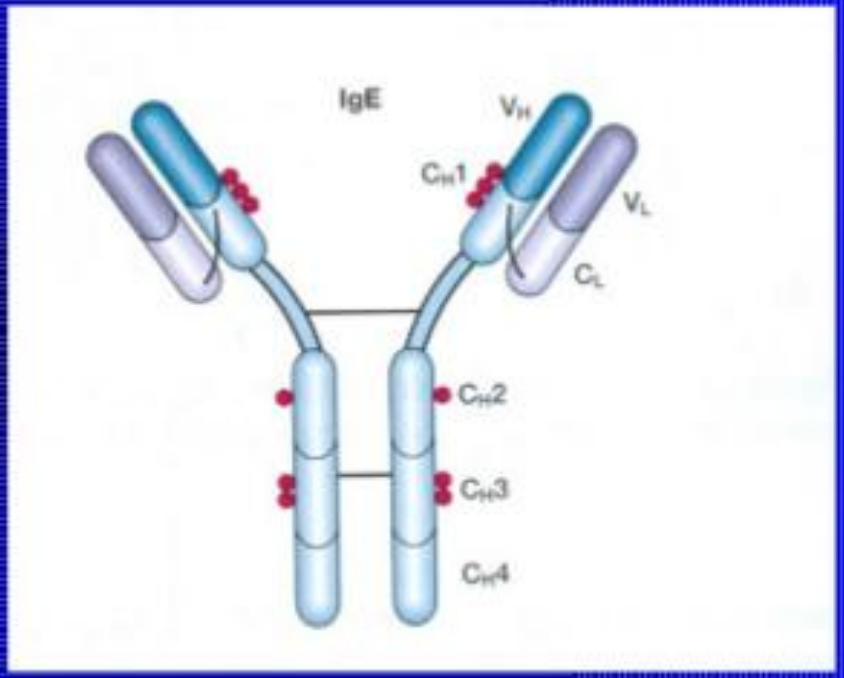
Immunoglobulin M (Ig M)

- Accounts for 5-10% of total serum proteins
- Polymer of five monomeric units (pentamer)
- Held together by disulfide bonds and 'J' chain
- Mol. Wt. of 900,000-10,00,000 (millionaire molecule)
- Half life: 5 days



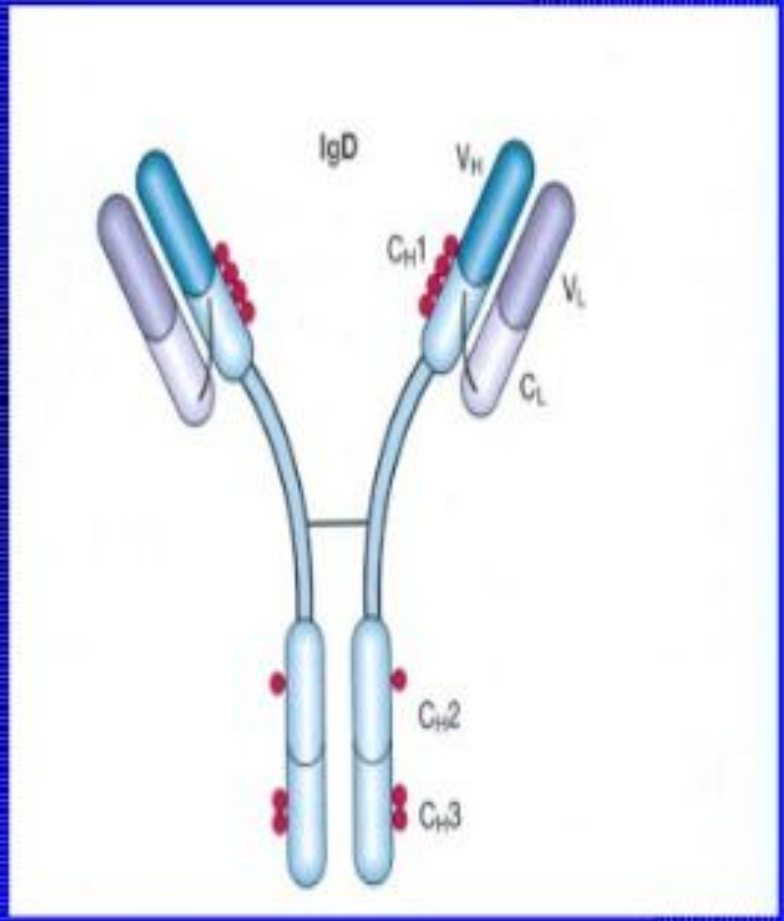
Immunoglobulin E (Ig E)

- Structure is similar to Ig G
- Has 4 constant region domains.
- Mol. Wt. 1,90,000
- Half life: 2 days
- Heat labile (inactivated at 56^{0}C in 1 hour)
- Normal serum concentration 0.3 ug/ml
- Mostly present extra cellularly
- Does not cross placenta



Immunoglobulin D (Ig D)

- Structure is similar to IgG
- Serum concentration 30 micrograms per ml
- Constitutes 0.2% of total immunoglobulins
- Half life: 3 days
- IgD together with IgM is major membrane bound immunoglobulin on unstimulated B lymphocytes-acts as recognition receptors for antigens



Antibodies exist in two forms

- Antibodies occur in 2 forms
  - Soluble Ag: secreted in blood and tissue
  - Membrane-bound Ag: found on surface of B-cell, also known as a B-cell receptor (BCR)
- Complete and incomplete *Ig*

According to the **TEMPERATURE** at which they react

- **Cold antibodies** – react at 4 degree Celsius to room temperature
- **Warm antibodies** – react at 37 degree Celsius

Immunoglobulin (Ig)M warm autoantibodies (AABs) usually cause severe autoimmune hemolytic anemia (AIHA) and, in some cases, red blood cell (RBC)-bound IgM cannot be detected.

According to **OCCURENCE**

- **Natural antibodies** – appear without any apparent stimulus
- **Immune antibodies** – appear following the introduction of an antigen

According to the **SPECIES** which produce them

- **Isoantibodies** – antibodies produced after the introduction of the antigen from the same species.

- **Heterophile antibodies** – antibodies produced after the introduction of the antigen from another species.

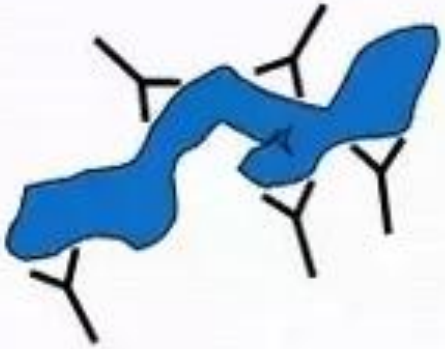
According to its **REACTION** with an antigen

- **Agglutinins** – antibodies responsible for immobilization of motile organisms and for cell clumping
- **Agglutinoids** – agglutinins that are modified by heat in such manner that they can no longer bring about agglutination but still are capable of combining with specific agglutinogens

Polyclonal vs. monoclonal

Polyclonal

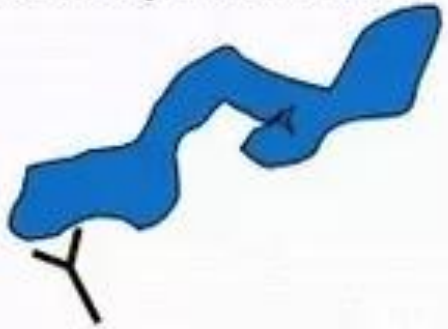
- Cheap to produce
- Mixed population of antibodies
- May bind to different areas of target molecule
- Tolerant of small changes in protein structure (denaturation, dimerisation, phosphorylation)



Polyclonal antibodies

Monoclonal

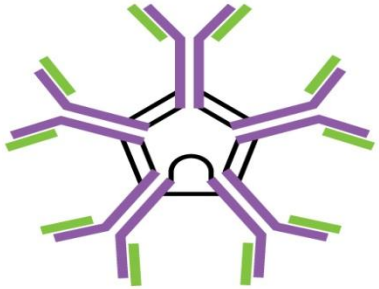
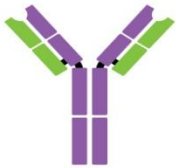
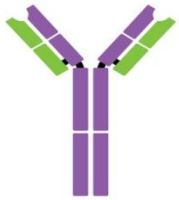
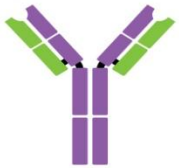
- Expensive to produce
- Single antibody species
- Will only bind single specific site
- May only recognise a particular protein form (phosphorylation, dimersied)
- Infinitely renewable



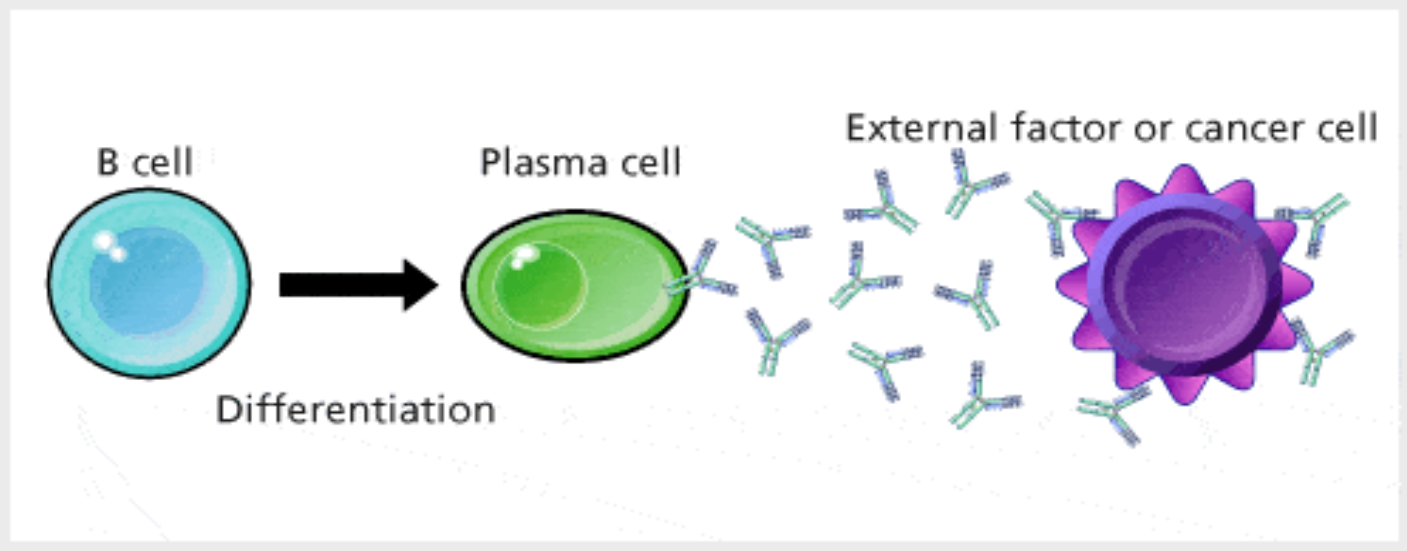
Monoclonal antibodies

- Monoclonal means “coming from one clone of antibody producing cells” these are called plasma cells. These antibodies are all the same and are all coming from the same clone of cells. And should all bind to the same antigen and binding site.
- -Monoclonal Antibodies are state-of-the-art stuff in pharmacology. They have only one mission and one life target i.e. to bind to the target antigens and destroy it. These drugs have revolutionized cancer treatment, and improved the five year survival rates of many cancer patients.
  -Proteins surround the cells (both normal and cancer cells) and few proteins are specifically expressed by the cancer cells; monoclonal antibodies are engineered to target one particular (vital oncogene) protein (antigen) responsible for the uncontrolled growth of the cell (causing Neoplasm
- **Polyclonal** antibodies are a **mixture of antibodies** from several clones of plasma cells. And should bind to more antigens or different binding sites on one kind of antigen.

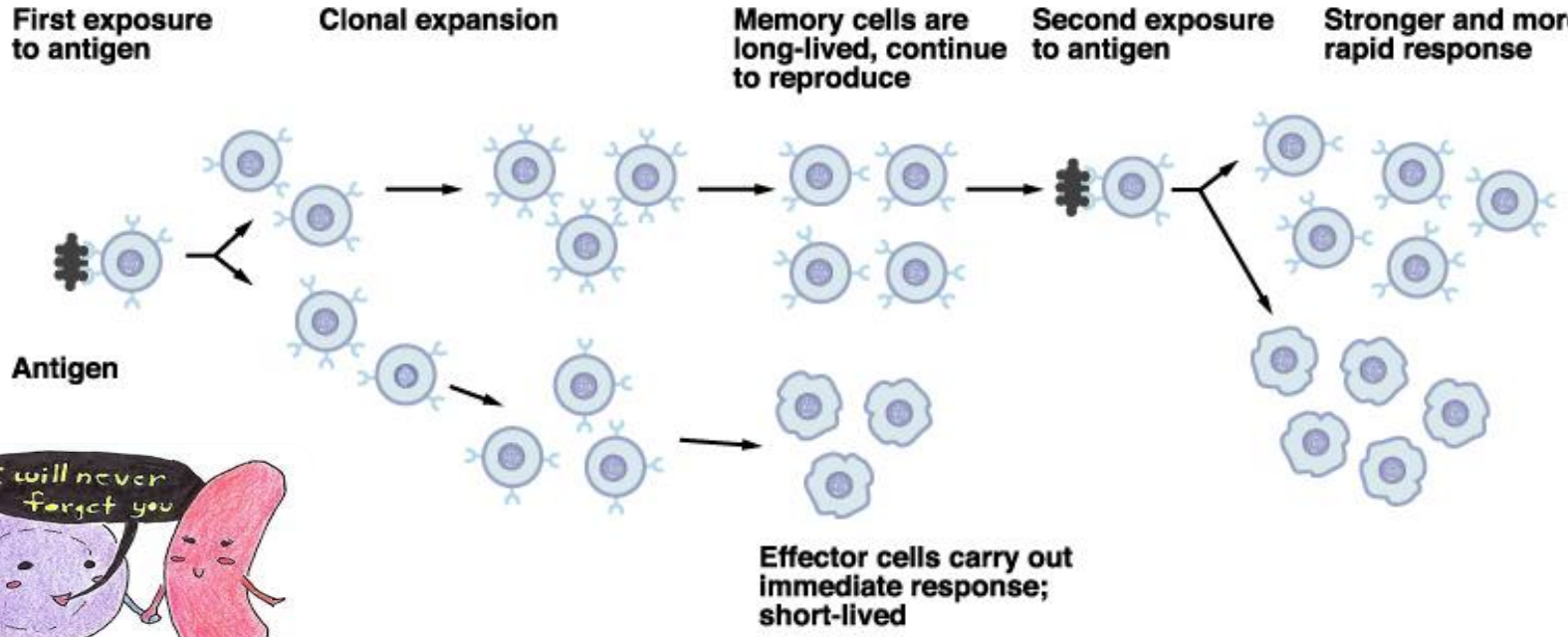
The Five Immunoglobulin (Ig) Classes

	IgM pentamer	IgG monomer	Secretory IgA dimer	IgE monomer	IgD monomer
					
Heavy chains	μ	γ	α	ε	δ
Number of antigen binding sites	10	2	4	2	2
Molecular weight (Daltons)	900,000	150,000	385,000	200,000	180,000
Percentage of total antibody in serum	6%	80%	13%	0.002%	1%
Crosses placenta	no	yes	no	no	no
Fixes complement	yes	yes	no	no	no
Fc binds to		phagocytes		mast cells and basophils	
Function	Main antibody of primary responses, best at fixing complement; the monomer form of IgM serves as the B cell receptor	Main blood antibody of secondary responses, neutralizes toxins, opsonization	Secreted into mucus, tears, saliva, colostrum	Antibody of allergy and antiparasitic activity	B cell receptor

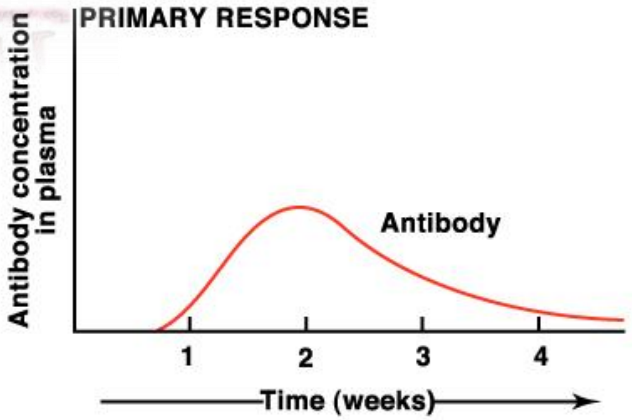
Antibody (Ab) also know as Immunoglobulin (Ig) is the large Y shaped protein produced by the body's immune system when it detects harmful substances, called antigens like bacteria and viruses. The production of antibodies is a major function of the immune system and is carried out by a type of white blood cell called a B cell (B lymphocyte), differentiated B cells called plasma cells. The produced antibodies bind to specific antigens express in external factors and cancer cells.



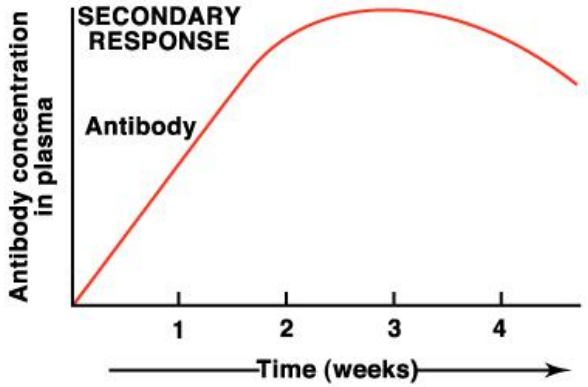
Immunologic Memory

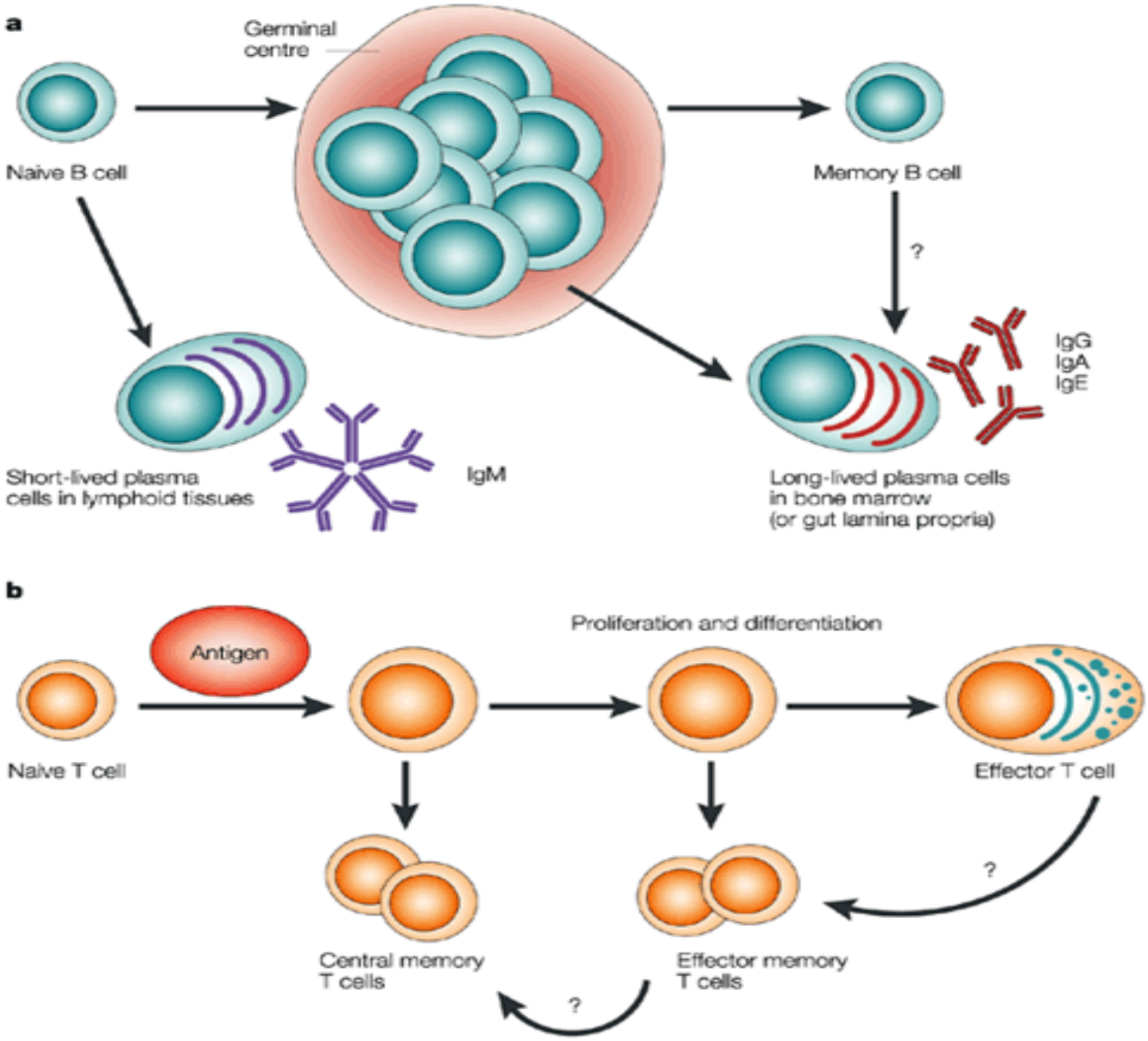


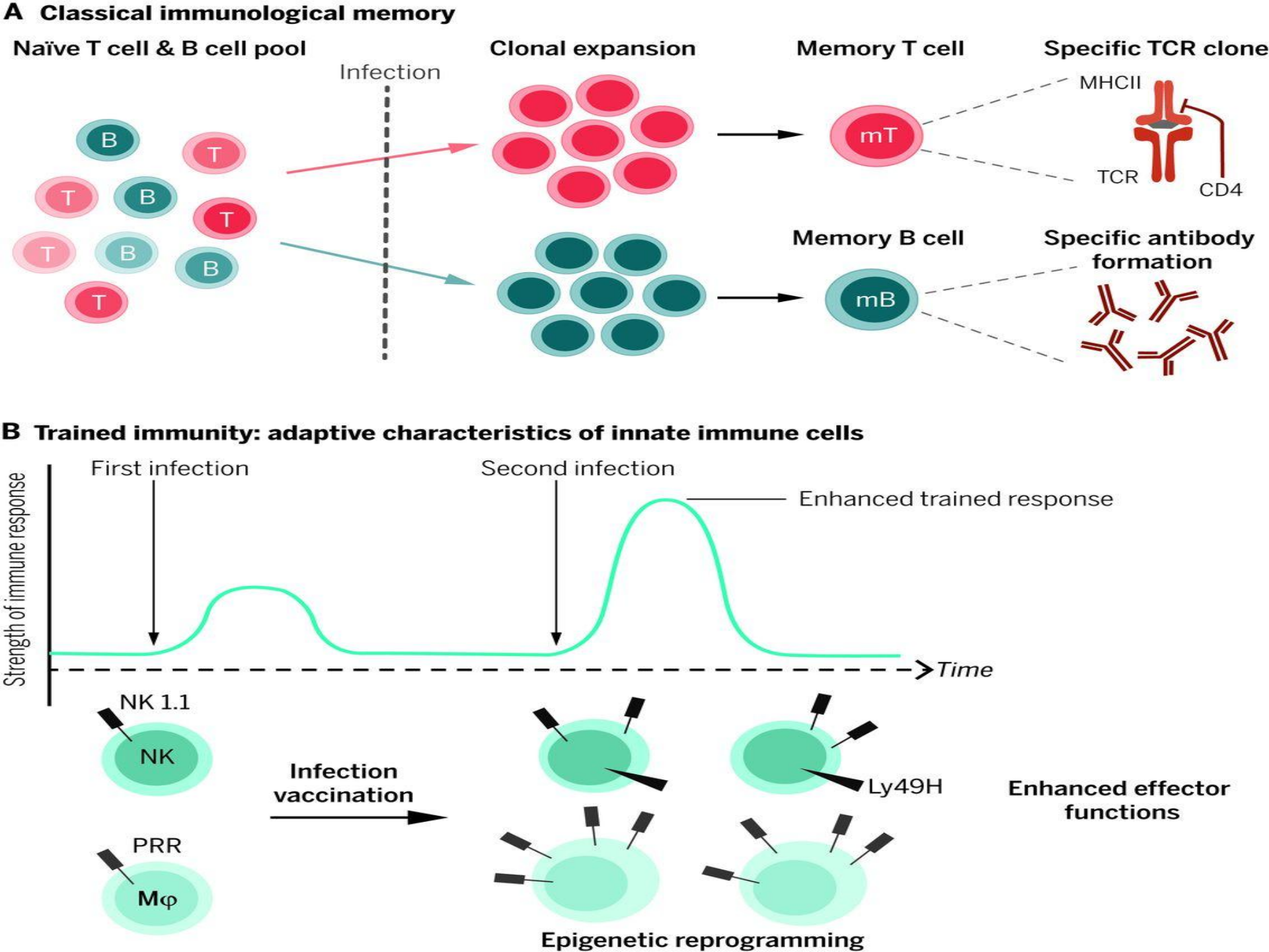
Primary response

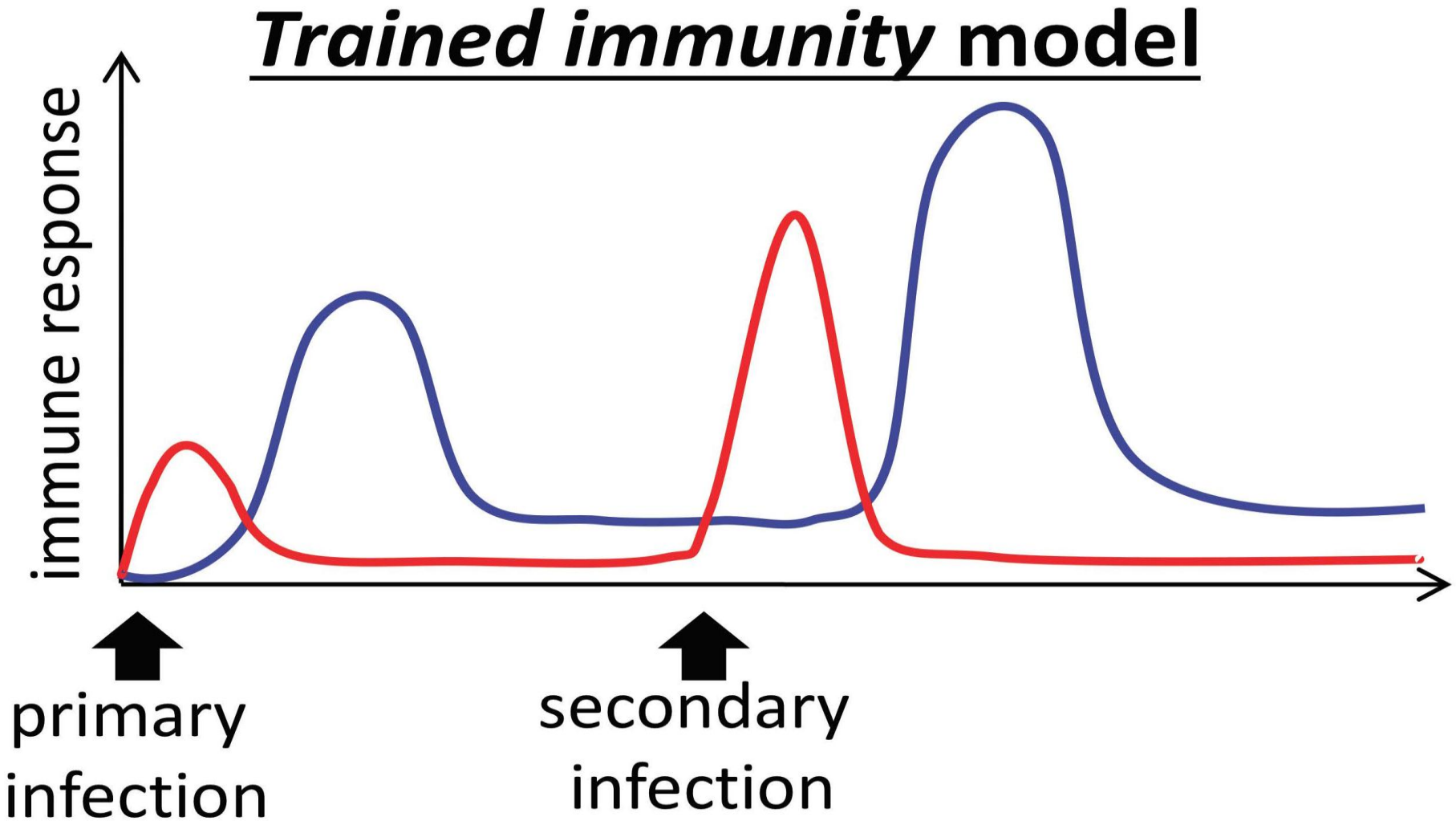


Secondary response



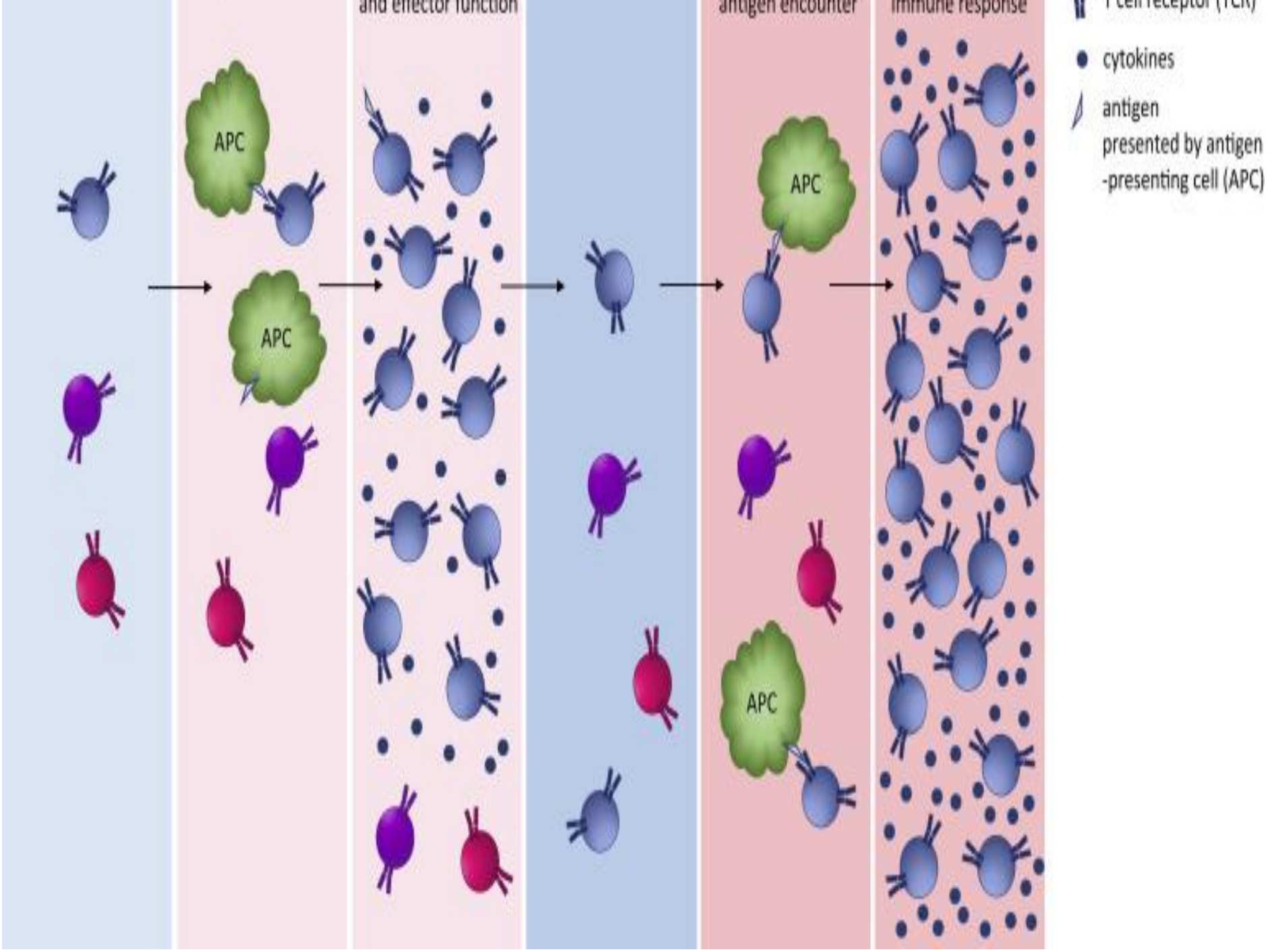

a
Germinal centre
Naive B cell
Memory B cell
?
IgG
IgA
IgE
IgM
Short-lived plasma cells in lymphoid tissues
Long-lived plasma cells in bone marrow (or gut lamina propria)
b
Antigen
Proliferation and differentiation
Naive T cell
Effector T cell
?
Central memory T cells
Effector memory T cells
?


A Classical immunological memory
Naïve T cell & B cell pool
Infection
Clonal expansion
Memory T cell
Specific TCR clone
MHCII
TCR
CD4
B
T
mT
Memory B cell
Specific antibody formation
mB
B Trained immunity: adaptive characteristics of innate immune cells
First infection
Second infection
Enhanced trained response
Strength of immune response
Time
NK 1.1
NK
Infection vaccination
Ly49H
Enhanced effector functions
PRR
Mφ
Epigenetic reprogramming

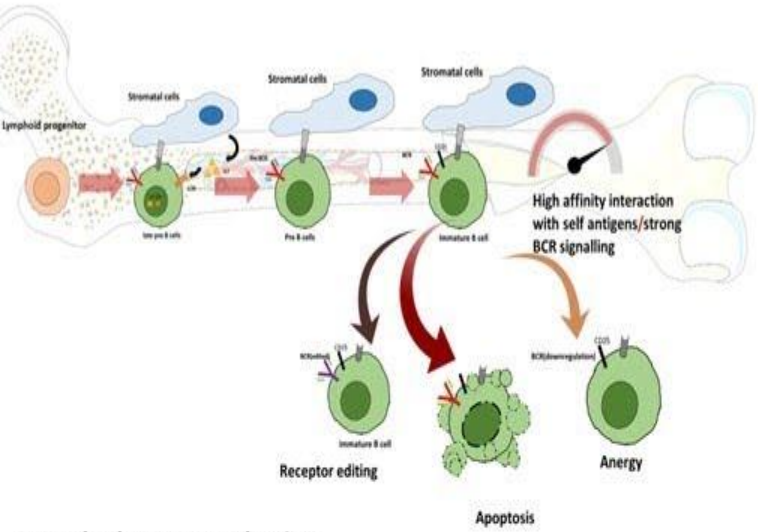


Innate immunity : memory

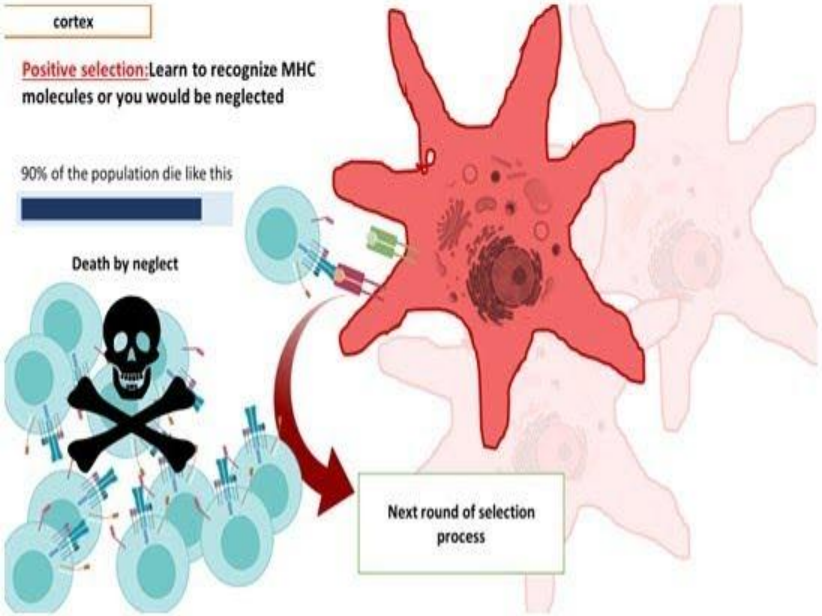
Adaptive immunity : memory

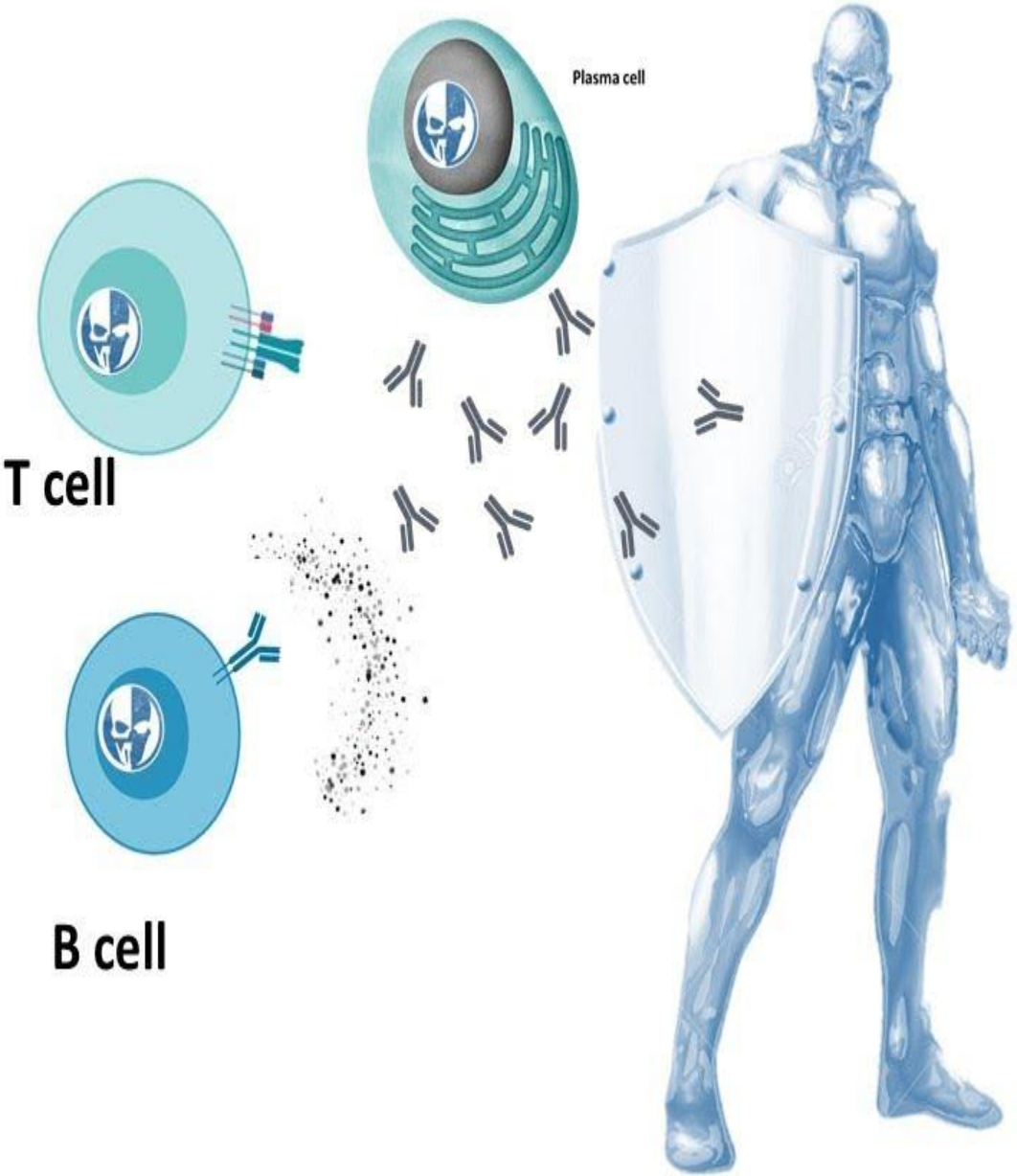

and effector function
antigen encounter
immune response
APC
APC
APC
APC
T cell receptor (TCR)
cytokines
antigen
presented by antigen
-presenting cell (APC)

Immune tolerance and autoimmunity



Central tolerance mechanism





General features of Immunologic tolerance

- Tolerance is **antigenic specific** and results from the recognition of antigens by specific lymphocytes.
- Normal individuals are tolerant of their own antigens(self antigen)----- **Self-tolerance**.
- Foreign antigens may be administered in ways that preferentially inhibit immune response by inducing tolerance in specific lymphocytes---**antigen induction**.

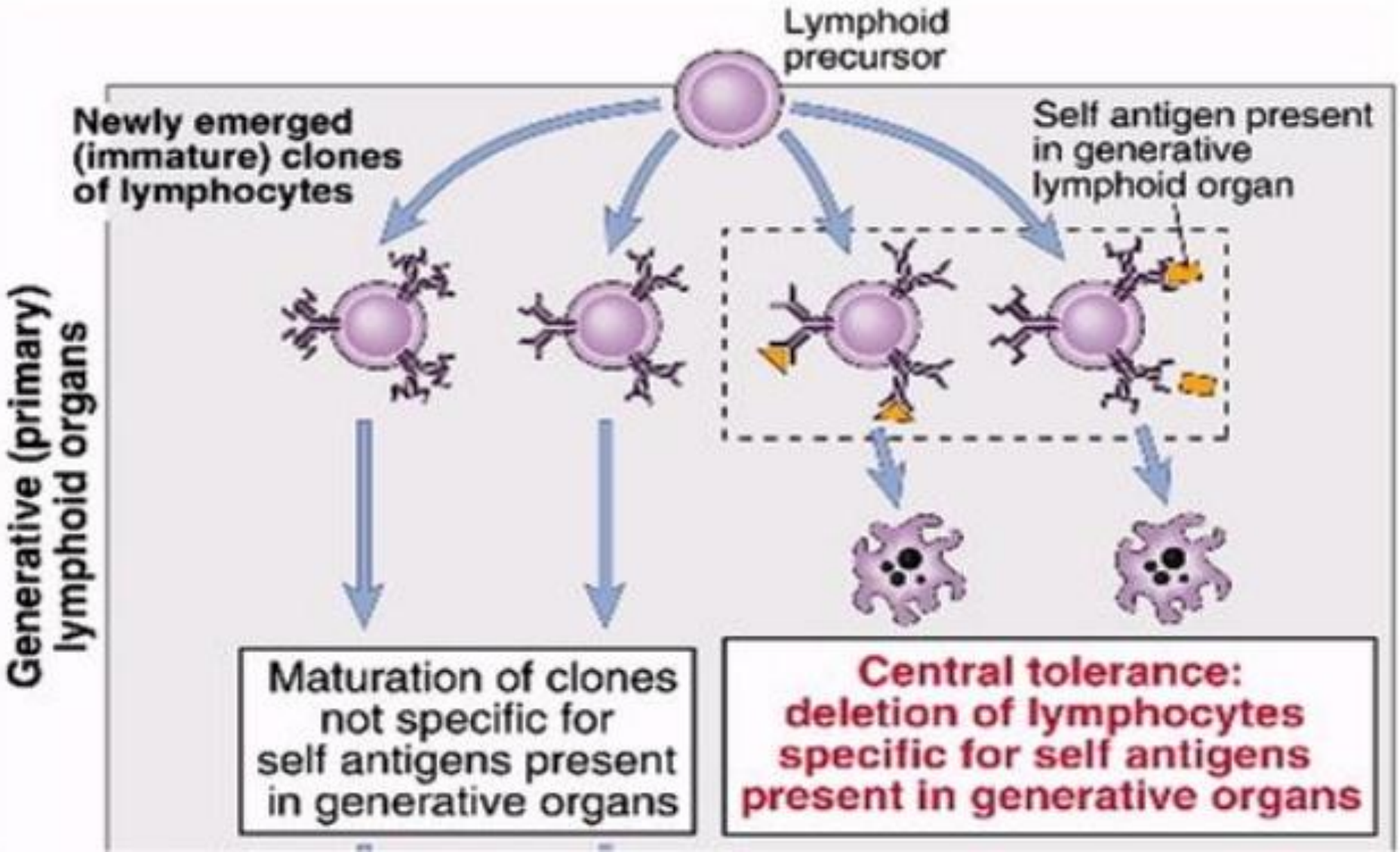
Immunological tolerance

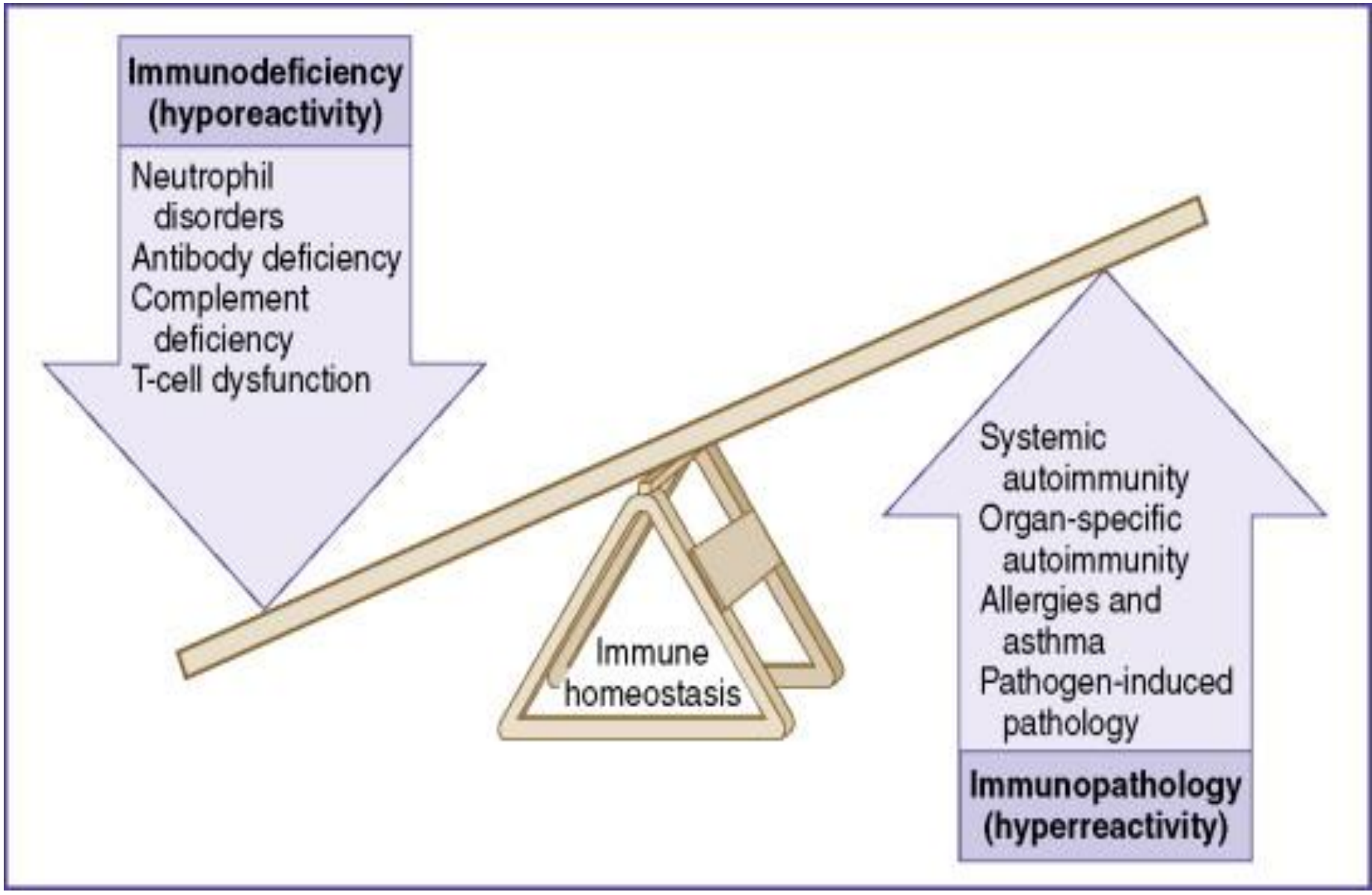
- **Definition:**
  - unresponsiveness to an antigen induced by exposure of lymphocytes to that antigen; antigen-specific (unlike "immunosuppression")

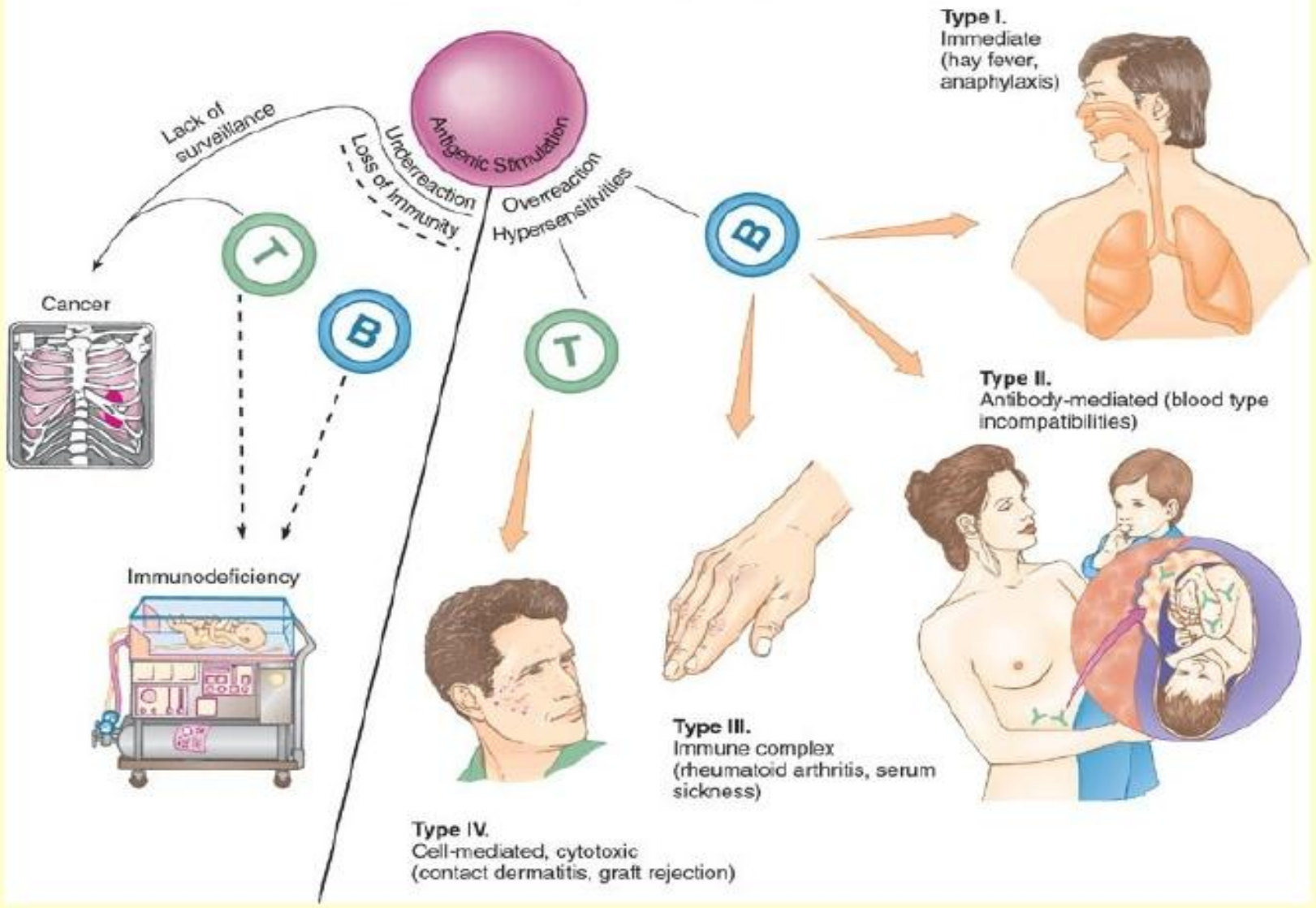
- **Significance:**
  - All individuals are tolerant of their own antigens (self-tolerance); breakdown of self-tolerance results in autoimmunity
  - Therapeutic potential: Inducing tolerance may be exploited to prevent graft rejection, treat autoimmune and allergic diseases, and prevent immune responses in gene therapy and stem cell transplantation

Central Tolerance

(this occurs during lymphocyte development.)



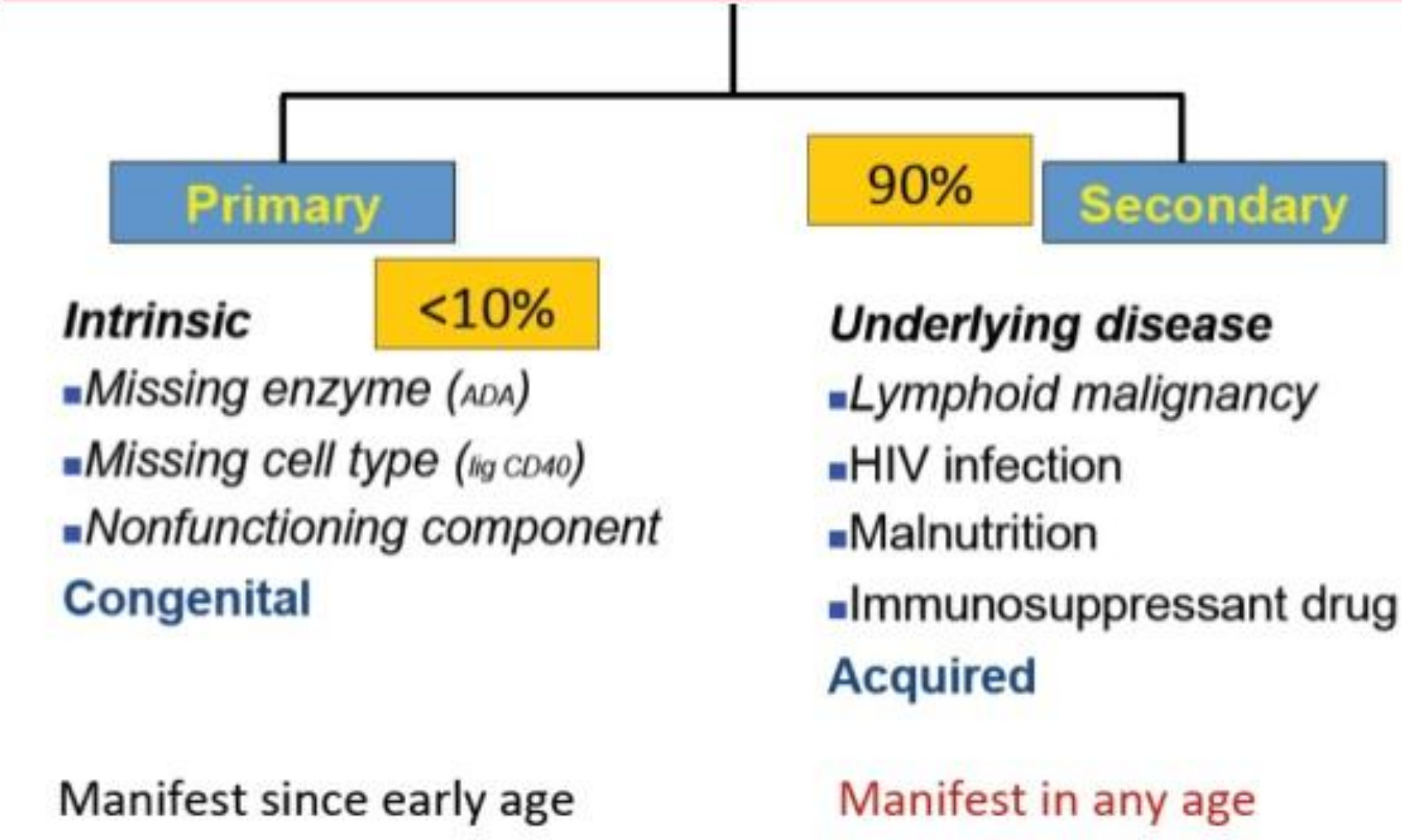

Immunodeficiency (hyporeactivity)
Neutrophil disorders
Antibody deficiency
Complement deficiency
T-cell dysfunction
Immune homeostasis
Systemic autoimmunity
Organ-specific autoimmunity
Allergies and asthma
Pathogen-induced pathology
Immunopathology (hyperreactivity)



Immunopathology

- Allergy, hypersensitivity – an exaggerated, misdirected expression of immune responses
- Involves the same types of immune reactions as those at work in protective immunities.
- Autoimmunity – abnormal responses to self Ag
- Immunodeficiency – deficiency or loss of immunity
- Cancer – results from a lack of surveillance

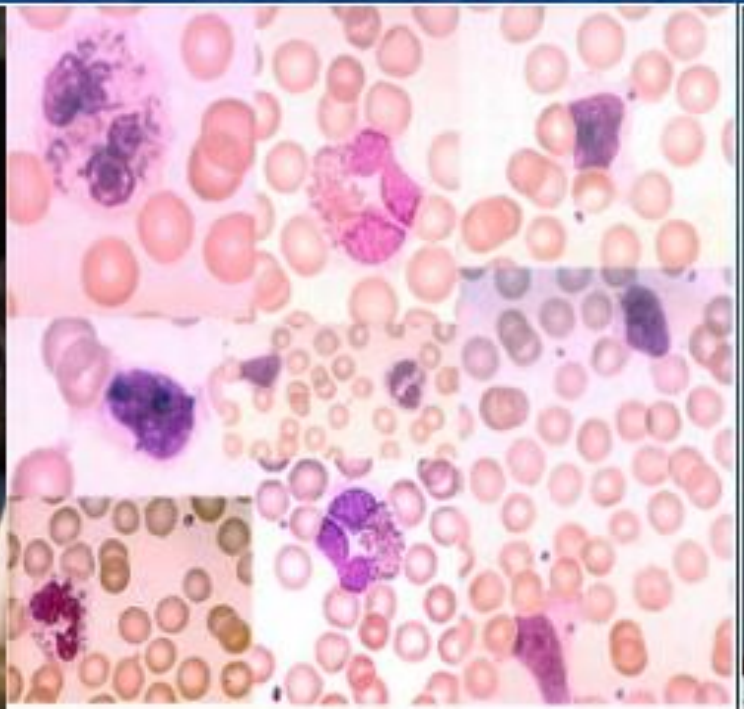
Immune Deficiency



Classification

T cell disorders	B cell defects
-Severe combined immunodeficiency -Wiskott aldrich syndrome(Xp11) -Ataxia telengectiasia(11q) -Digeorge anomaly	-XL agammaglobulinemia -Common variable immunodeficiency -Selective IgA deficiency -AR agammaglobulinemia -Hyper-IgM syndromes- XL
Phagocyte disorders	**Complement disorders**
-Chronic granulomatous disease -Leukocyte adhesion defect -Chediac higashi syndrome -Myeloperoxidase deficiency -Cyclic neutropenia (elastase defect)	-C1q deficiency -Factor I deficiency -Factor H deficiency -Factor D deficiency -Properdin deficiency

CHEDIAK HIGASHI SYNDROME



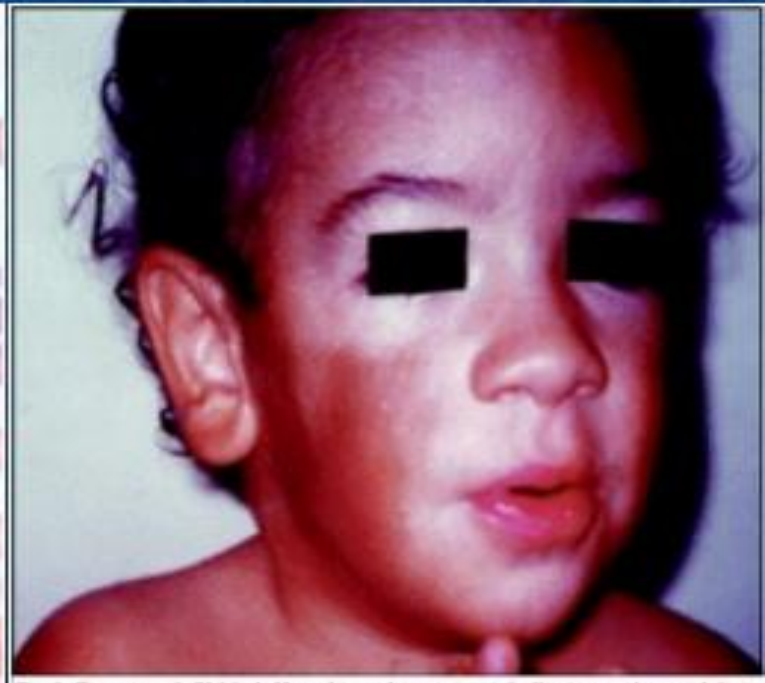
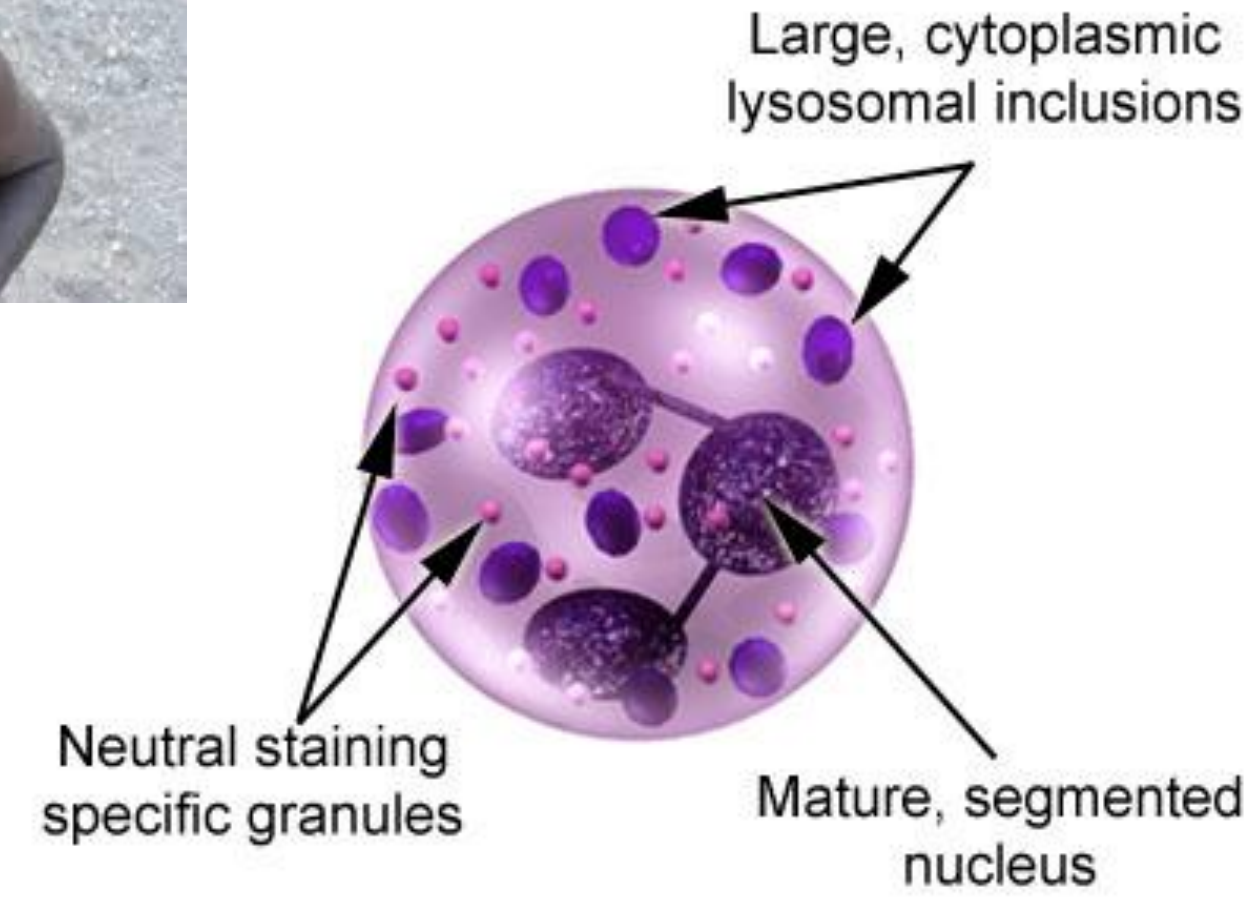


Fig 1. Features of Chédiak-Higashi syndrome: partial albinism and grayish hair.

CHEDIAK-HIGASHI NEUTROPHIL



Rashidi H MD, Nguyen J MD et al. HematologyOutlines.com

Chediak-Higashi Disease

- Rare autosomal recessive
- Abnormal lysosome: myeloperoxidase positive fused 1° granules
- Impaired PMN locomotion
- Hypopigmentation, photophobia
- Usually die at 5-10 years of age due to opportunistic and pyrogenic infections

Bruton agammaglobulinemia

or X-linked agammaglobulinemia (XLA) is an inherited immunodeficiency **disorder** characterized by the absence of mature B cells, resulting in severe antibody deficiency and recurrent infections

ANTIBODY DEFICIENCY
INABILITY TO CLEAR EXTRACELLULAR BACTERIA

- **X-LINKED AGAMMAGLOBULINEMIA XLA**
  (Bruton's agammaglobulinemia)

Genetic defect

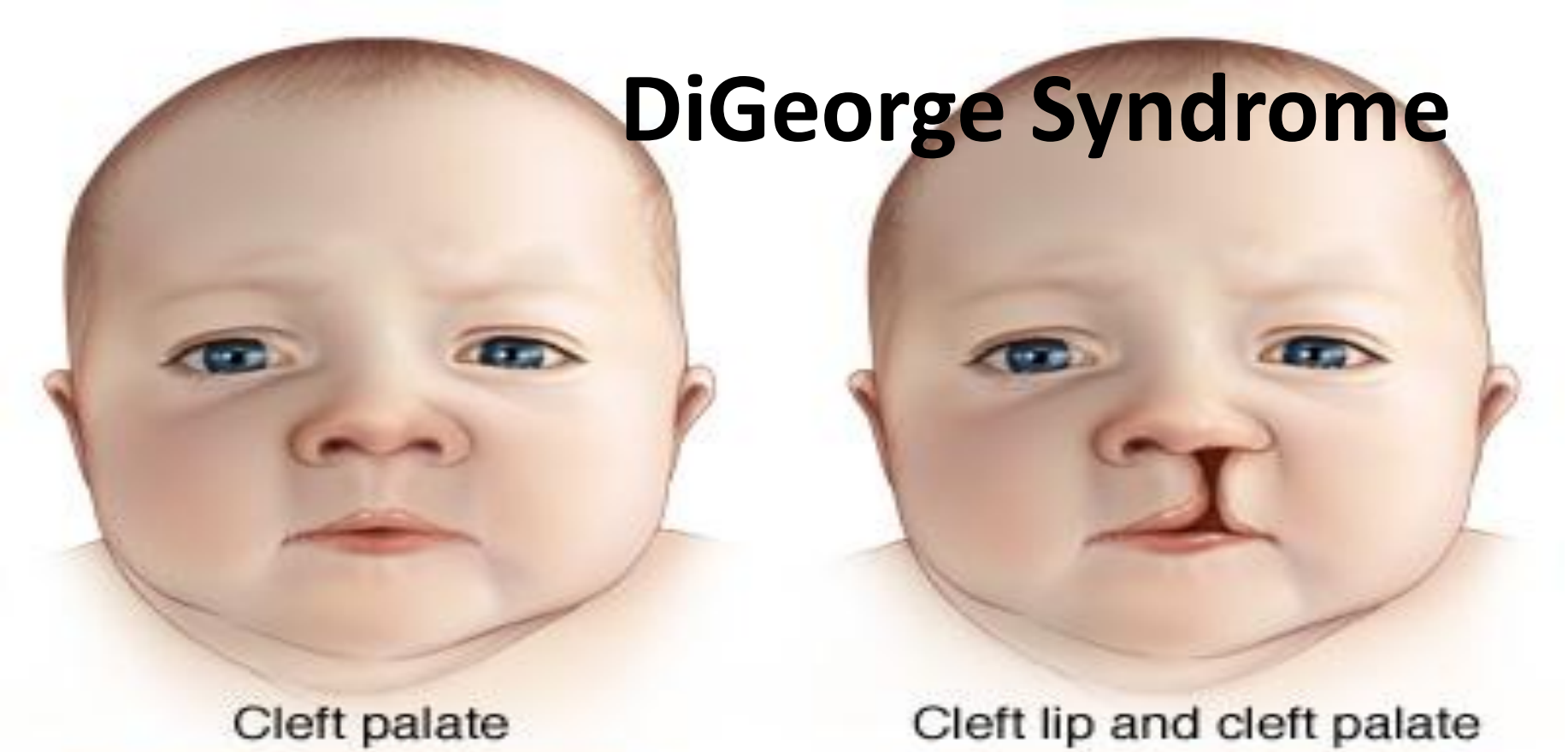
- Mutation in the Bruton's tyrosine kinase, essential for B cell activation and development
- NO B CELLS IN THE PERIPHERY – block at pre-B cell stage
- Carrier mother XX HEALTHY non-random inactivation of X in B cells
- Son XY DISEASE Son XY HEALTHY
- Increased susceptibility to bacteria and enteroviruses

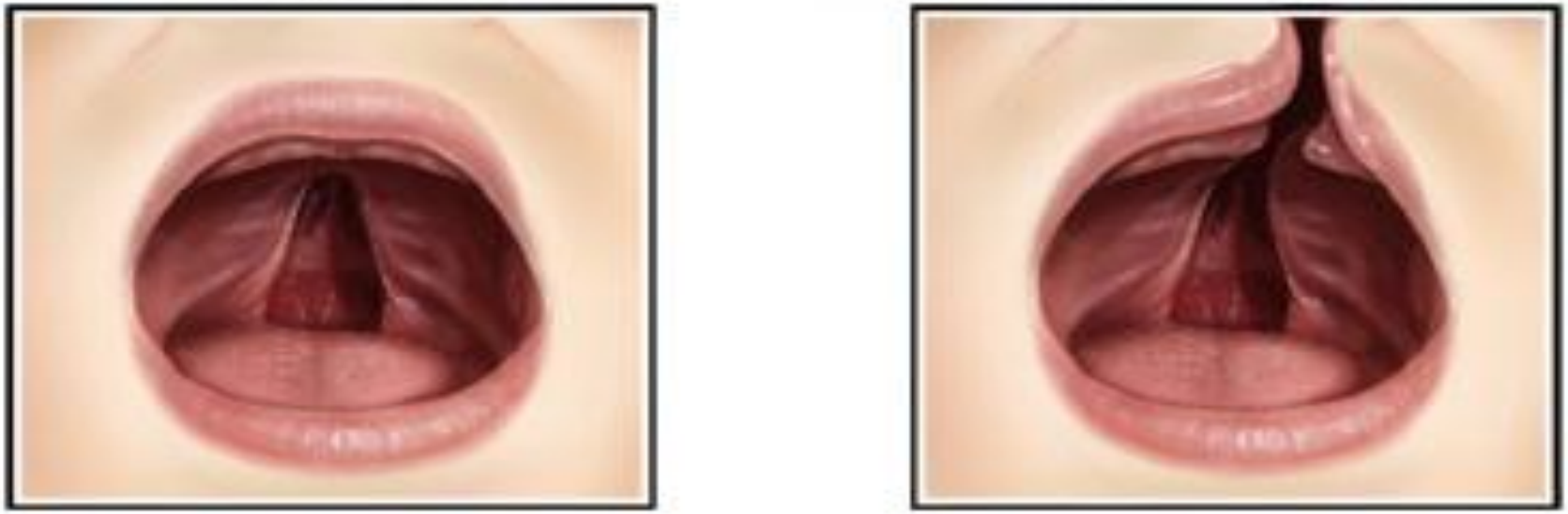
Treatment

– monthly injections of Gamma glob. (IVIG)

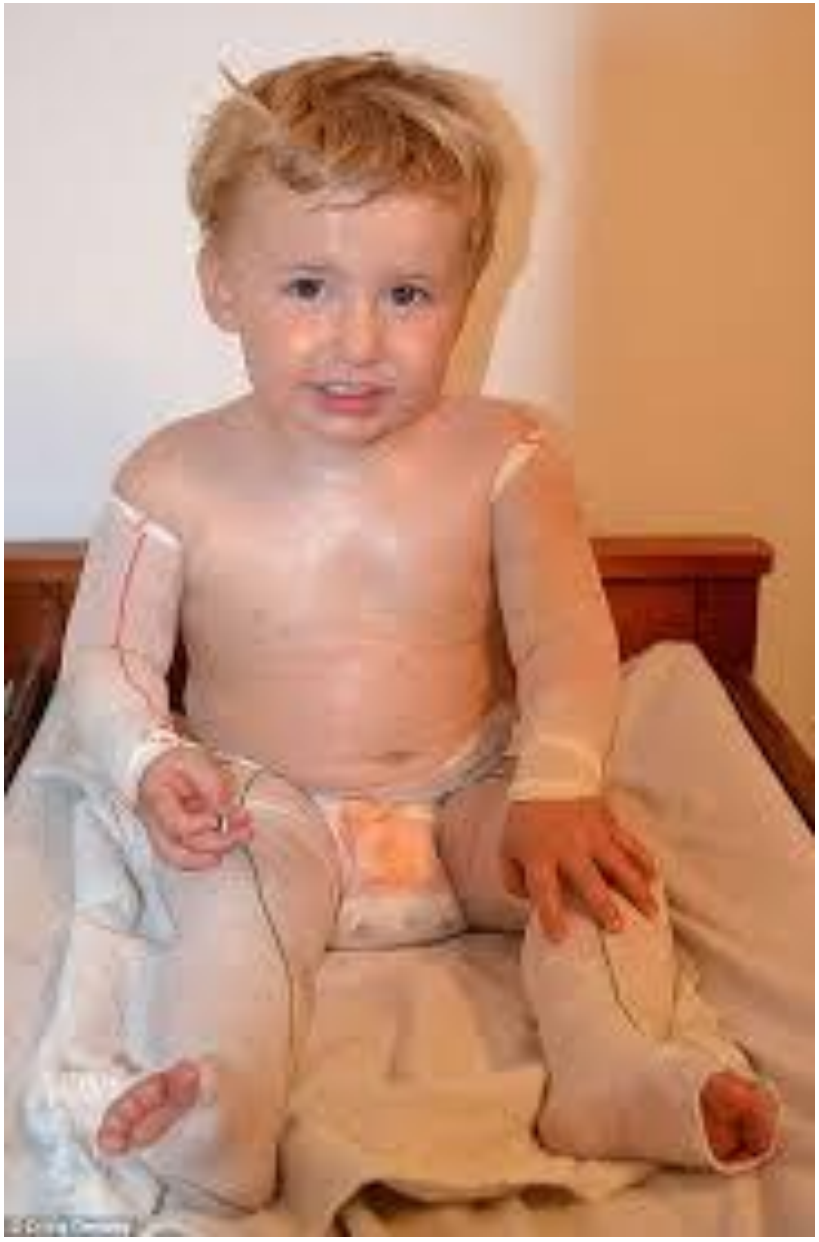
- **DiGeorge syndrome**, also known as 22q11.2 deletion **syndrome**, is a **syndrome** caused by the deletion of a small segment of chromosome 22.
- While the symptoms can vary, they often include congenital heart problems, specific facial features, frequent infections, developmental delay, learning problems and cleft palate.

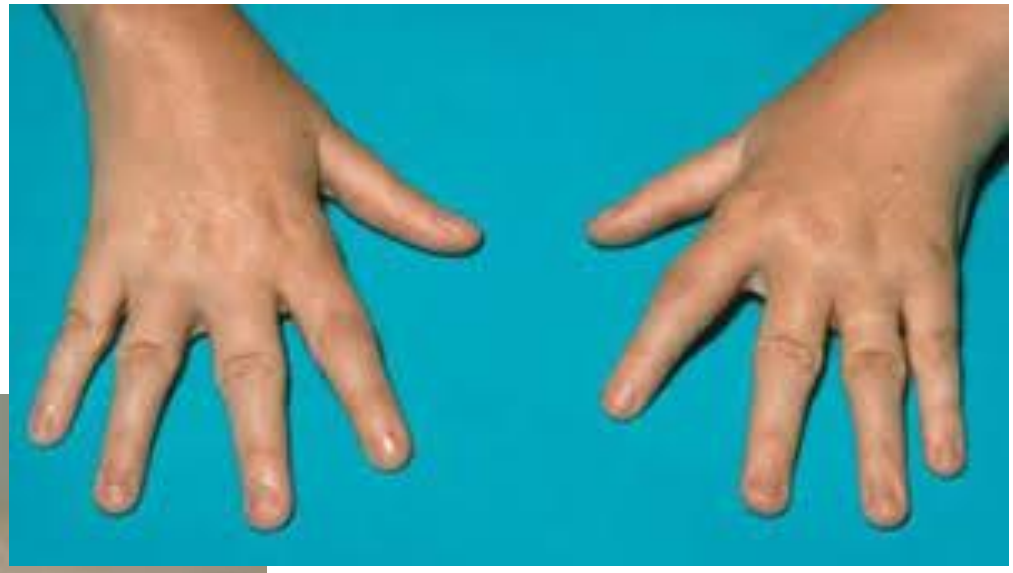
DiGeorge Syndrome

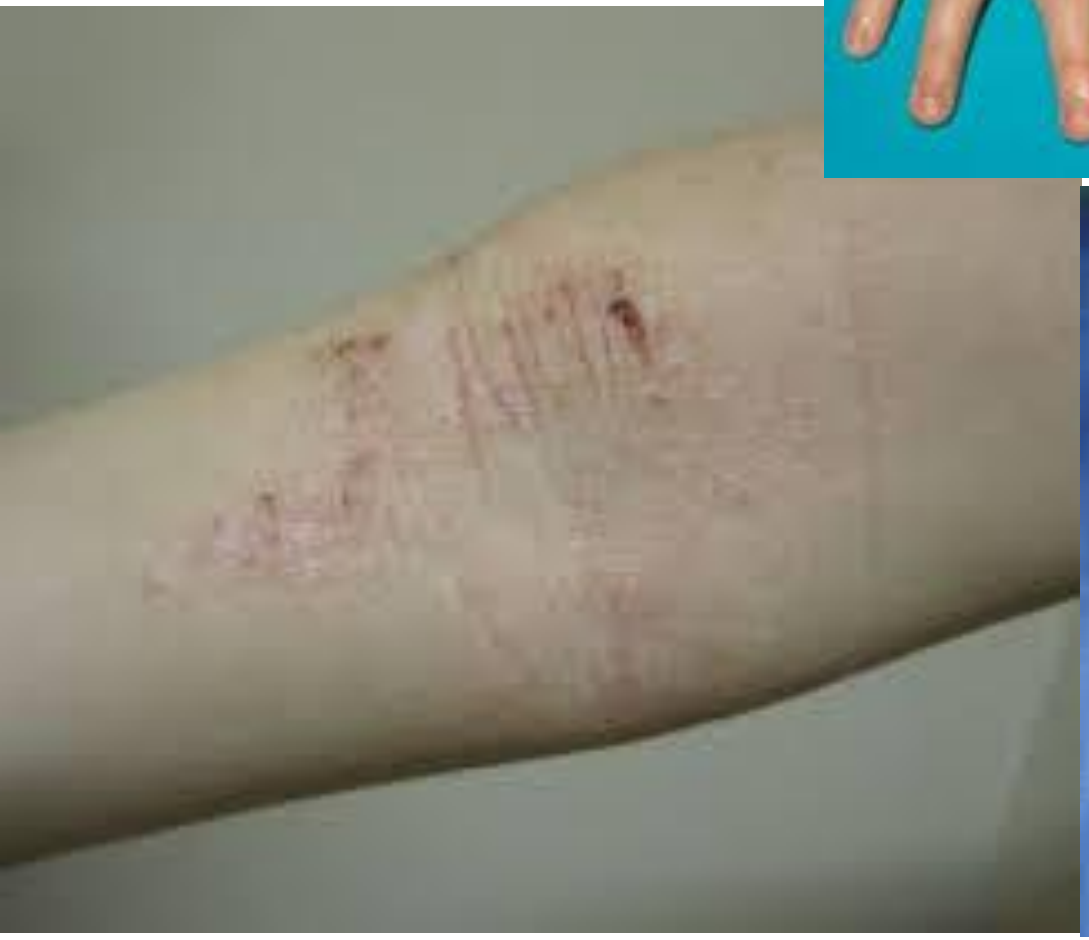




Wiskott–**Aldrich syndrome** (WAS) is a rare X-linked recessive disease characterized by eczema, thrombocytopenia (low platelet count), immune deficiency, and bloody diarrhea (secondary to the thrombocytopenia).







Hypersensitivity (Allergy, immune mediated injury)

-Hypersensitivity: A change in the tissue reaction following re-exposure to antigen

-Antigen (first time) → No harmful effect + stimulation of formation of specific antibodies

(Second time) → Ag will react with the specific antibody fixed on the cells

Cellular damage with severe inflammatory reaction = hypersensitivity

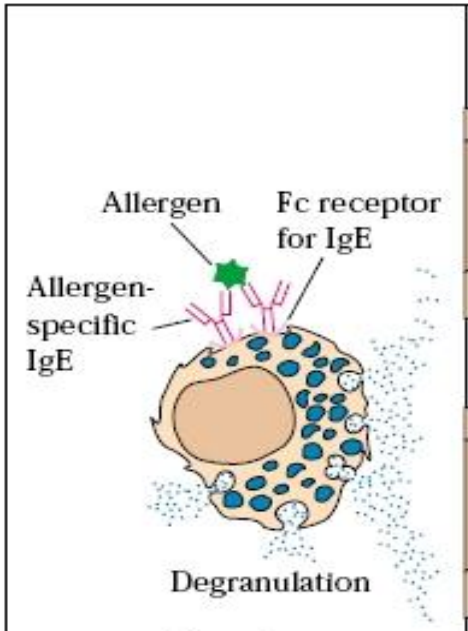
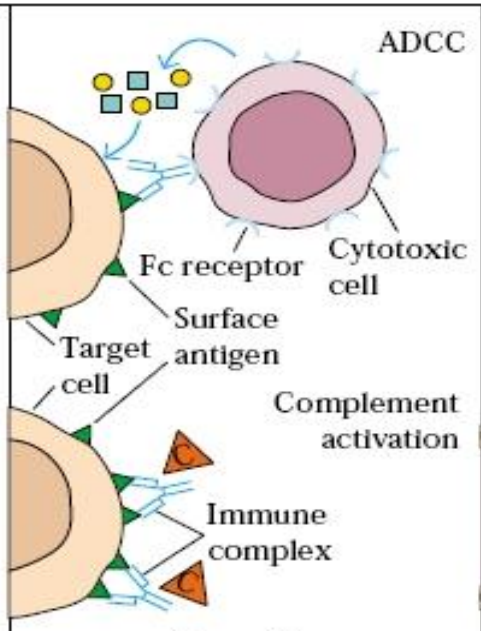
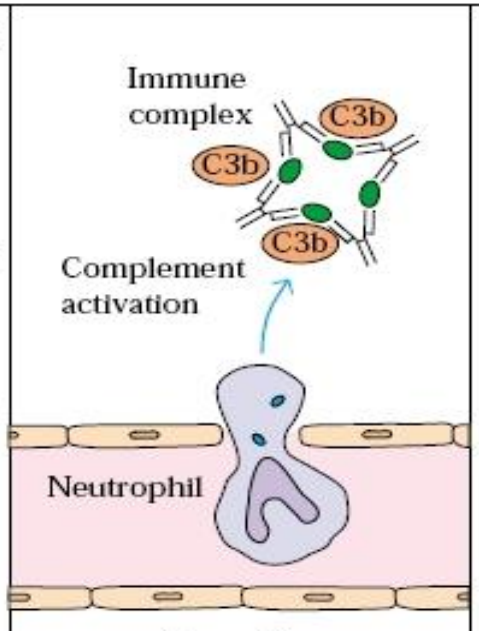
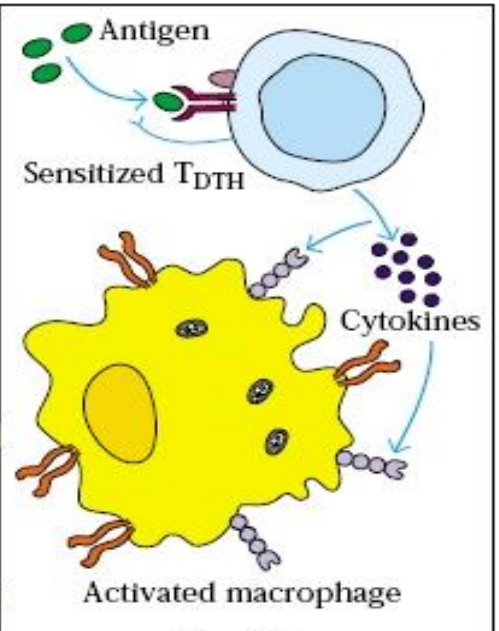
OR

Hypersensitivity is a state of altered immune responsiveness in which a severe and harmful immune reaction occurs on exposure to the antigen.

IMMUNE MECHANISMS OF TISSUE INJURY
Hypersensitivity reactions/diseases

- Classified into 4 types based on the immune mechanisms of tissue injury:
- Type I, Type II, Type III and Type IV.

Hypersensitivity Reactions

 Type I	 Type II	 Type III	 Type IV
IgE-Mediated Hypersensitivity	IgG-Mediated Cytotoxic Hypersensitivity	Immune Complex-Mediated Hypersensitivity	Cell-Mediated Hypersensitivity
Ag induces crosslinking of IgE bound to mast cells and basophils with release of vasoactive mediators	Ab directed against cell surface antigens meditates cell destruction via complement activation or ADCC	Ag-Ab complexes deposited in various tissues induce complement activation and an ensuing inflammatory response mediated by massive infiltration of neutrophils	Sensitized T_H1 cells release cytokines that activate macrophages or T_C cells which mediate direct cellular damage
Typical manifestations include systemic anaphylaxis and localized anaphylaxis such as hay fever, asthma, hives, food allergies, and eczema	Typical manifestations include blood transfusion reactions, erythroblastosis fetalis, and autoimmune hemolytic anemia	Typical manifestations include localized Arthus reaction and generalized reactions such as serum sickness, necrotizing vasculitis, glomerulnephritis, rheumatoid arthritis, and systemic lupus erythematosus	Typical manifestations include contact dermatitis, tubercular lesions and graft rejection

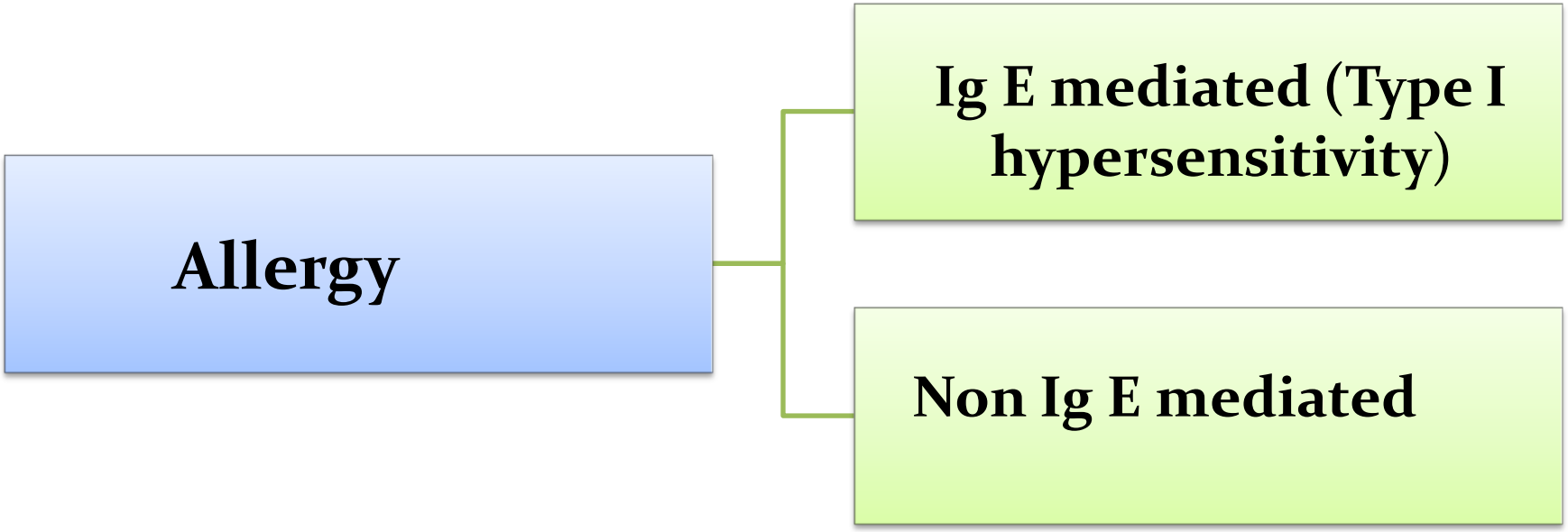
Type I Hypersensitivity

- Atopy – any chronic local allergy such as hay fever or asthma
- Anaphylaxis – a systemic, often explosive reaction that involves airway obstruction and circulatory collapse

Mechanism of Type I

- **sensitizing dose** – on first contact with allergen, specific B cells form IgE which attaches to mast cells and basophils
- **provocative dose** - subsequent exposure with the same allergen binds to the IgE-mast cell complex
- degranulation releases mediators with physiological effects such as vasodilation and bronchoconstriction
- symptoms are rash, itching, redness, increased mucous discharge, pain, swelling, and difficulty breathing

Allergy


Allergy
Ig E mediated (Type I hypersensitivity)
Non Ig E mediated

Type I Hypersensitivity
A sequence of Events

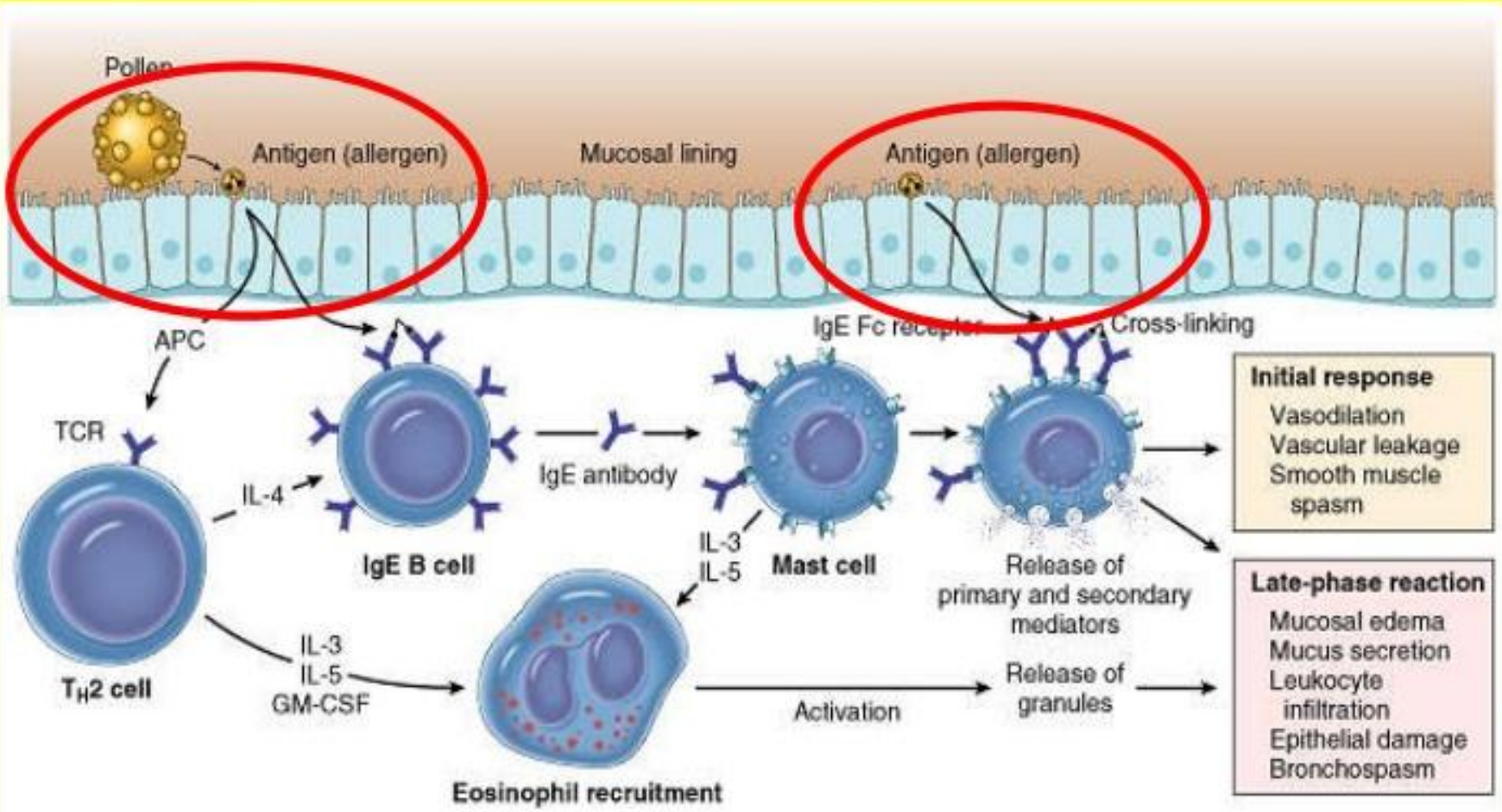
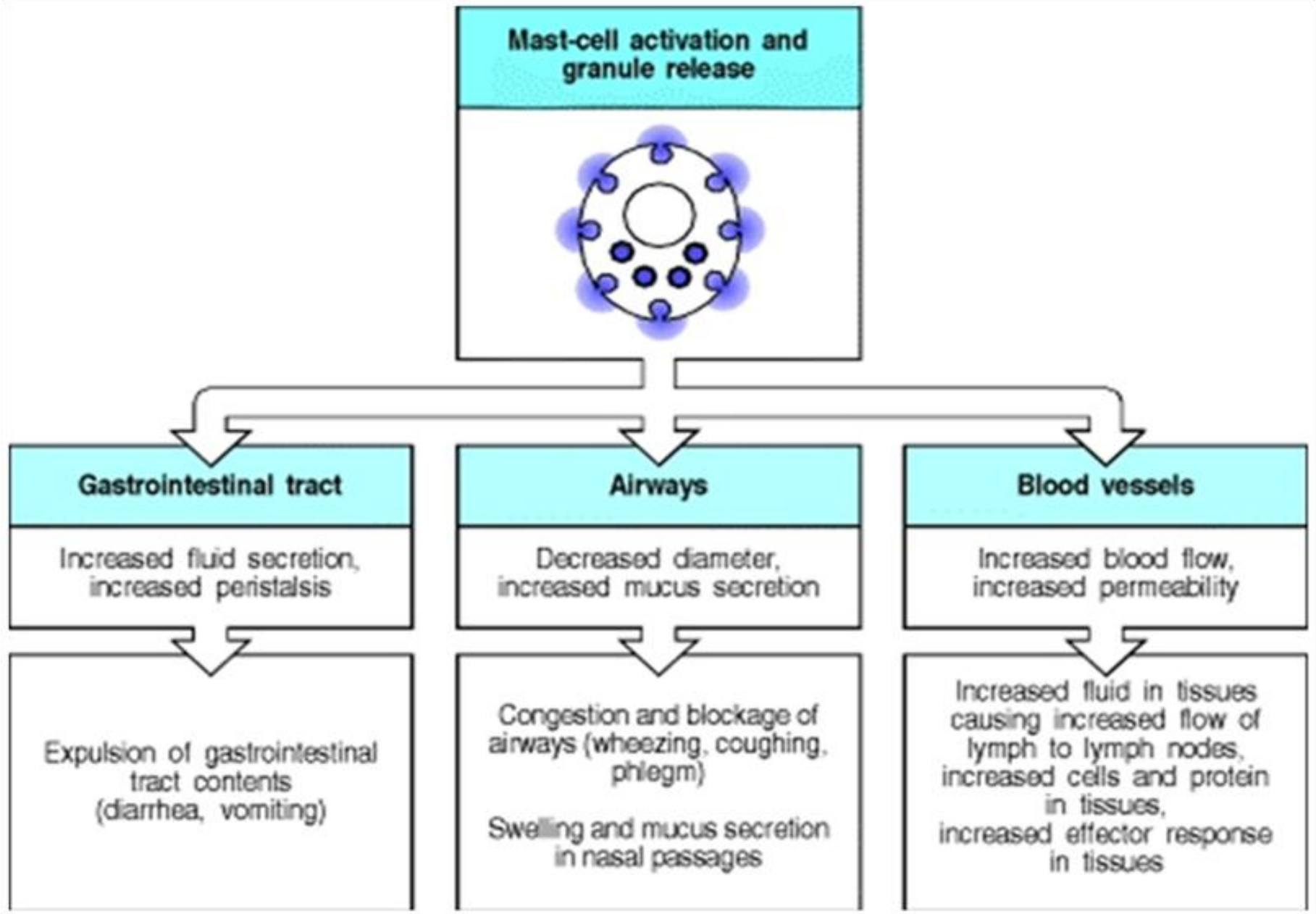


Photo: Kumar, Cotran, Robbins. Robbins Basic pathology, 7th ed., Saunders, Philadelphia, 2003.

Mast Cell Activation

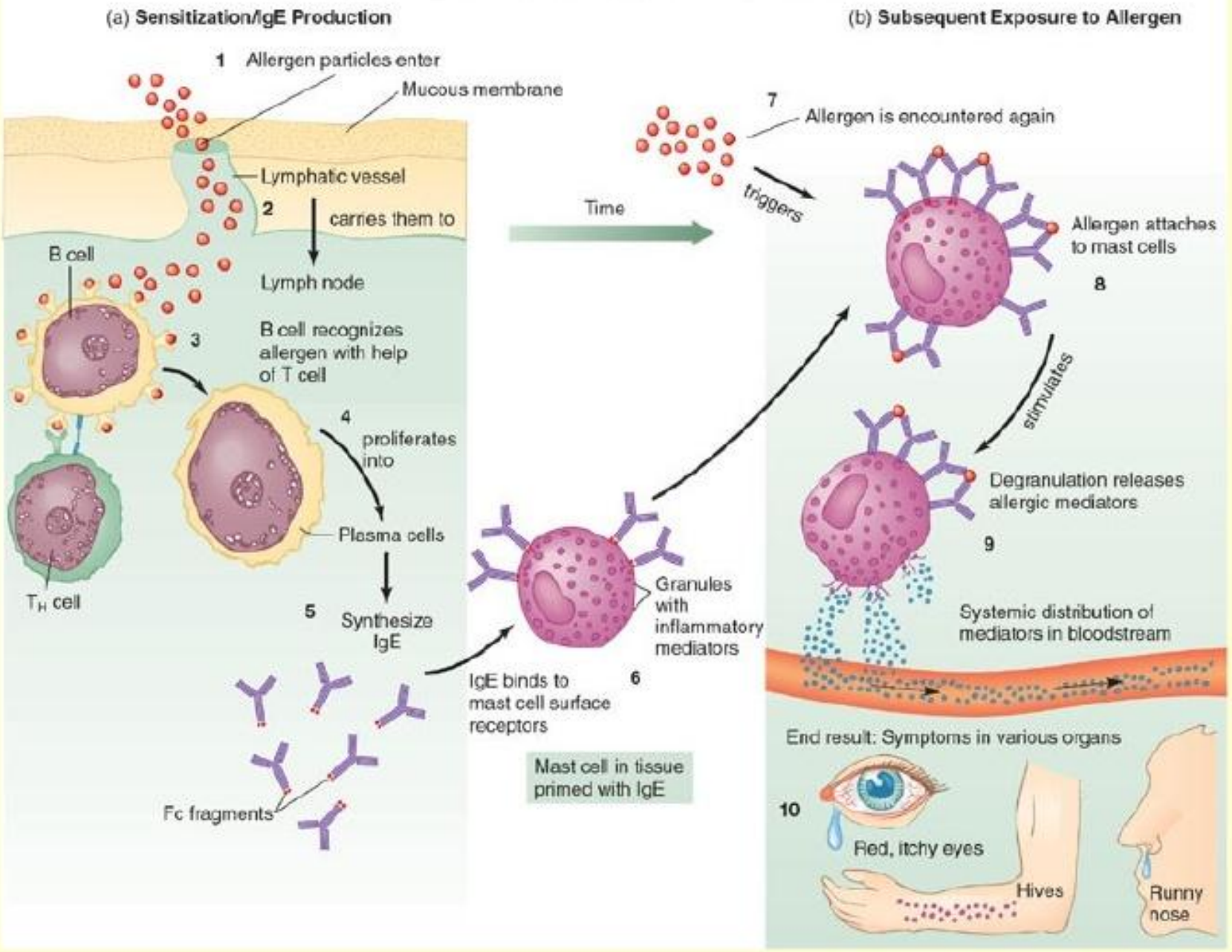


Type I Hypersensitivity Reaction
Clinical Manifestations

- **Systemic anaphylaxis:**
  - -- Acute asthma
  - -- Laryngeal edema
  - -- Diarrhea
  - -- Urticaria
  - -- Shock (Anaphylactic shock)

Typically follows oral administration pf allergen as:

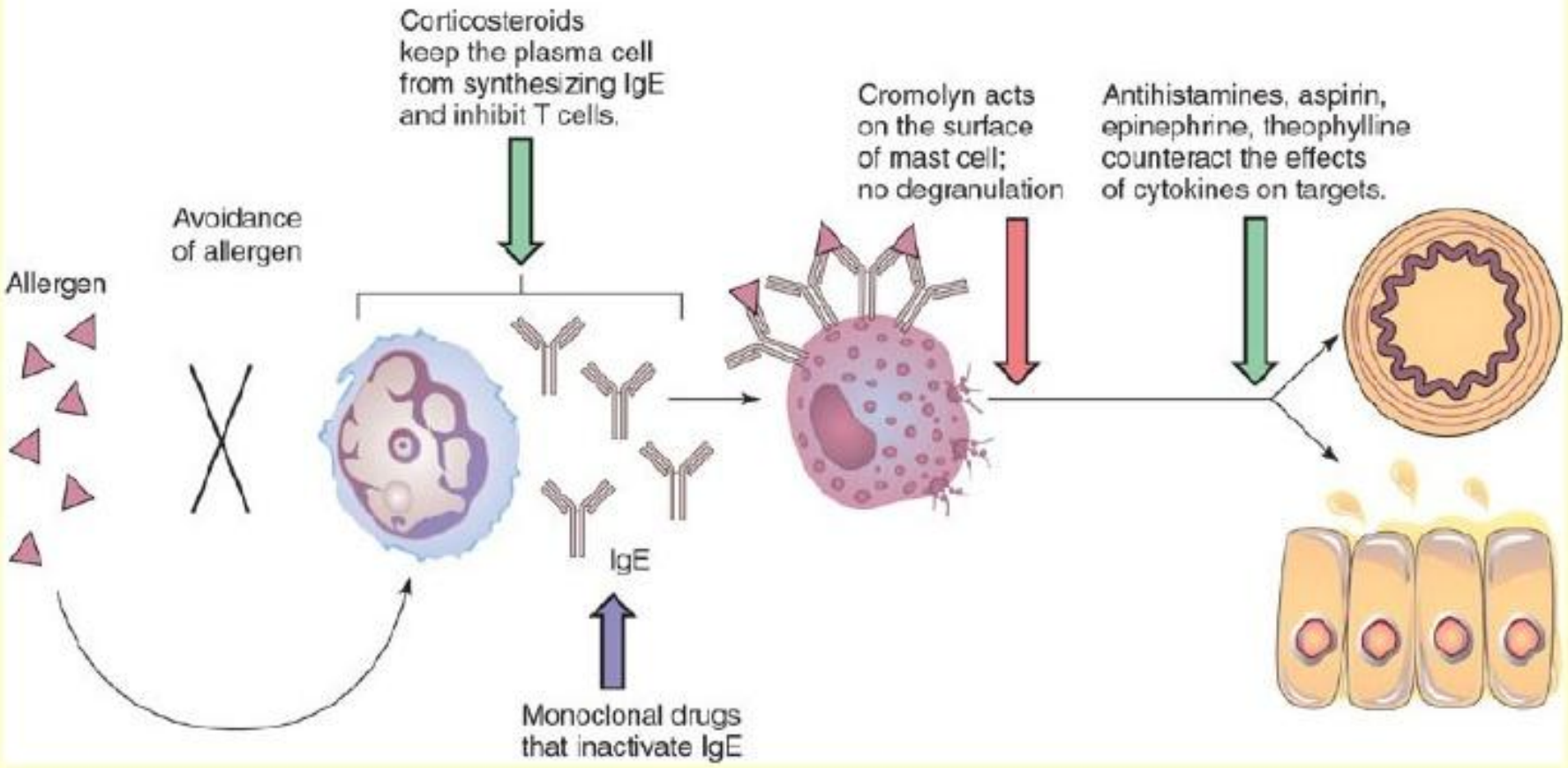
- E.g.: penicillin allergy
- E.g.: bee sting allergy
- Antisera, Drugs, Hormones



Systemic Anaphylaxis

- Sudden respiratory and circulatory disruption that can be fatal in a few minutes
- Allergen and route are variable
- Bee stings, antibiotics or serum injection

Strategies for circumventing allergic attacks



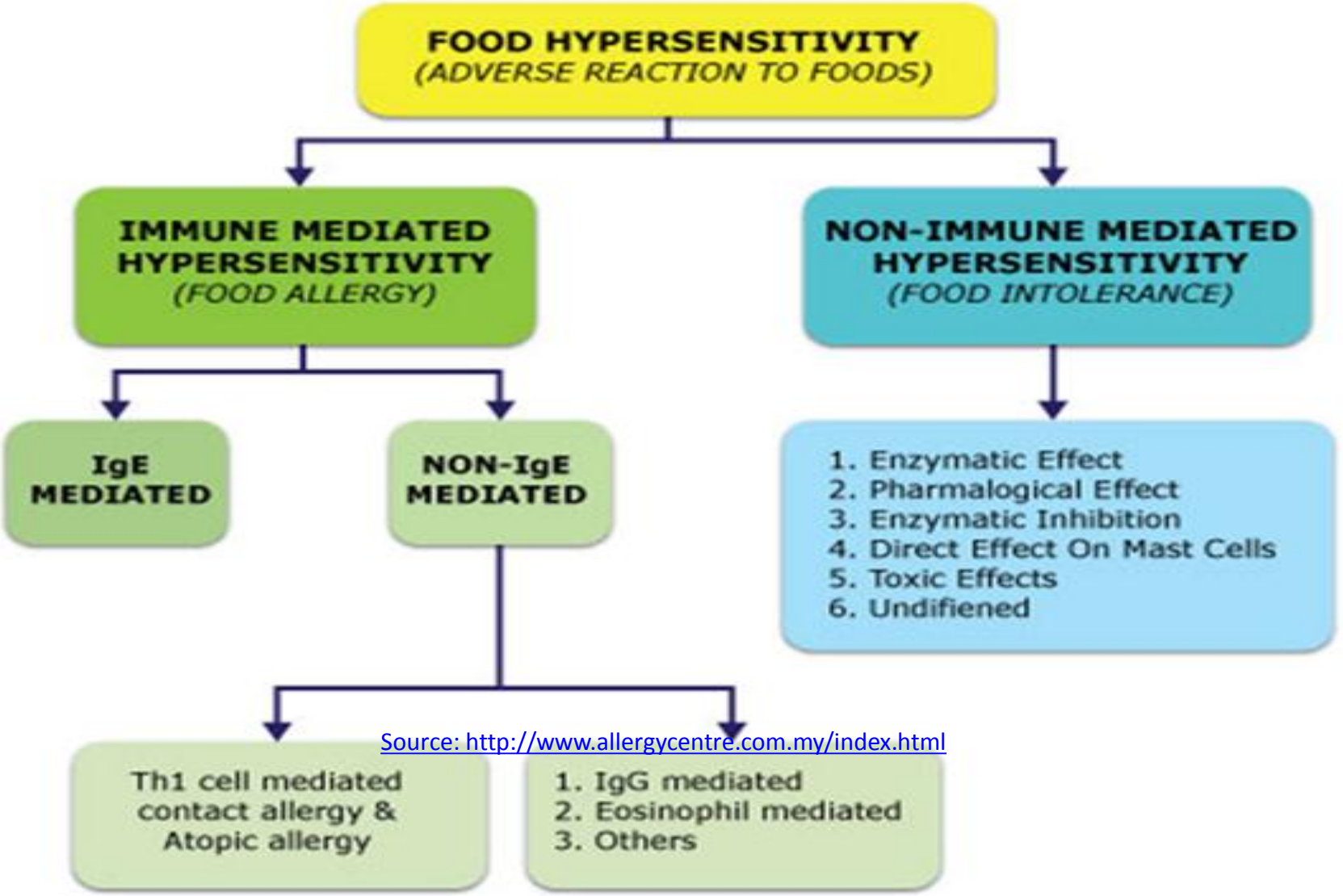
Type II Hypersensitivity

- Reactions that lyse foreign cells
- Involve antibodies, complement, leading to lysis of foreign cells
- Transfusion reactions
  - ABO blood groups
  - Rh factor – hemolytic disease of the newborn

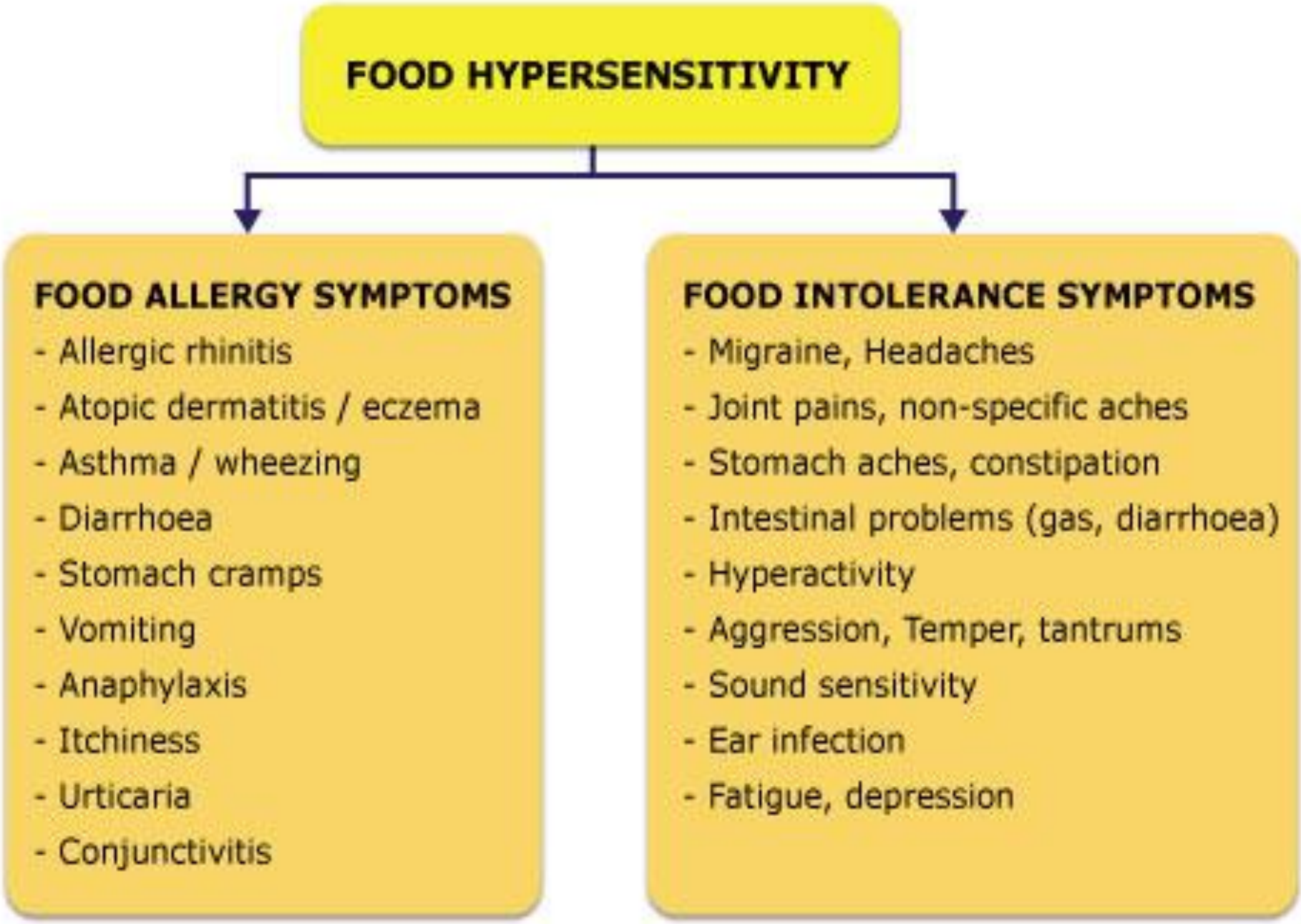
ABLE 16-3 Principal mediators involved in type I hypersensitivity

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)

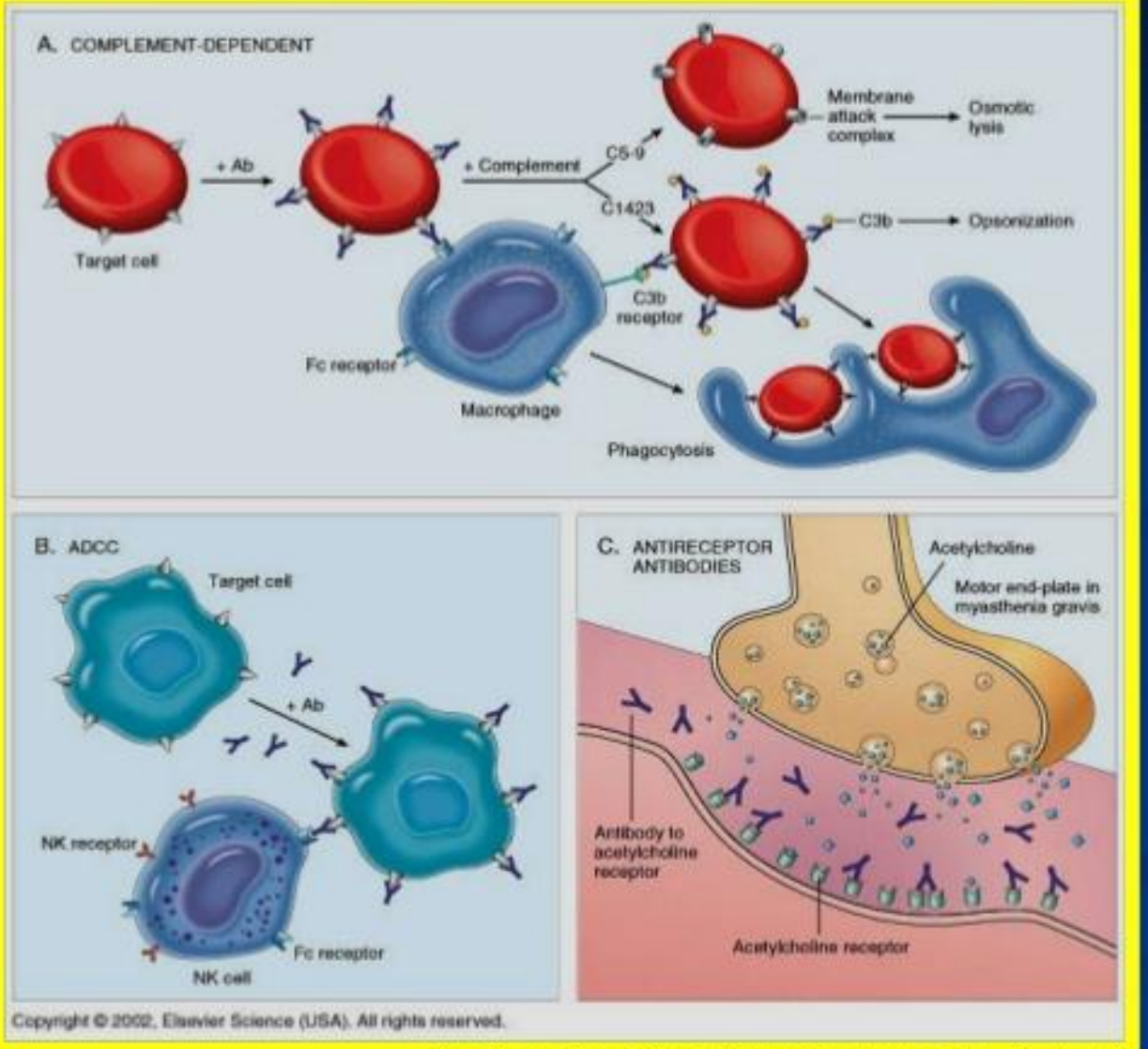
Food Hypersensitivity



Source: http://www.allergycentre.com.my/index.html

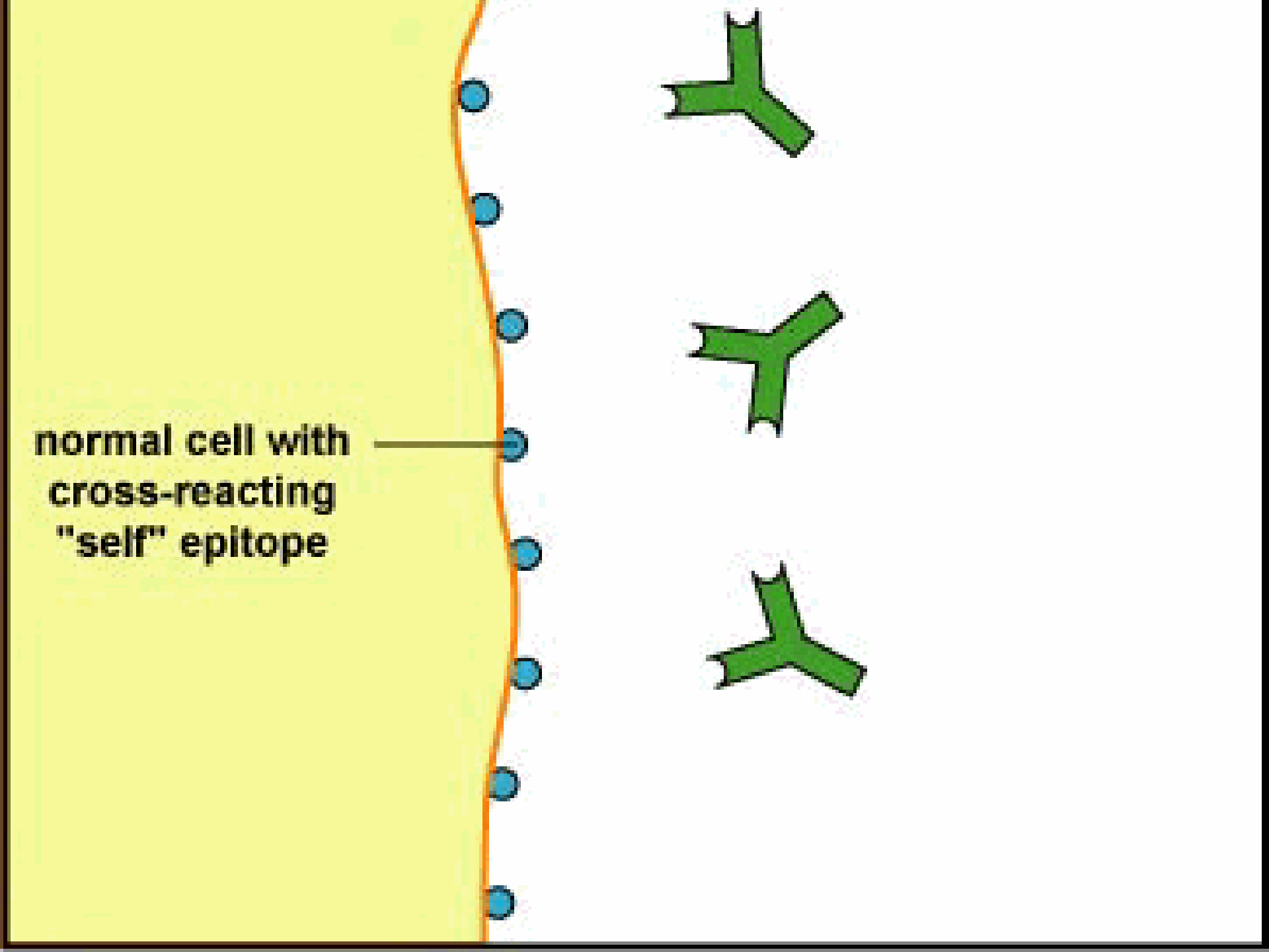

FOOD HYPERSENSITIVITY
FOOD ALLERGY SYMPTOMS
- Allergic rhinitis
- Atopic dermatitis / eczema
- Asthma / wheezing
- Diarrhoea
- Stomach cramps
- Vomiting
- Anaphylaxis
- Itchiness
- Urticaria
- Conjunctivitis
FOOD INTOLERANCE SYMPTOMS
- Migraine, Headaches
- Joint pains, non-specific aches
- Stomach aches, constipation
- Intestinal problems (gas, diarrhoea)
- Hyperactivity
- Aggression, Temper, tantrums
- Sound sensitivity
- Ear infection
- Fatigue, depression

Type II Hypersensitivity
Antibody-Mediated Injury



Myasthenia gravis (Acetylcholine receptor antibody)

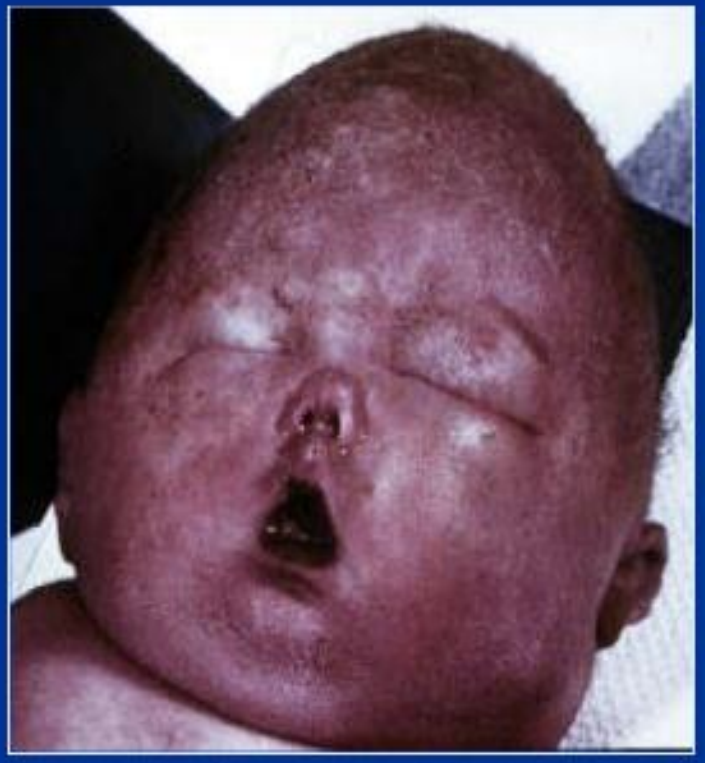
Photo: Kumar, Cotran, Robbins. Robbins Basic pathology, 7th ed., Saunders, Philadelphia, 2003.


normal cell with
cross-reacting
"self" epitope

Type II Hypersensitivity Reaction

Clinical Manifestations

- Transfusion and transplant reactions
- Rhesus incompatibility between Rh-negative mother and Rh-positive fetus (erythroblastosis fetalis)



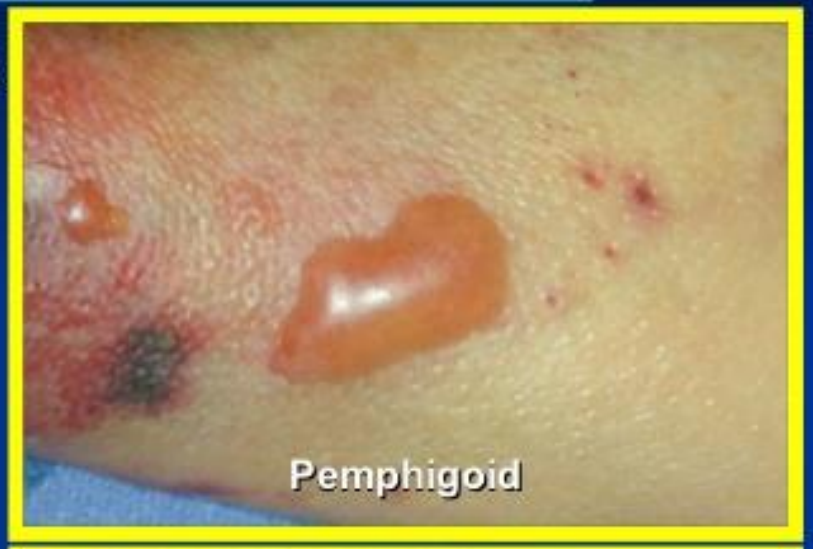
Immune hydrops from Rh hemolysis

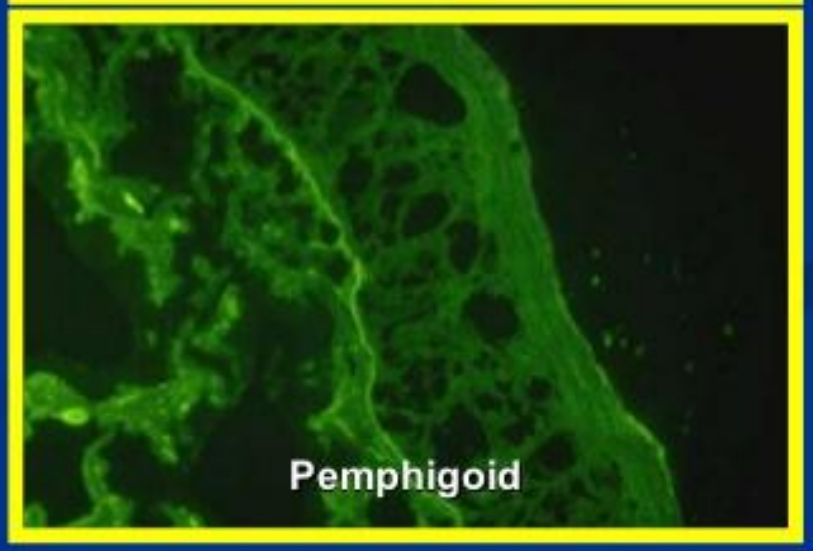
Erythroblastosis fetalis

- Elevated Rh antibody titers
- Many immature RBCs in blood
- Excess bilirubin from RBC breakdown
  -- Hyperbilirubinemia (yellow tissues)
- First baby = OK, because IgM cannot cross placenta, after that, IgG takes over
- Progressive anemia, ischemia, death
- Brain damage from bilirubin: kernicterus
- Prevention: Rh- mother gets anti-D immunoglobulin after birth (covers antigenic sites on baby's RBCs in mother's blood
- Rx: phototherapy of baby (breaks bilirubin)

Type II Hypersensitivity Reaction
Clinical Manifestations

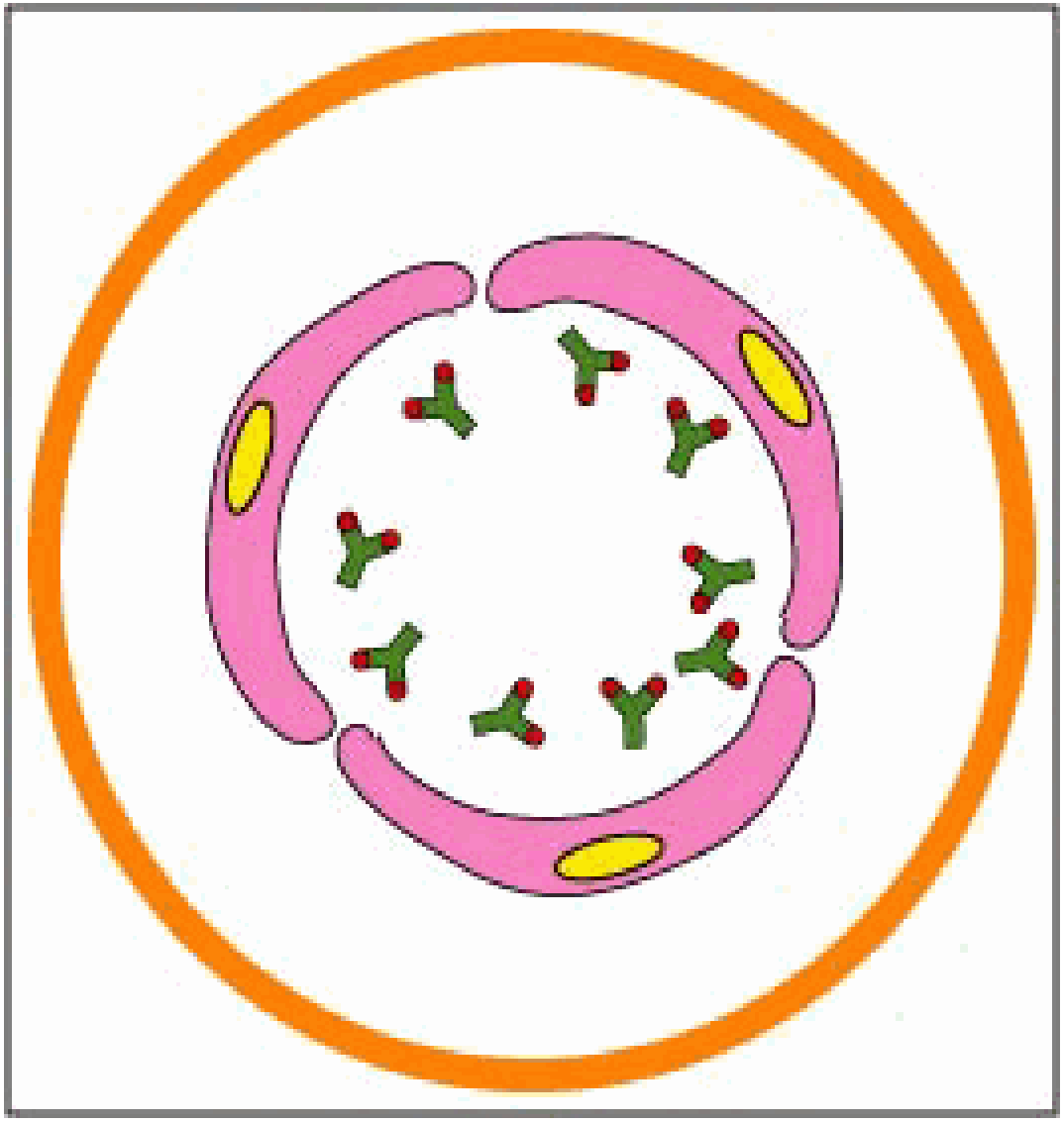
- Autoimmune hemolytic anemia
- Agranulocytosis
- Thrombocytopenia
- Pemphigus vulgaris
- Pemphigoid
  (Cicatricial pemphigoid)

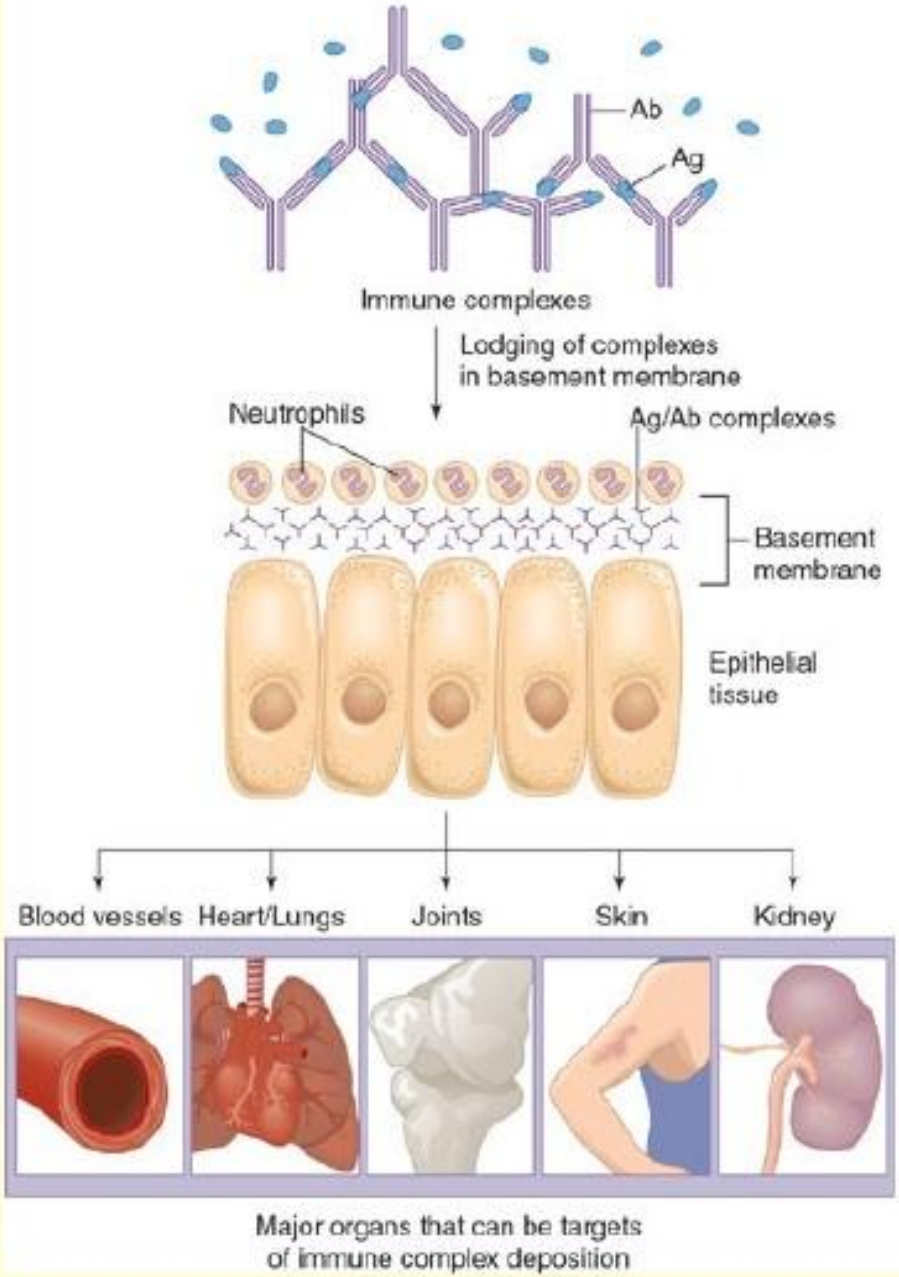




Type III Hypersensitivity

- A large quantity of soluble foreign Ag stimulates Ab that produce small, soluble Ag-Ab complexes
- Immune complexes become trapped in tissues & incite a damaging inflammatory response
  - Arthus reaction – local reaction to series of injected Ag to same body site
  - Serum sickness – systemic disease resulting from repeated injections of foreign proteins



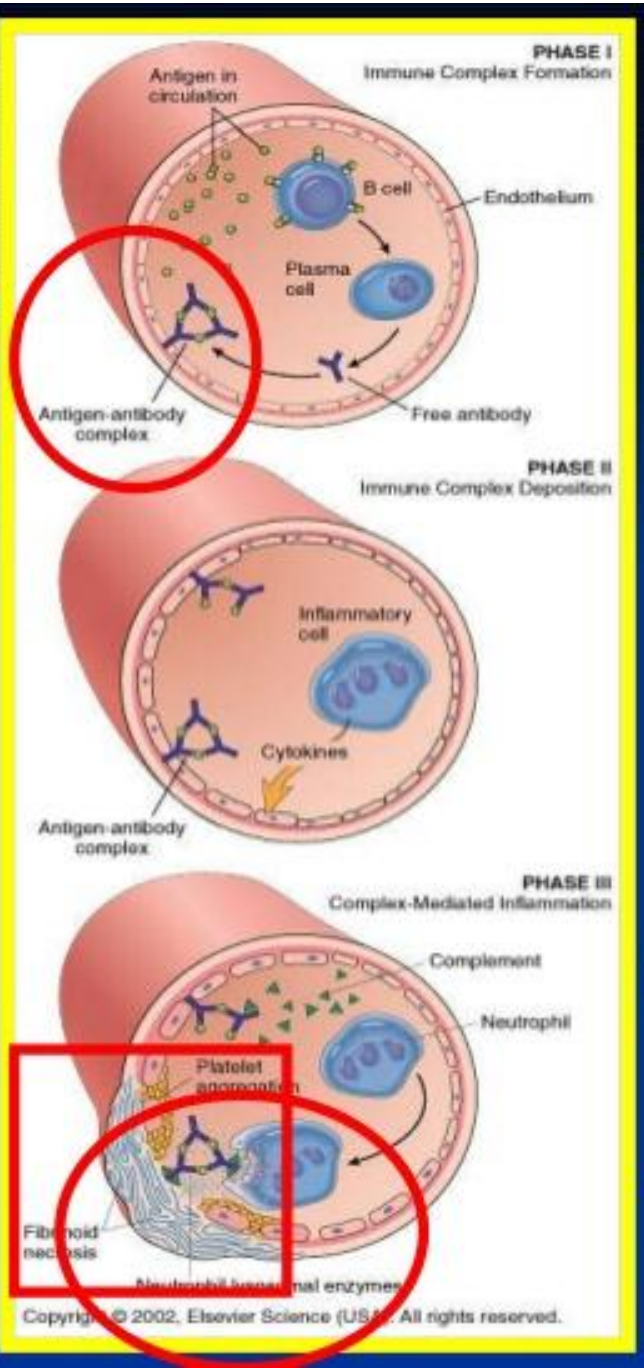


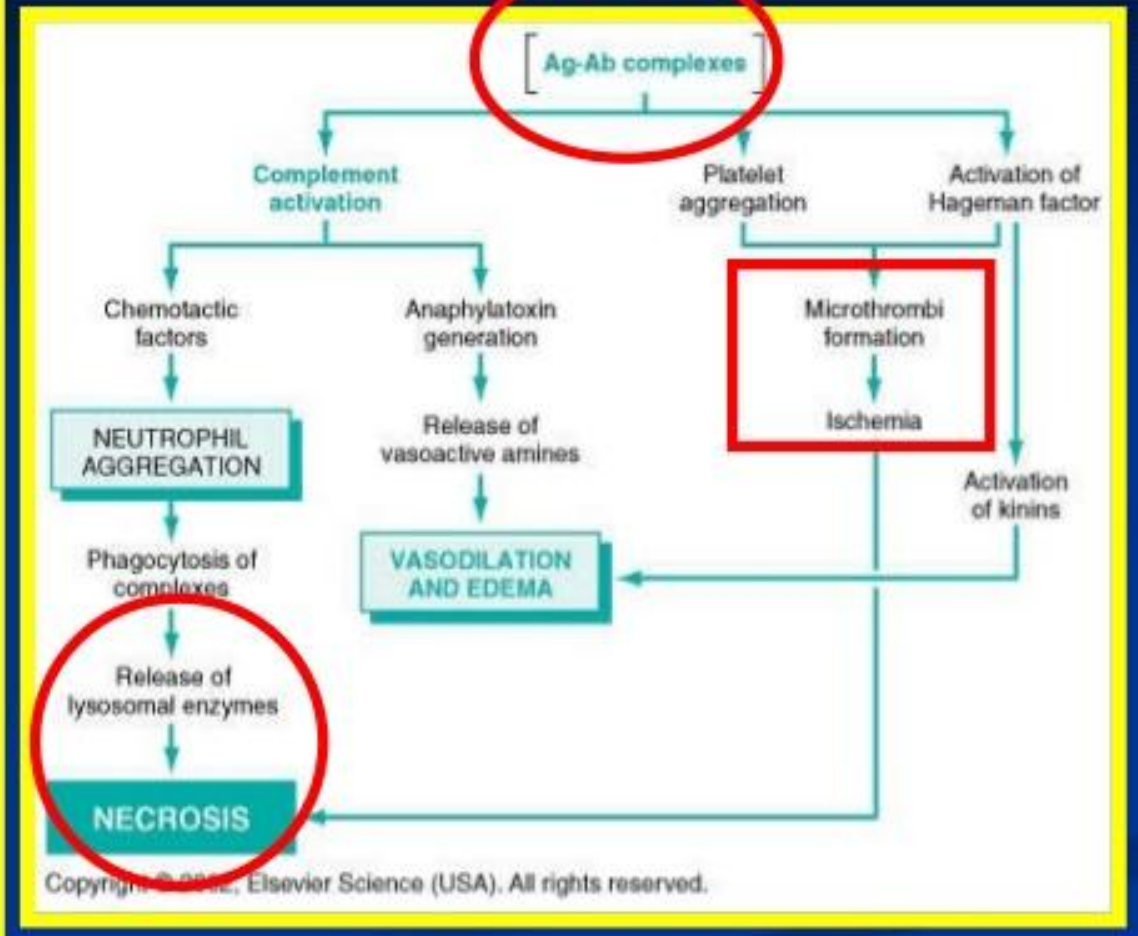
Major organs that can be targets of immune complex deposition

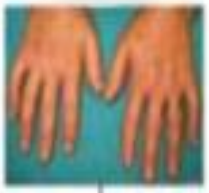
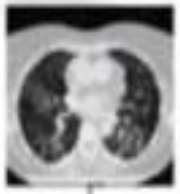
Steps:

1. Antibody combines with excess soluble antigen, forming large quantities of Ab/Ag complexes.
2. Circulating immune complexes become lodged in the basement membrane of epithelia in sites such as kidney, lungs, joints, skin.
3. Fragments of complement cause release of histamine and other mediator substances.
4. Neutrophils migrate to the site of immune complex deposition and release enzymes that cause severe damage in the tissues and organs involved.

I- Systemic Immune Complex Disease






Hidroksixlorokin

NSAİDs

Tənəffüs terapiyası

Kortikosteroid

Bikarbonat və Kalium əvəzedilməsi

Kortikosteroid

Mg

Ataksik nevro[illegible]

Metilprednizalon

Hidroksixlorokin

Siklofosfamid

Kortikosteroid

Azatioprin

Siklofosfamid

Rituksimab

Plasma terapiya

Rituksimab

Metilterksat

Mikofenol turşusu və Siklosporin A

Mikofenol turşusu və Azatropin

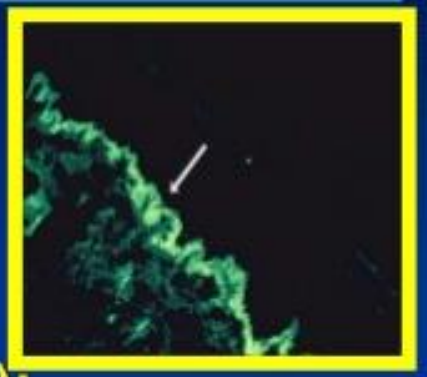
Plasma terapiya

Rituksimab

Rituksimab

Rituksimab

Immune Complex Mediated (Type III) Damage Systemic

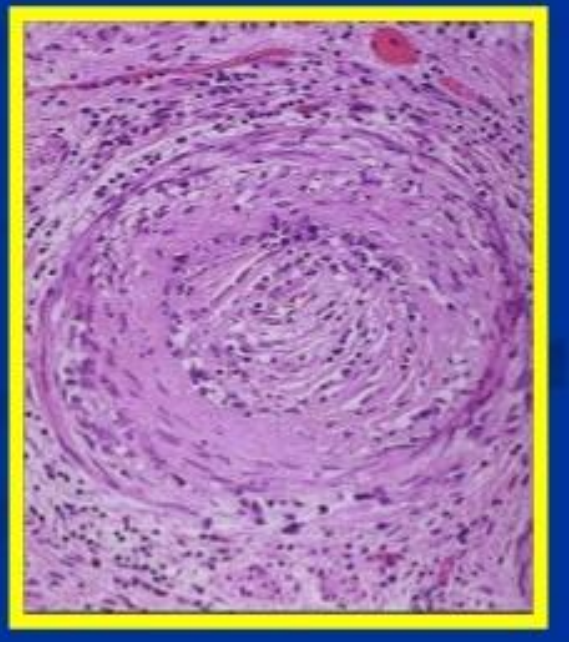


Acute (single large dose of Ag exposure):

- Acute serum sickness
- Poststreptococcal glomerulonephritis

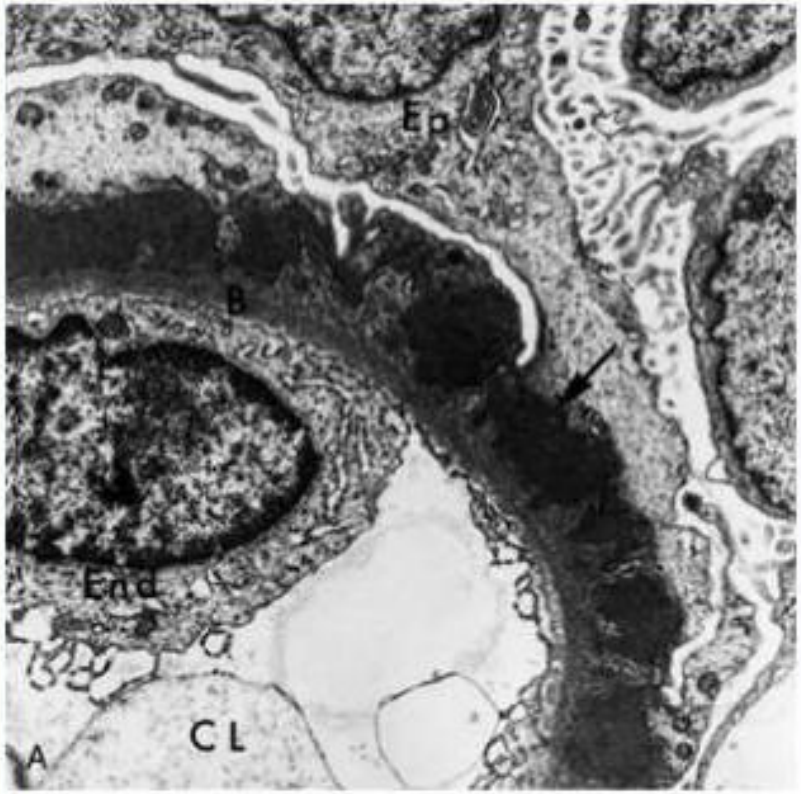
Chronic (persistent/repeated Ag exposure):

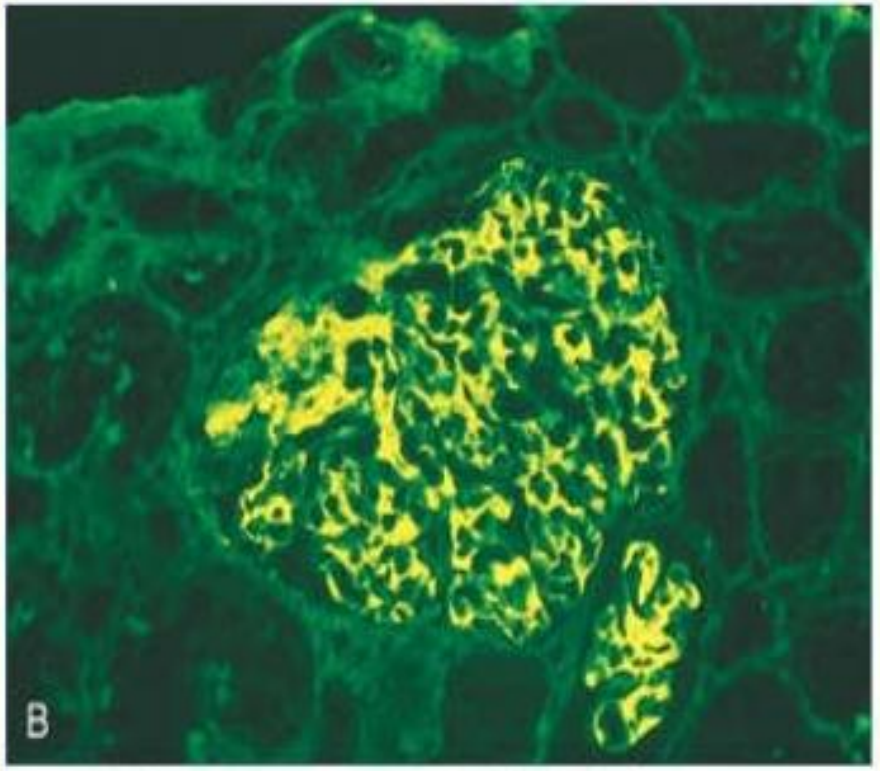
- Systemic lupus erythematosus
- Rheumatoid arthritis
- Membranous glomerulonephritis
  -- Inciting antigens = unknown



Immune Complex Deposition in Glomerulus

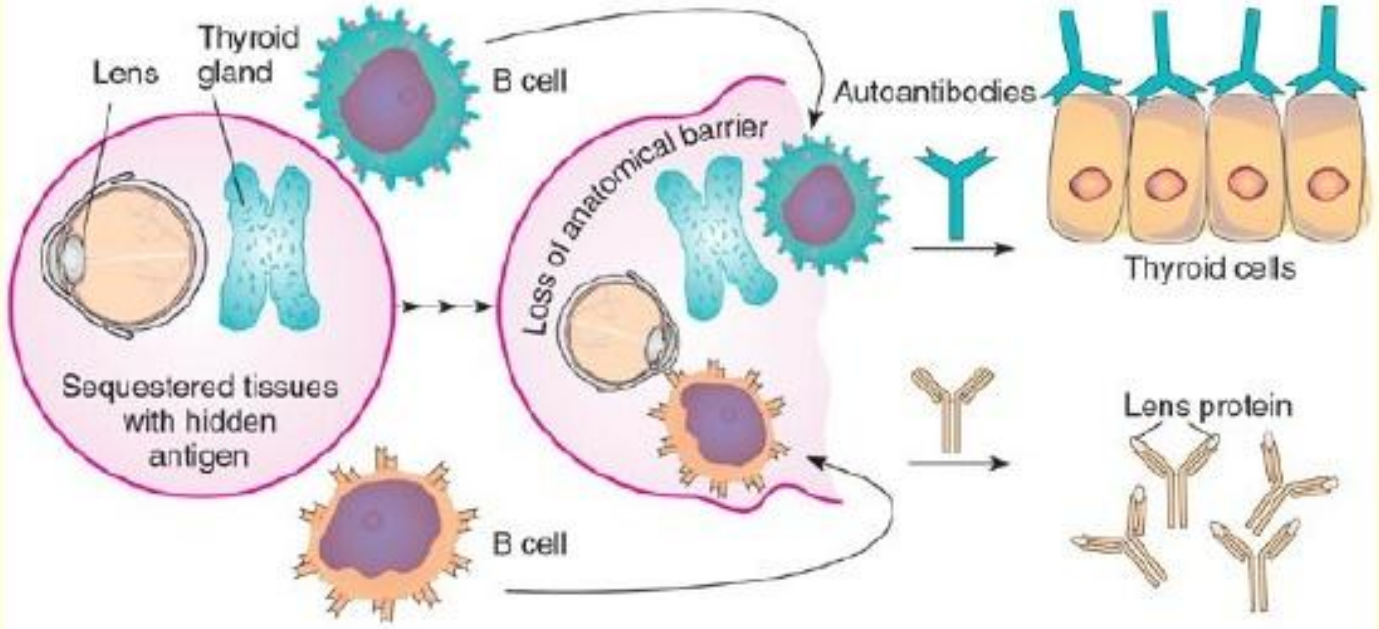
Type III Hypersensitivity



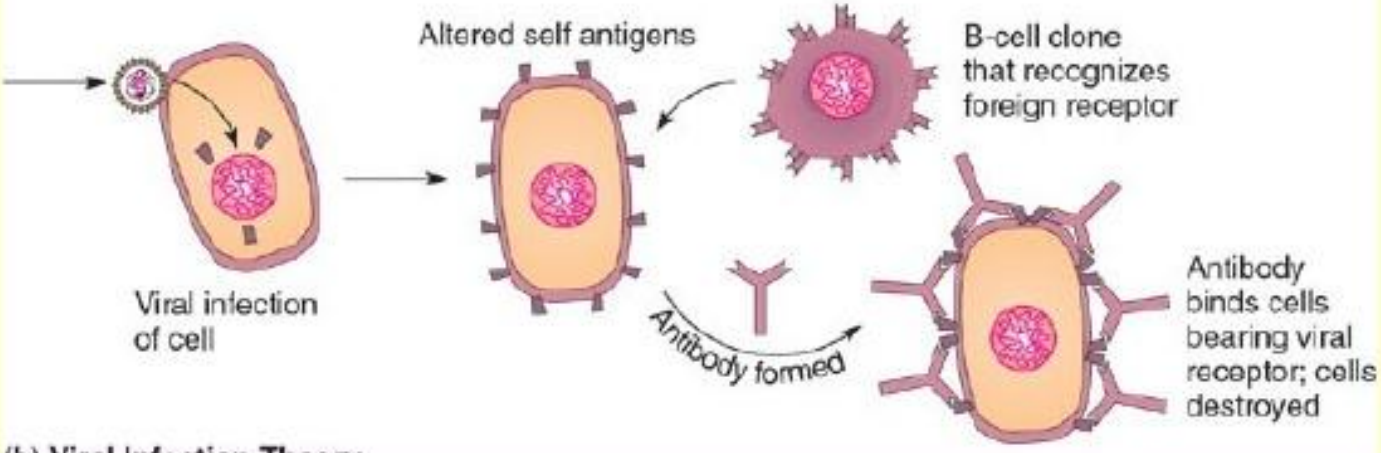


Autoimmunity

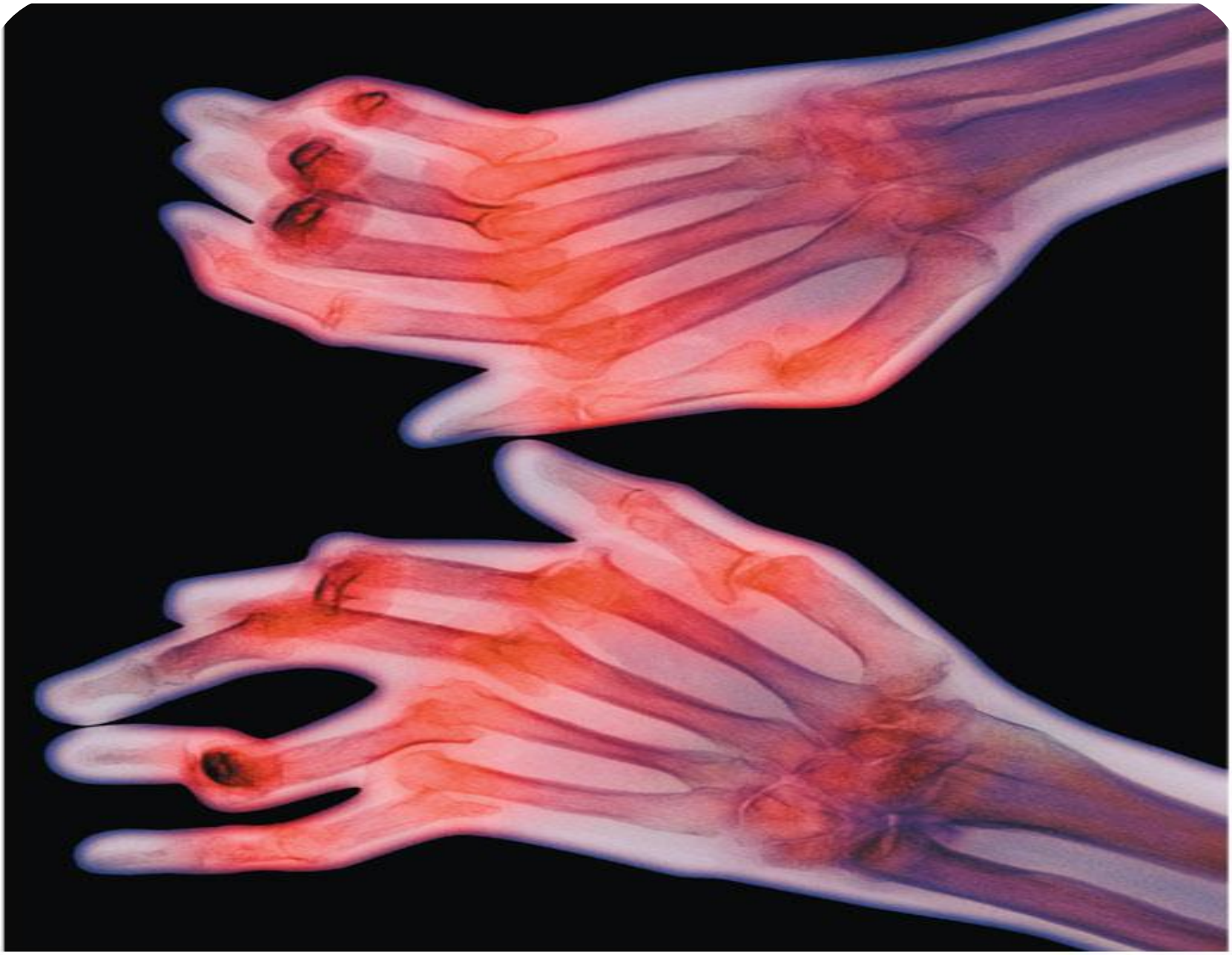
- In certain type I & II hypersensitivities, the immune system has lost tolerance to self molecules and forms autoantibodies and sensitized T cells against them.
- More common in females
- Disruption of function can be systemic or organic specific
  - Systemic lupus erythematosus
  - Rheumatoid arthritis
  - Endocrine autoimmunities
  - Myasthenia gravis
  - Multiple sclerosis



(a) **Sequestered Antigen Theory**



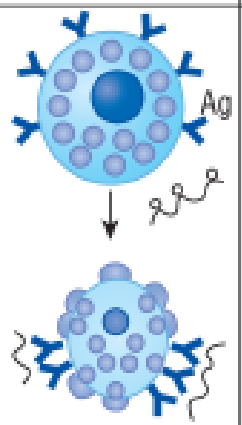
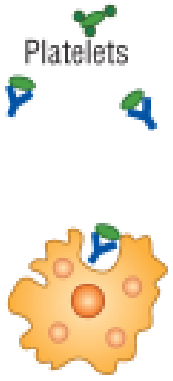
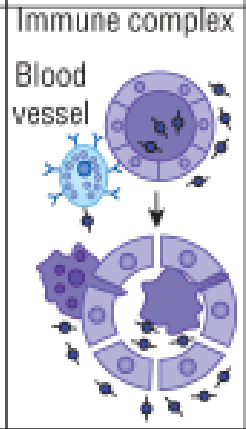
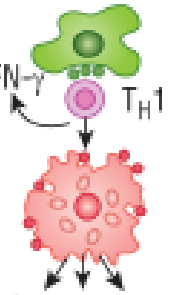
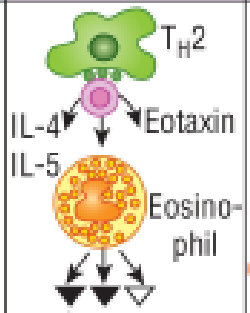
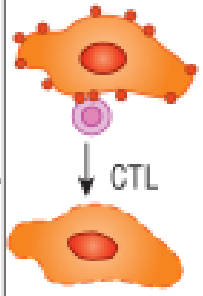
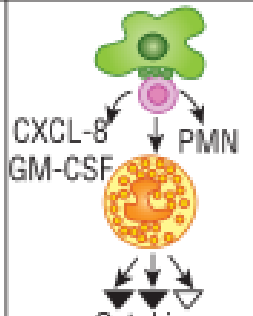
(b) **Viral Infection Theory**



Type IV Hypersensitivity

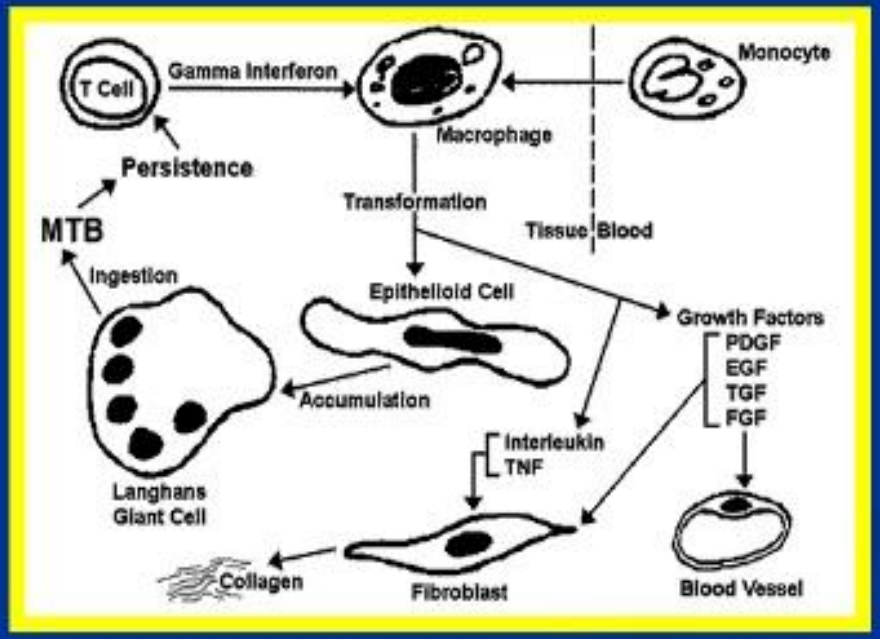
- Cell-mediated
- A delayed response to Ag involving activation of and damage by T cells
- Delayed allergic response – skin response to allergens – tuberculin skin test, contact dermititis from plants, metals, cosmetics
- Graft rejection – reaction of cytotoxic T cells directed against foreign cells of a grafted tissue; involves recognition of foreign HLA

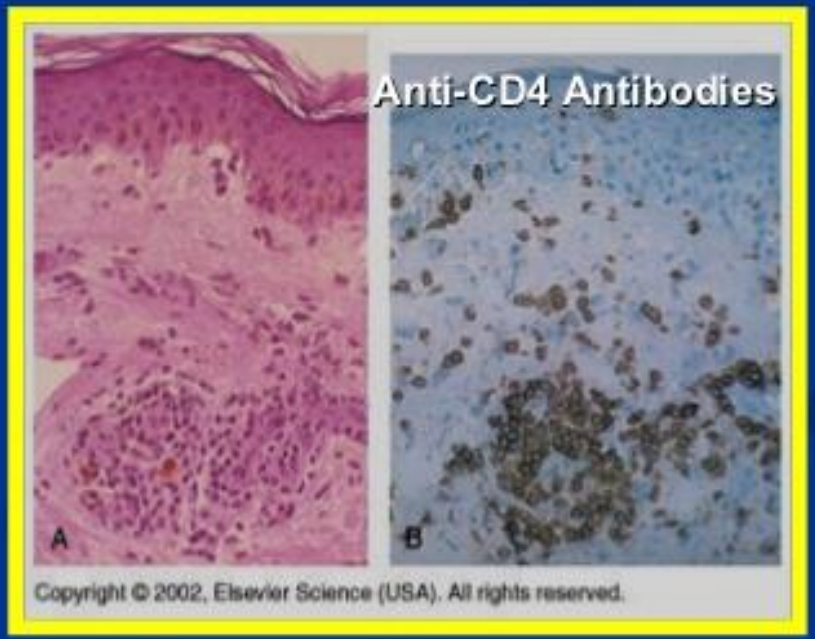
Antibody (I-III) and T-cell-orchestrated hypersensitivity reactions (IVa-d)

	Type I	Type II	Type III	Type IVa	Type IVb	Type IVc	Type IVd
Immune reactant	IgE	IgG	IgG	IFNγ, TNFα T_H1 cells)	IL-5,IL-4/IL-13 (T_H2 cells)	Perforin/ granzyme B (CTL)	CXCL-8, IL-17 GM-CSF (T-cells)
Antigen	Soluble antigen	Cell-or matrix-associated antigen	Soluble antigen	Antigen presented by cells or direct T-cell stimulation	Antigen presented by cells or direct T-cell stimulation	Cell-associated antigen or direct T-cell stimulation	Soluble antigen presented by cells or direct T-cell stimulation
Effector	Mast cell activation	FcR^+ cells (phagocytes, NK cells)	FcR^+ cells complement	Macrophage activation	Eosinophils	T-cells	Neutrophils
							
Example of hypersensitivity reaction	Allergic rhinitis, asthma, systemic anaphylaxis	Hemolytic anemia, thrombocytopenia (e.g., penicillin)	Serum sickness, Arthus reaction	Tuberculin reaction, contact dermatitis (with IVc)	Chronic asthma, chronic allergic rhinitis Maculopapular exanthema with eosinophilia	Contact dermatitis Maculopapular and bullous exanthema hepatitis	AGEP Behcet's disease

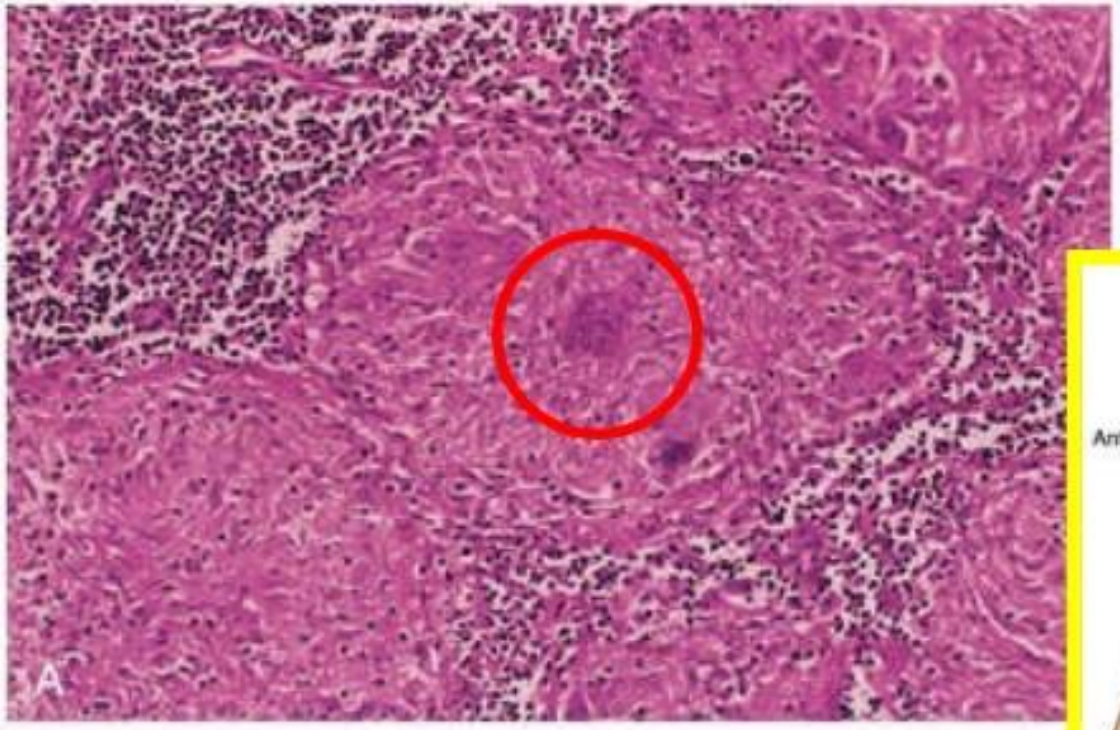
Type IV Hypersensitivity
Delayed Hypersensitivity Reaction

- CD4+ T lymphocytes + class II HLA molecules
  - Numerous cytokines
  - Macrophages

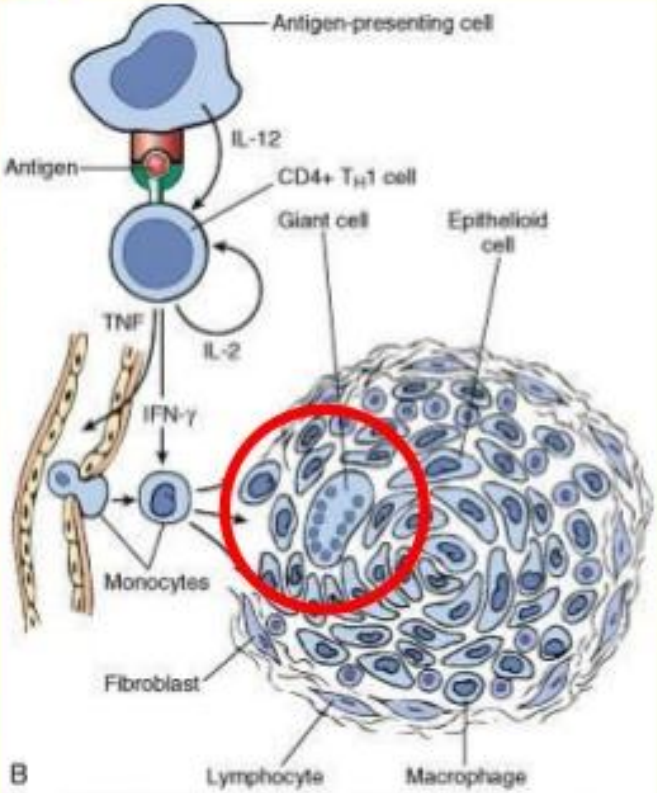


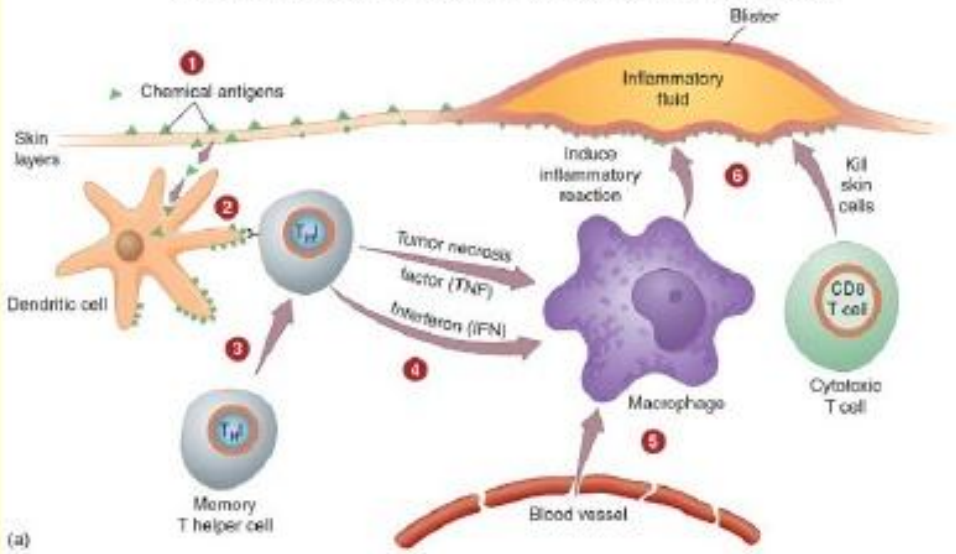


Granuloma Formation

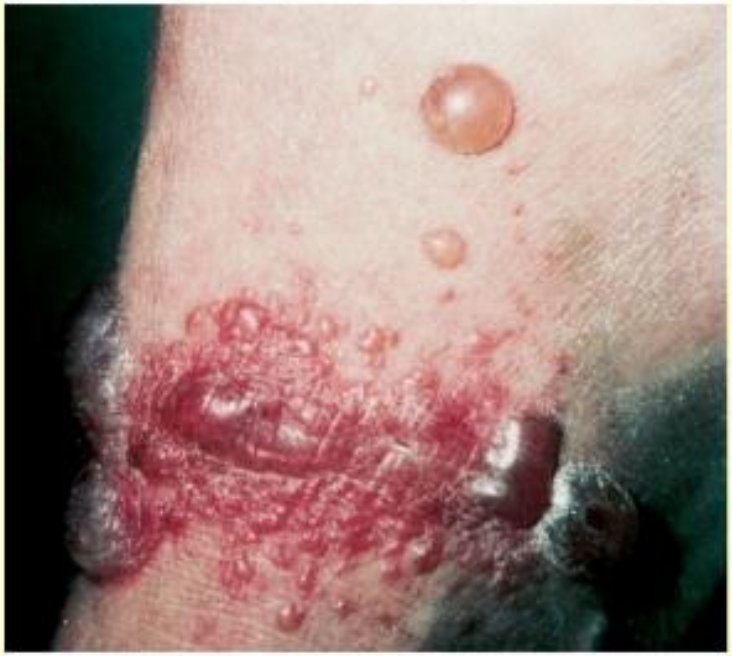


Multinucleated giant cell





1. Lipid-soluble chemicals are absorbed by the skin.
2. Dendritic cells close to the epithelium pick up the allergen, process it, and display it on MHC receptors.
3. Previously sensitized T_H cells recognize the presented allergen.
4. Sensitized T_H cells are activated to secrete cytokines (IFN, TNF) that attract macrophages and cytotoxic T cells to the site.
5. Macrophage releases mediators that stimulate a strong, local inflammatory reaction. Cytotoxic T cells directly kill cells and damage the skin. Fluid-filled blisters result.

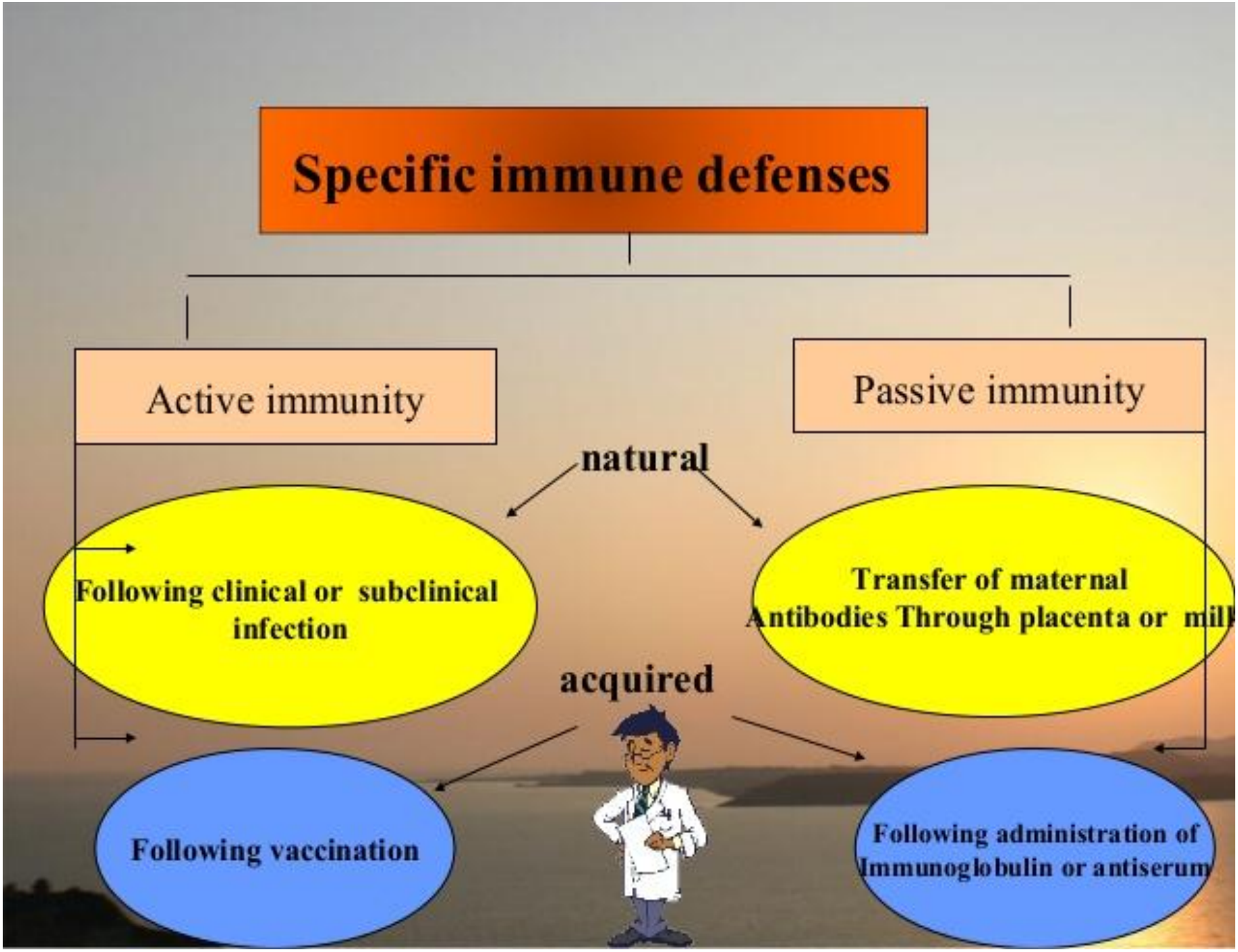


(b)

immunoprophylaxis:

Prevention of diseases by the administration of vaccines, immunoglobulins or immunostimulants

- Immunoprophylaxis have led to a significant decline in worldwide morbidity and mortality .


Specific immune defenses
Active immunity
Passive immunity
natural
Following clinical or subclinical infection
Transfer of maternal Antibodies Through placenta or mil
acquired
Following vaccination
Following administration of Immunoglobulin or antiserum

A vaccine is any preparation intended to produce immunity to a disease by stimulating the production of antibodies.

Types of vaccines

1. Live pathogens – attenuated
2. Killed micro-orgs
3. Microbial extracts
4. Vaccine conjugates
5. Toxoids

Types of vaccines

Live vaccines	Live Attenuated vaccines	Killed Inactivated vaccines	Toxoids	Cellular fraction vaccines	Recombinant vaccines
• Small pox variola vaccine	• BCG • Typhoid oral • Plague • Oral polio • Yellow fever • Measles • Mumps • Rubella • Intranasal Influenza • Typhus	• Typhoid • Cholera • Pertussis • Plague • Rabies • Salk polio • Intra-muscular influenza • Japanise encephalitis	• Diphtheria • Tetanus	• Meningococcal polysaccharide vaccine • Pneumococcal polysaccharide vaccine • Hepatitis B polypeptide vaccine	• Hepatitis B vaccine

Application of vaccines

- Infants and children expanded immunization.
- Active immunization for adults
- Active immunization for adult females
- Immunizing pregnant women
- Vaccines for Healthcare Workers
- Vaccinations in travel
- Vaccinations for immunocompromised perso

Recommended Childhood and Adolescent Immunization Schedule UNITED STATES • 2006

Vaccine ▼ Age ▶	Birth	1 month	2 months	4 months	6 months	12 months	15 months	18 months	24 months	4–6 years	11–12 years	13–14 years	15 years	16–18 years
Hepatitis B[1]	HepB	HepB		*HepB*[1]	HepB				HepB Series					
Diphtheria, Tetanus, Pertussis[2]			DTaP	DTaP	DTaP		DTaP			DTaP	Tdap	Tdap		
Haemophilus influenzae type b[3]			Hib	Hib	*Hib*[3]	Hib								
Inactivated Poliovirus			IPV	IPV	IPV					IPV				
Measles, Mumps, Rubella[4]						MMR				MMR	MMR			
Varicella[5]						Varicella			Varicella					
Meningococcal[6]							Vaccines within broken line are for selected populations		MPSV4		MCV4	MCV4	MCV4	
Pneumococcal[7]			PCV	PCV	PCV	PCV			PCV		PPV			
Influenza[8]					Influenza (Yearly)				Influenza (Yearly)					
Hepatitis A[9]									HepA Series					

This schedule indicates the recommended ages for routine administration of currently licensed childhood vaccines, as of December 1, 2005, for children through age 18 years. Any dose not administered at the recommended age should be administered at any subsequent visit when indicated and feasible. Indicates age groups that warrant special effort to administer those vaccines not previously administered. Additional vaccines may be licensed and recommended during the year. Licensed combination vaccines may be used whenever any components of the combination are indicated and other components of the vaccine are not contraindicated and if approved by the Food and Drug Administration for that dose of the series. Providers should consult the respective ACIP statement for detailed recommendations. Clinically significant adverse events that follow immunization should be reported to the Vaccine Adverse Event Reporting System (VAERS). Guidance about how to obtain and complete a VAERS form is available at www.vaers.hhs.gov or by telephone, 800-822-7967.

Range of recommended ages Catch-up immunization 11–12 year old assessment

Figure 1. Recommended adult immunization schedule, by vaccine and age group

VACCINE ▼ / AGE GROUP ▶	19–26 years	27–49 years	50–59 years	60–64 years	≥65 years
Tetanus, diphtheria, pertussis (Td/Tdap)[1,*]	Substitute 1-time dose of Tdap for Td booster; then boost with Td every 10 yr				Td booster every 10 yrs
Human papillomavirus (HPV)[2,*]	3 doses (females)				
Varicella[3,*]	2 doses				
Zoster[4]				1 dose	
Measles, mumps, rubella (MMR)[5,*]	1 or 2 doses		1 dose		
Influenza[6,*]	1 dose annually				
Pneumococcal (polysaccharide)[7,8]	1 or 2 doses				1 dose
Hepatitis A[9,*]	2 doses				
Hepatitis B[10,*]	3 doses				
Meningococcal[11,*]	1 or more doses				

*Covered by the Vaccine Injury Compensation Program.

For all persons in this category who meet the age requirements and who lack evidence of immunity (e.g., lack documentation of vaccination or have no evidence of prior infection)

Recommended if some other risk factor is present (e.g., on the basis of medical, occupational, lifestyle, or other indications)

No recommendation

Report all clinically significant postvaccination reactions to the Vaccine Adverse Event Reporting System (VAERS). Reporting forms and instructions on filing a VAERS report are available at www.vaers.hhs.gov or by telephone, 800-822-7967.

Information on how to file a Vaccine Injury Compensation Program claim is available at www.hrsa.gov/vaccinecompensation or by telephone, 800-338-2382. To file a claim for vaccine injury, contact the U.S. Court of Federal Claims, 717 Madison Place, N.W., Washington, D.C. 20005; telephone, 202-357-6400.

Additional information about the vaccines in this schedule, extent of available data, and contraindications for vaccination is also available at www.cdc.gov/vaccines or from the CDC-INFO Contact Center at 800-CDC-INFO (800-232-4636) in English and Spanish, 24 hours a day, 7 days a week.

Use of trade names and commercial sources is for identification only and does not imply endorsement by the U.S. Department of Health and Human Services.

Swine flu vaccine

Intranasal live attenuated influenza vaccine”

Intramuscular inactivated influenza vaccine”

Immunoprophylaxis in pregnancy:

- **Safe vaccines :**

Diphtheria, Tetanus, Influenza, and Hepatitis B.

- **Contraindicated vaccines :**

Measles, Mumps, and Rubella; Varicella and (BCG)

- **Immunoglobulins :**
- Considered in pregnant women exposed to hepatitis B , rabies, tetanus, varicella, and hepatitis A.
- **Tetanus toxoid :**
- appear safe during pregnancy and are administered to prevent neonatal tetanus.

Vaccination for healthcare workers :

- Hepatitis B
- Influenza
- MMR
- Varicella (chickenpox)
- Tetanus, diphtheria, pertussis
- Meningococcal :For specific healthcare personnel

Traveller's Vaccines :

Specific vaccine according to the country traveled to:

- TAB, YF, cholera, meningiococcal, pneuomococcal, HIB, influenza, rabies, plague, Japanese encephalitis.
- Hajj for instance necessates meningococcal vaccination from all over, and YF from places like south Africa, and cholera from places like India.

Vaccination for special occupations

- Vets and animal handlers: rabies, plague and anthrax
- Sewage workers: DT, hepatitis A, polio, TAB
- Food handlers: TAB
- Military troops and camp dwellers: pneumococcal, meningococcal, influenza, BCG (for non reactors), tetanus

Immunoglobulins:

Two types of immunoglobulin preparations are available for passive immunization:

1. Normal human immunoglobulin
2. Specific (hyper-immune) human immunoglobulin

Immunostimulants

Immunomodulators used in immunodeficiency disorders, chronic infections and cancer.

1) Cytokines like INF alpha, INF beta, INF gamma
2) IL-2 –malignant melanoma.
3) TNF alpha- malignant melanoma and soft tissue sarcoma of extremity.
4) Oral bacterial extracts
5) Levamisole – anti helminthic.
6) BCG – used as intravesical therapy
7) Echinacea
8) Thalidomide

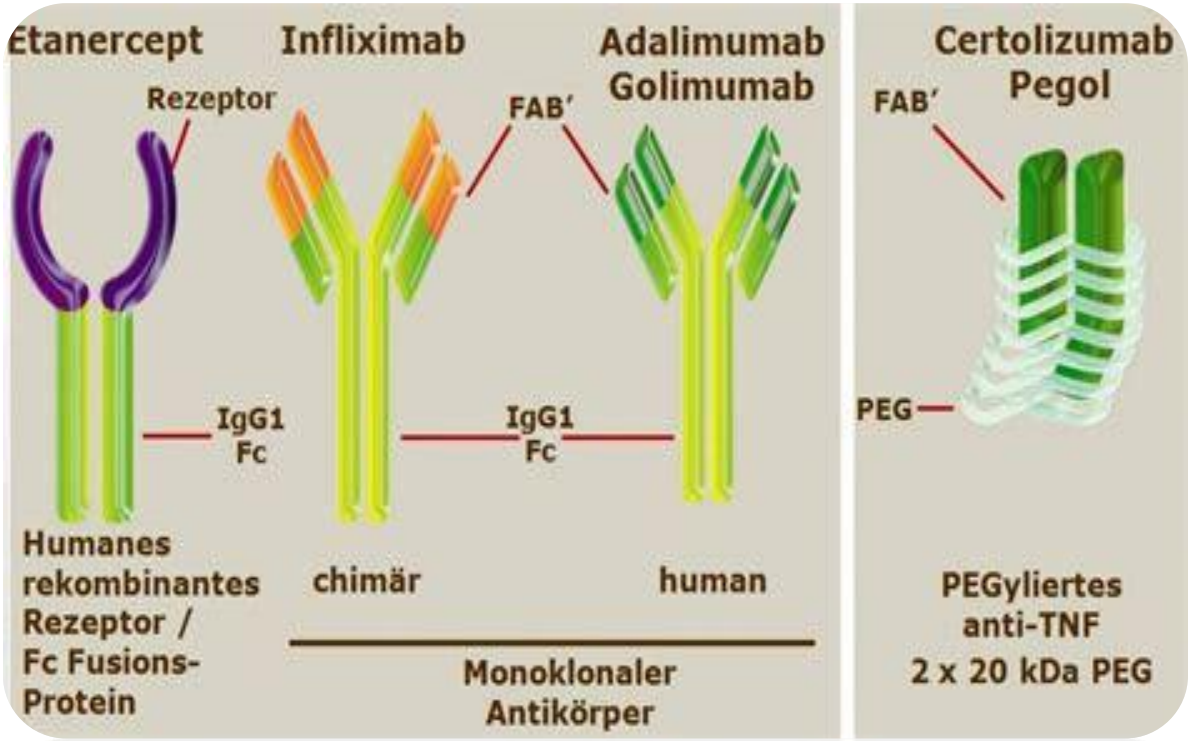
TNF blokator

- Adalimumab (Humira)
- Adalimumab-adbm (Cyltezo), a biosimilar to Humira
- Adalimumab-adaz (Hyrimoz), a biosimilar to Humira
- Adalimumab-atto (Amjevita), a biosimilar to Humira
- Certolizumab pegol (Cimzia)
- Etanercept (Enbrel)
- Etanercept-szzs (Ereizi), a biosimilar to Enbrel
- Golimumab (Simponi, Simponi Aria)
- Infliximab (Remicade)
- Infliximab-abda
- (Renflexis),

a biosimilar to Remicade

- Infliximab-dyyb
- (Inflectra),

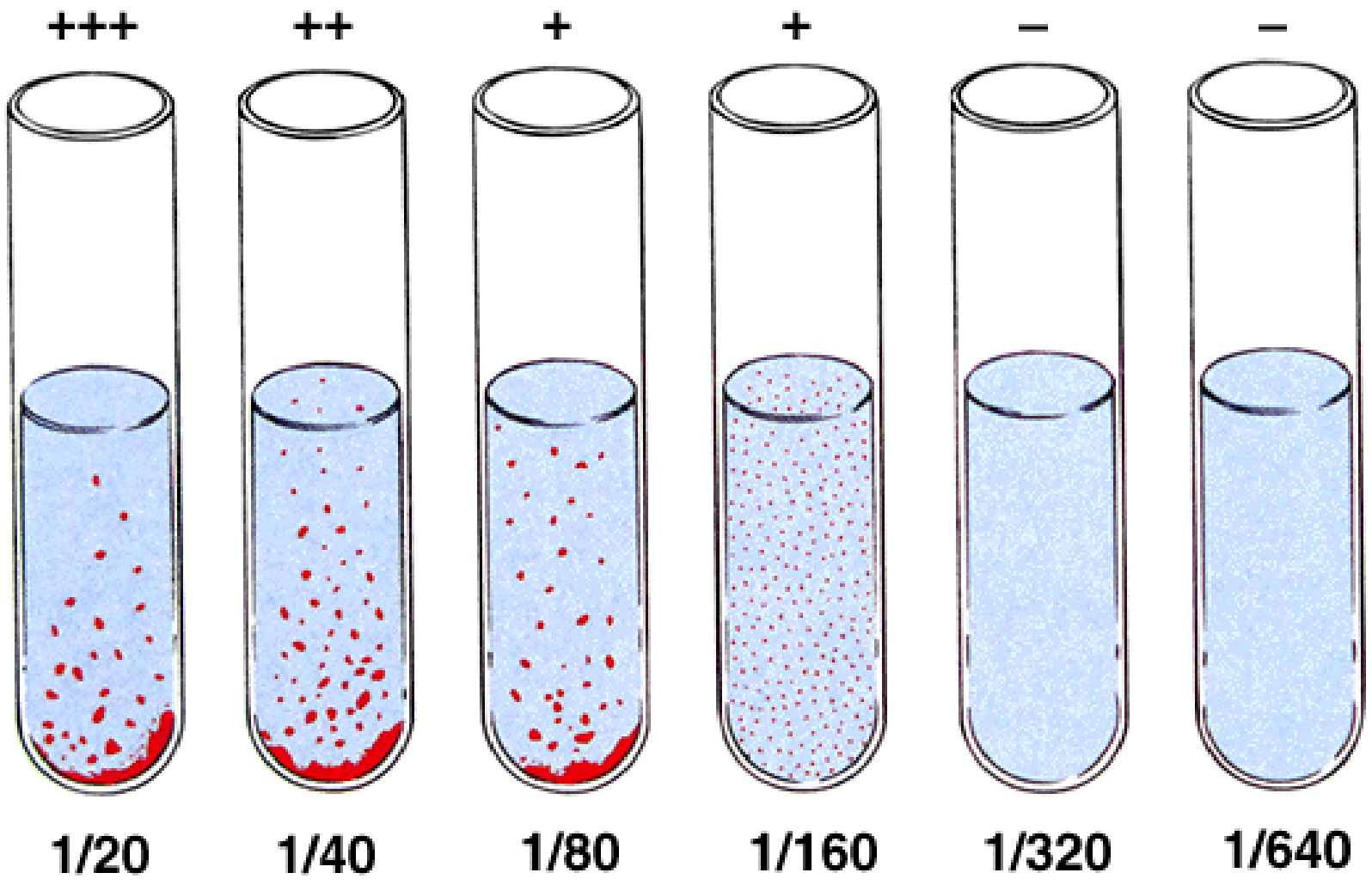
a biosimilar to Remicade



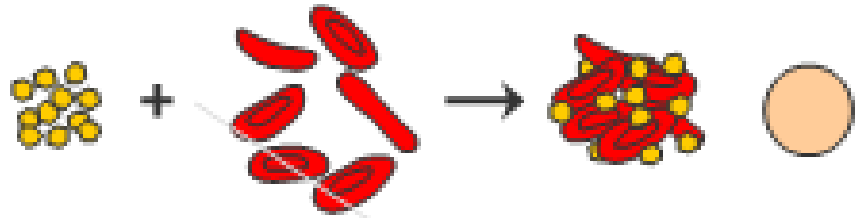
Antigen antibody reactions (serological tests)

- Agglutination reactions
- Precipitation reactions
- Toxin-antitoxin neutralization test
- Virus neutralization test
- Complement fixation test
- Immuno fluorescence test
- Radioimmuno assay
- Enzyme- linked immunosorbent assay(ELISA
- Immunoelectroblot eg., westren blot
- Immunochromatographic test.

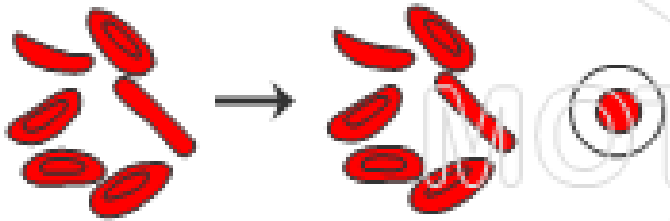
Agglutination test



Hemagglutination and hemagglutination-inhibition test



Viruses RBC Hemagglutination

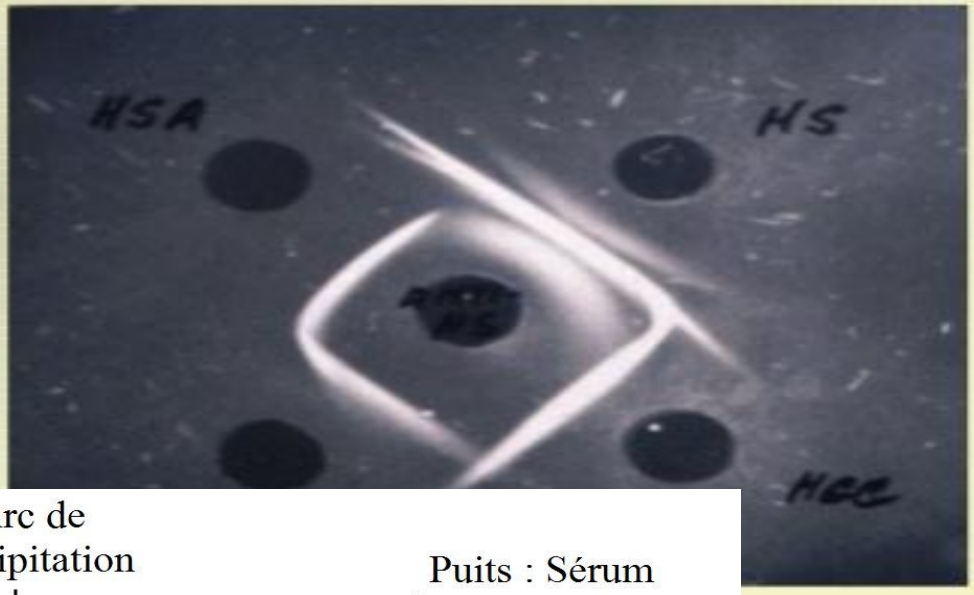


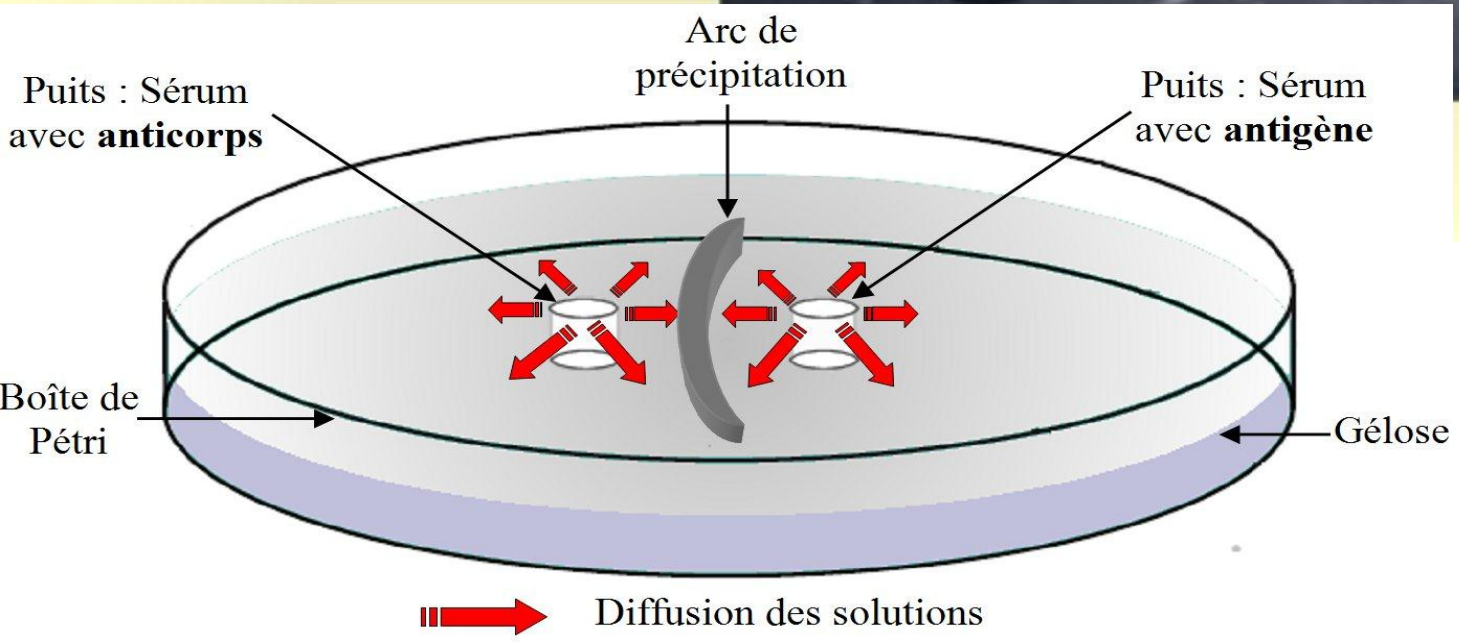
No hemagglutination

Viruses Antibodies from patient's serum Viruses coated with antibodies RBC Hemagglutination inhibition

2011217

Immunodiffusion - precipitin formation





Ring PR

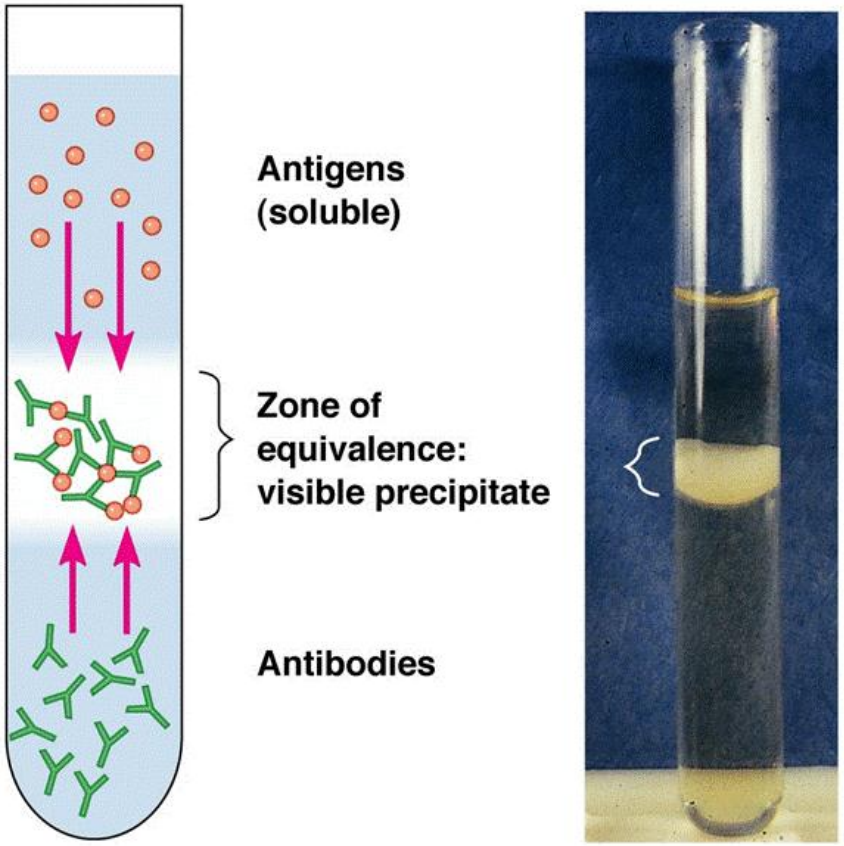
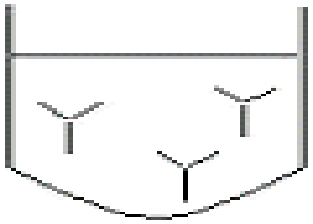
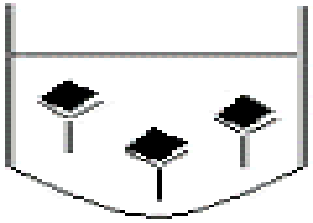


Figure 18.4 - Overview

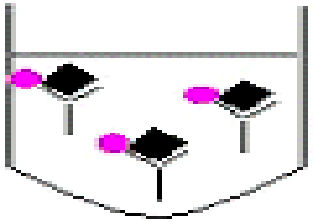
Complement Fixation Test



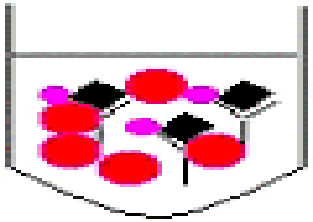
Serum with antibodies



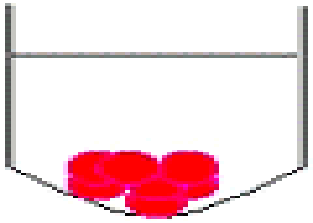
Antigen binds with antibodies



Complement binds with Ag/Ab complex



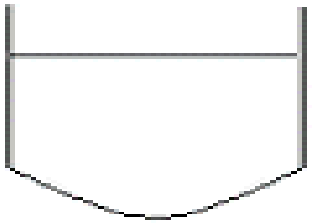
Hemolysin Sensitized red blood cells serve as an indicator



RBCs settle into a pellet

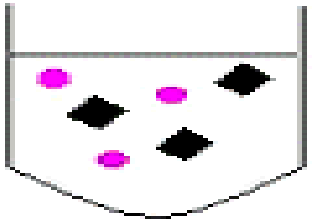
no lysis

Reactive

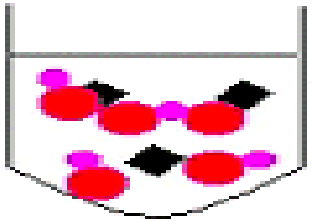


Serum without antibodies

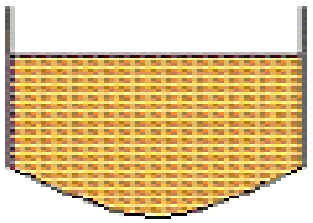
Unbound Antigen



Unbound complement



Hemolysin Sensitized RBCs serve as an indicator

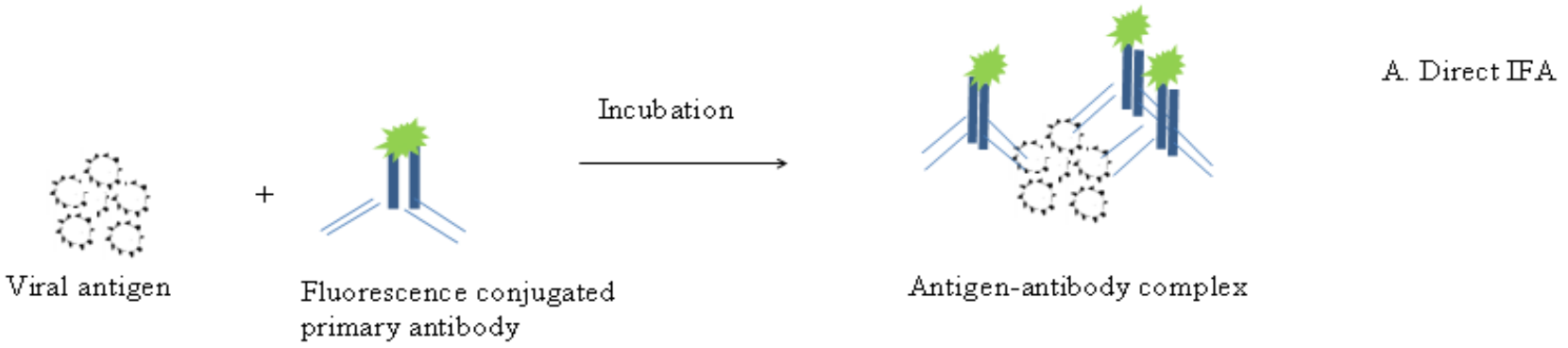


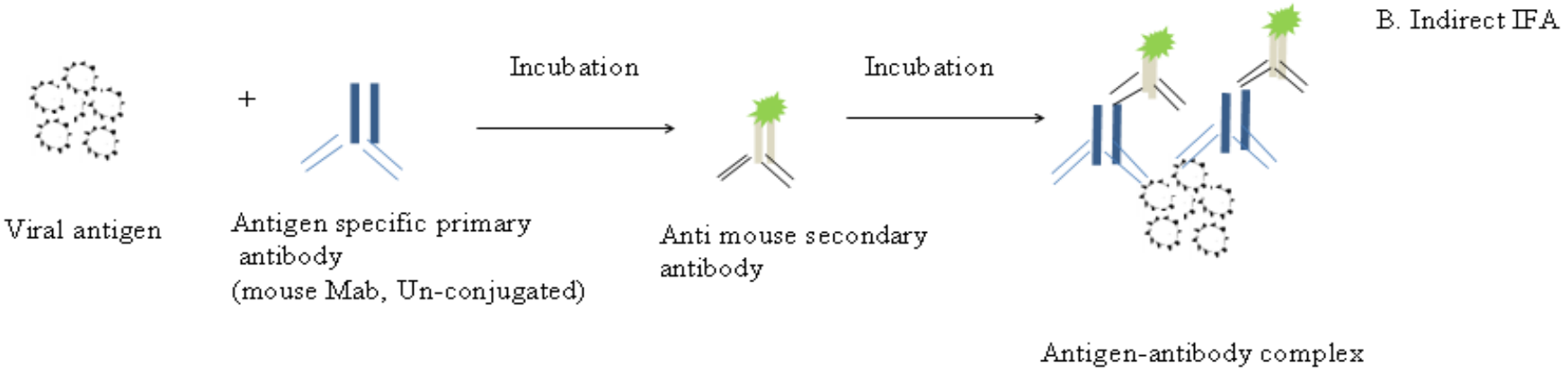
RBCs lysed by unbound complement

lysis

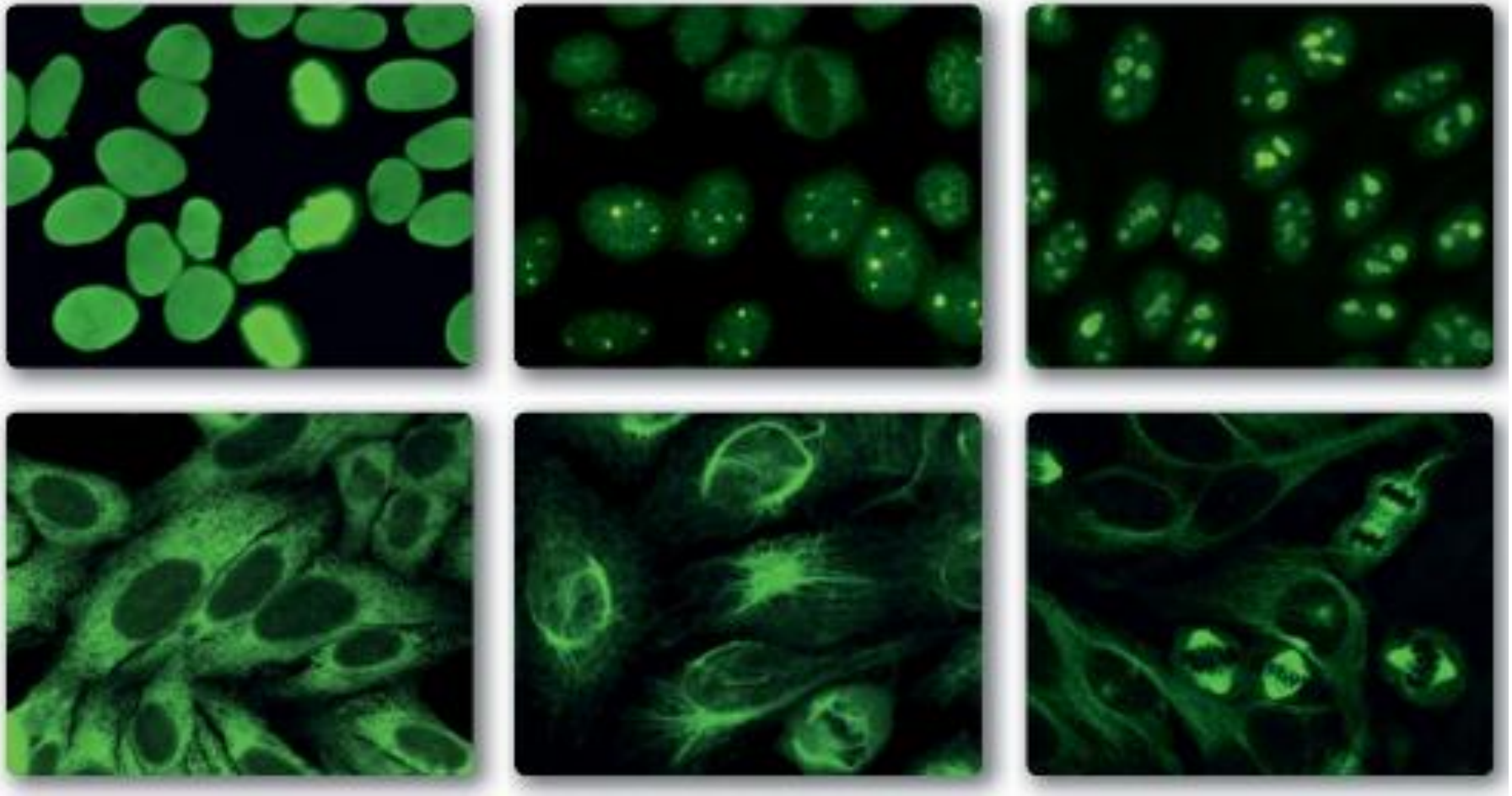
Nonreactive

IFM


Incubation
A. Direct IFA
Viral antigen
Fluorescence conjugated primary antibody
Antigen-antibody complex


Incubation
Incubation
B. Indirect IFA
Viral antigen
Antigen specific primary antibody (mouse Mab, Un-conjugated)
Anti mouse secondary antibody
Antigen-antibody complex

ANA diagnostics using indirect immunofluorescence



More than 100 autoantigens are presented in HEp-2 cells.

The most important among them are:

Polynucleotides	Double-stranded DNA, single-stranded DNA, RNA
Histones	H1, H2A, H2B, H3, H4, H2A-H2B complex
Ribonucleoproteins	U1-(n)RNP, Sm, SS-A (Ro), SS-B (La)
Nucleolar antigens	U3-(n)RNP/fibrillarin, RNA polymerase I, PM-Scl (PM-1), 7-2-RNP (To), 4-6-S-RNA, NOR-90 (nucleolar organiser)
Centromeres	Kinetochore proteins
Other proteins	Topoisomerase I (Scl-70), PCNA (cyclin I), nuclear granules, Ku, Mi-2, lamins, lamin receptors

Autoantibodies in systemic lupus erythematosus (SLE)

Antigen	Prevalence (%)
Double-stranded DNA	60–90
Single-stranded DNA	70–95
Nucleosomes	50–70
RNA	50
RNA helicase A	6
Histones	50–80
U1-nRNP	15–40
Sm	5–40
SS-A (Ro)	20–60
SS-B (La)	10–20
PCNA-like	3
Ku	10
Ribosomal P proteins	10

Direct ELISA for HIV

Antigen coating

Blocking

Primary Ab

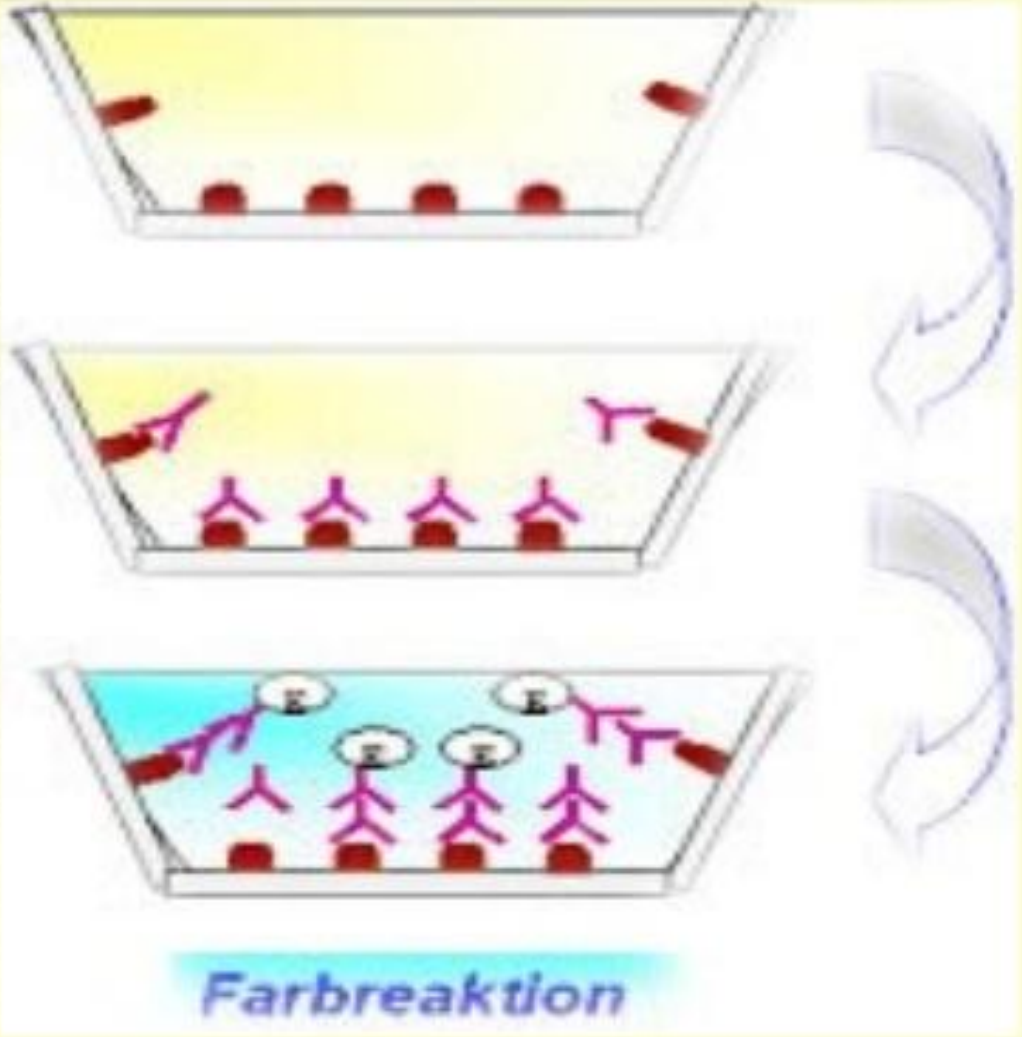
Washing

Secondary Ab

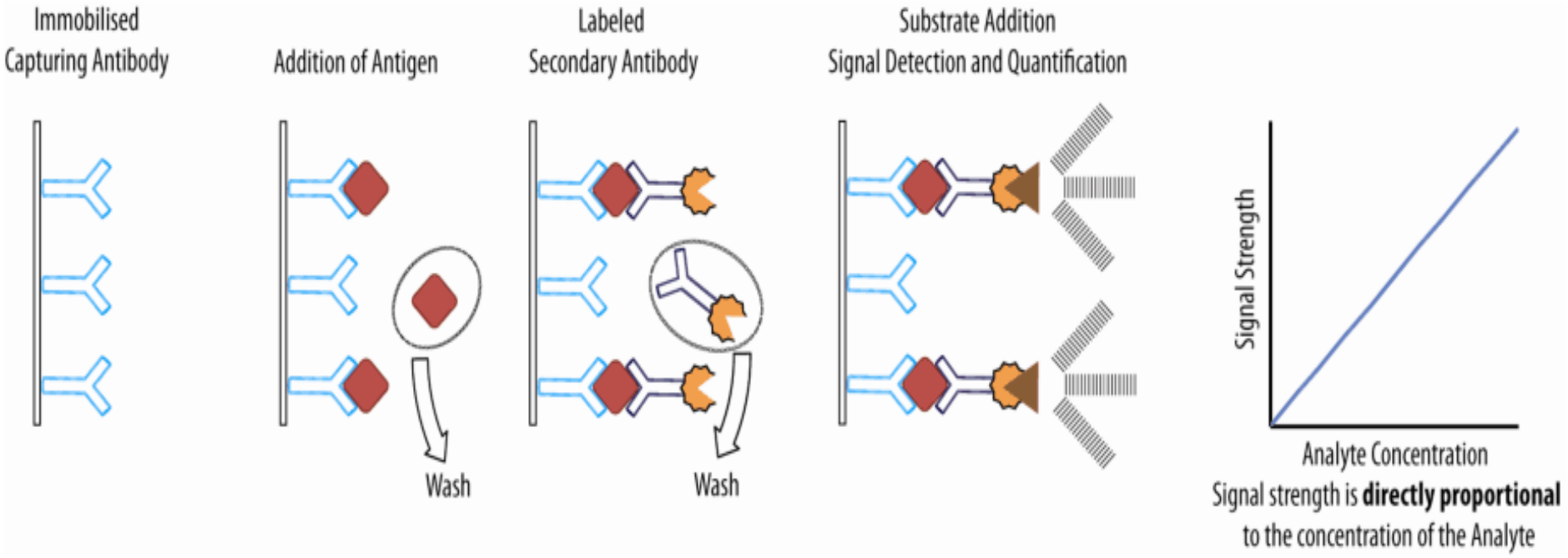
Washing

Substrate addition

Colour development



Sandwich ELISA for HBsAg



TORCH - panel (IgM & IgG)

- Toxoplasma
- Rubella
- Cytomegalo virus
- Herpes

- IgM - Acute or Recent infection
- IgG - Chronic infection


ids
ids-isys

Radioimmunuassays (1960)

This technology was employed for a few products capable of providing results that cannot be delivered by other technologies. It is used for tests that have to be carried out manually by experienced professionals

Calorimetric assay/ ELISA (1980)

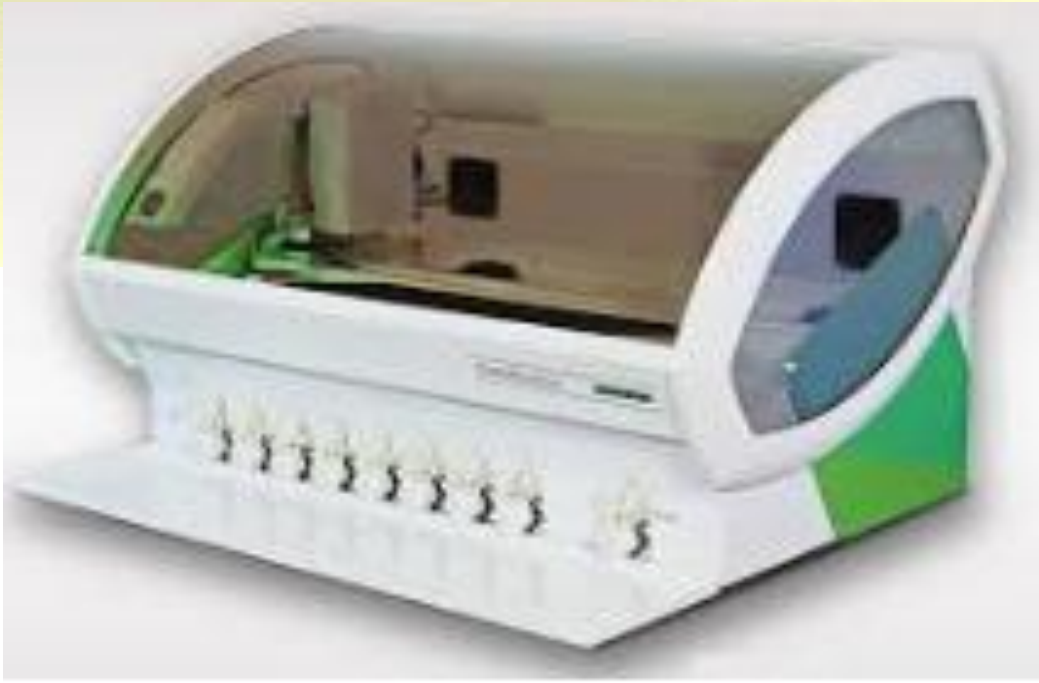
It can perform diagnostic tests with the aid of minimally sophisticated instrumentation; ELISA can automate some of the manual operations performed by laboratory staff.

Chemiluminsecence/ CLIA (1990)

CLIA can be adapted to products and instruments with features providing a high level of usage flexibility in terms of menus and the performance speed of the test.

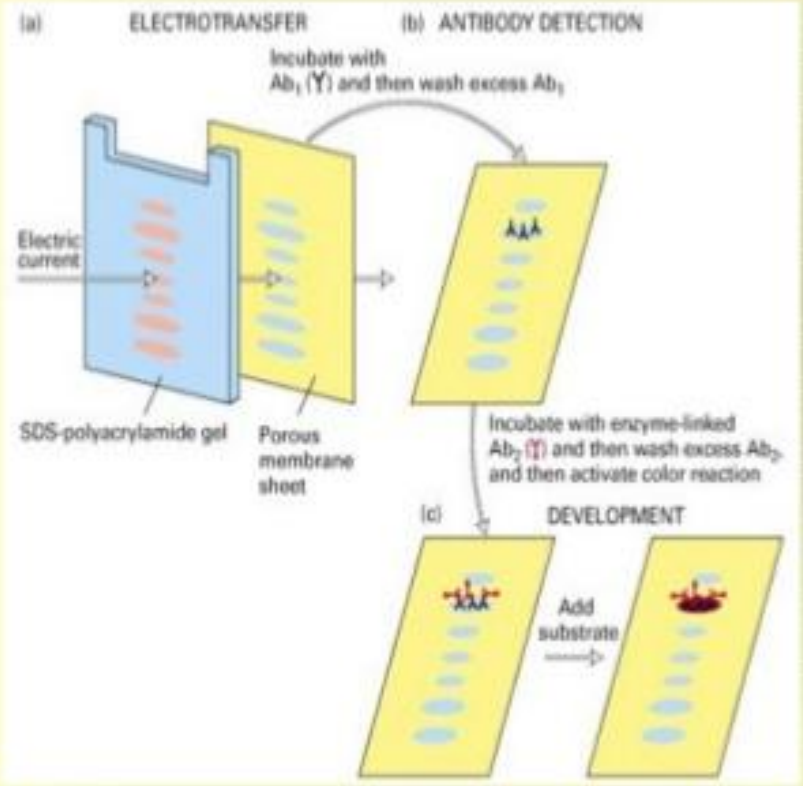
Western blot

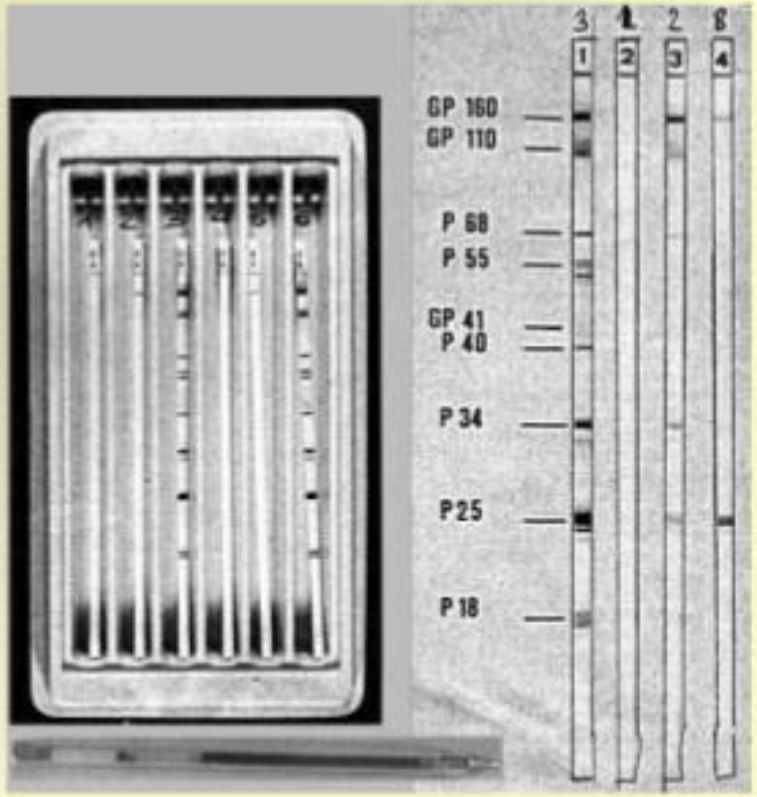
- ELISA is similar to Western blot but is more informative.
- HIV detection by ELISA and Western blot
- HIV - I and HIV - II

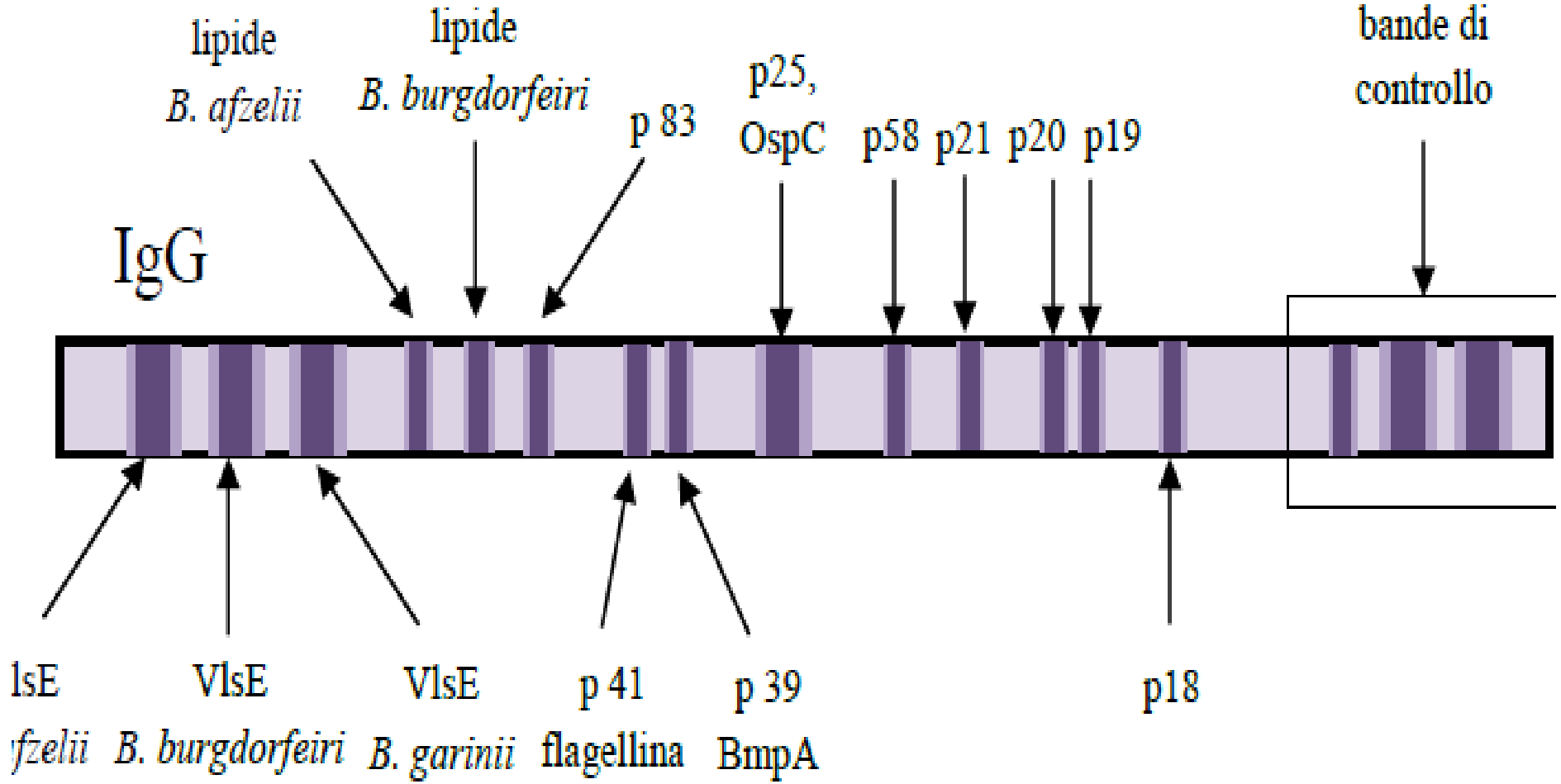


Automatic immunoblot analyzer - EURO...
medicalexpo.com

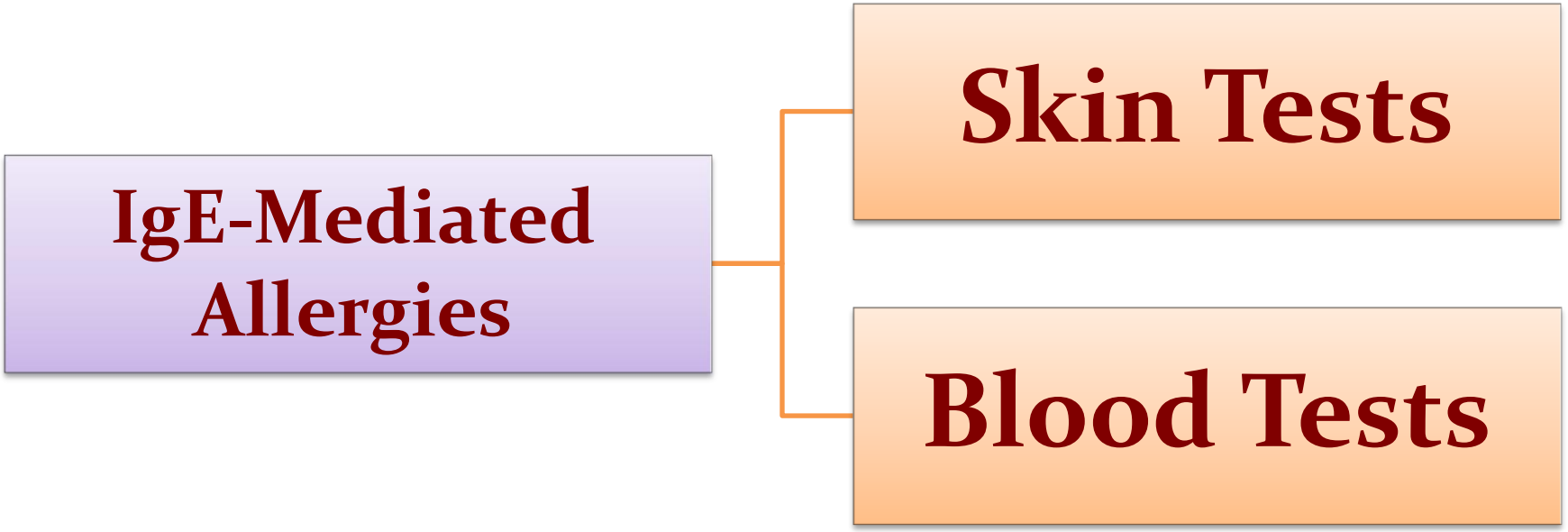
Western blot






lipide
B. afzelii
lipide
B. burgdorferiri
p 83
p25,
OspC
p58
p21
p20
p19
bande di
controllo
IgG
lsE
fzelii
VlsE
B. burgdorferiri
VlsE
B. garinii
p 41
flagellina
p 39
BmpA
p18

Laboratory Diagnosis



Skin Tests

- The cutaneous test
- (prick test, puncture test epicutaneous test)
  - Routine diagnosis in diseases (atopic or anaphylactic).
  - A single drop of concentrated aqueous allergen extract placed on the skin which is then pricked lightly with a needle point at the center of the drop. After 20 minutes the reaction is graded and recorded