Immunopathoogy

Hypersensitivity Reactions

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Lec.2

2.Antibody-Mediated Diseases (Type II Hypersensitivity)

- Are caused by **Antibodies(Ab)** directed against target **antigens** on the surface of cells or other tissue components.
- **The antigens are either:**
- **intrinsic antigen: normal antigens** in the cell or
- **extrinsic antigens** (drug metabolites) that deposit in tissues

Antibodies can cause disease via the following mechanisms :

1-opsonization *and* phagocytosis.

2-Inflammation

3- Antibody-mediated cellular dysfunction.

1.Opsonization and phagocytosis

- Ab target circulating cells (like RBC and platelet) and coat their surfaces (opsonize them) with or without complement proteins.

- **Complement-dependent reaction**
- **A-Direct lysis**: It is effected by complements activation, formation of membrane attack complex **MAC (C5 –9)** . This MAC then **disrupts cell membrane integrity** by **drilling a hole** through cell membrane lipid bilayer causing **osmotic lysis of the cells.**

- **B- Opsoinization**: By C3b, fragment of the complement to the cell surface **enhances Phagocytosis**

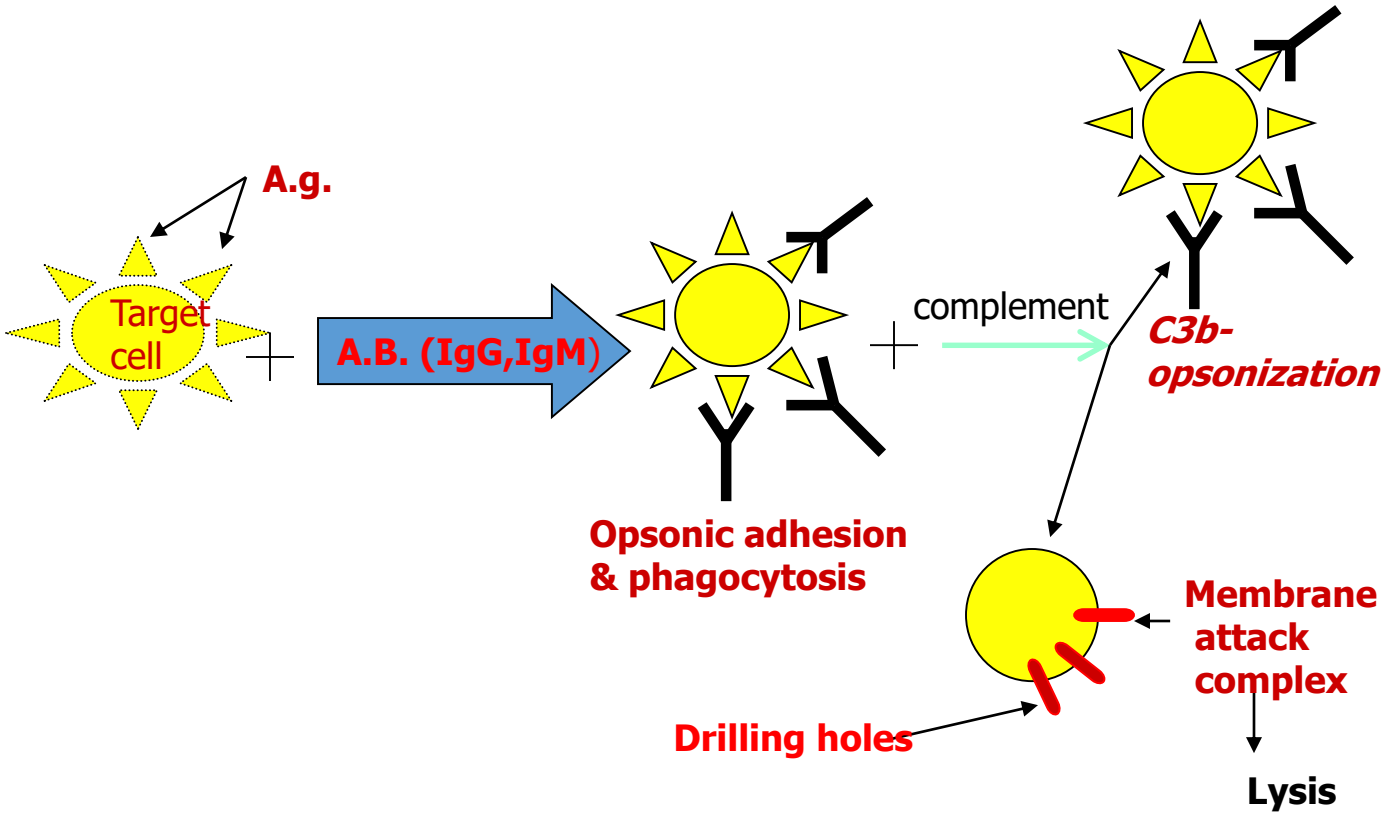
- then phagocytes (neutrophils and macrophages) attack these cells through their receptors for the antibodies, or through their receptors for complement proteins.

Examples

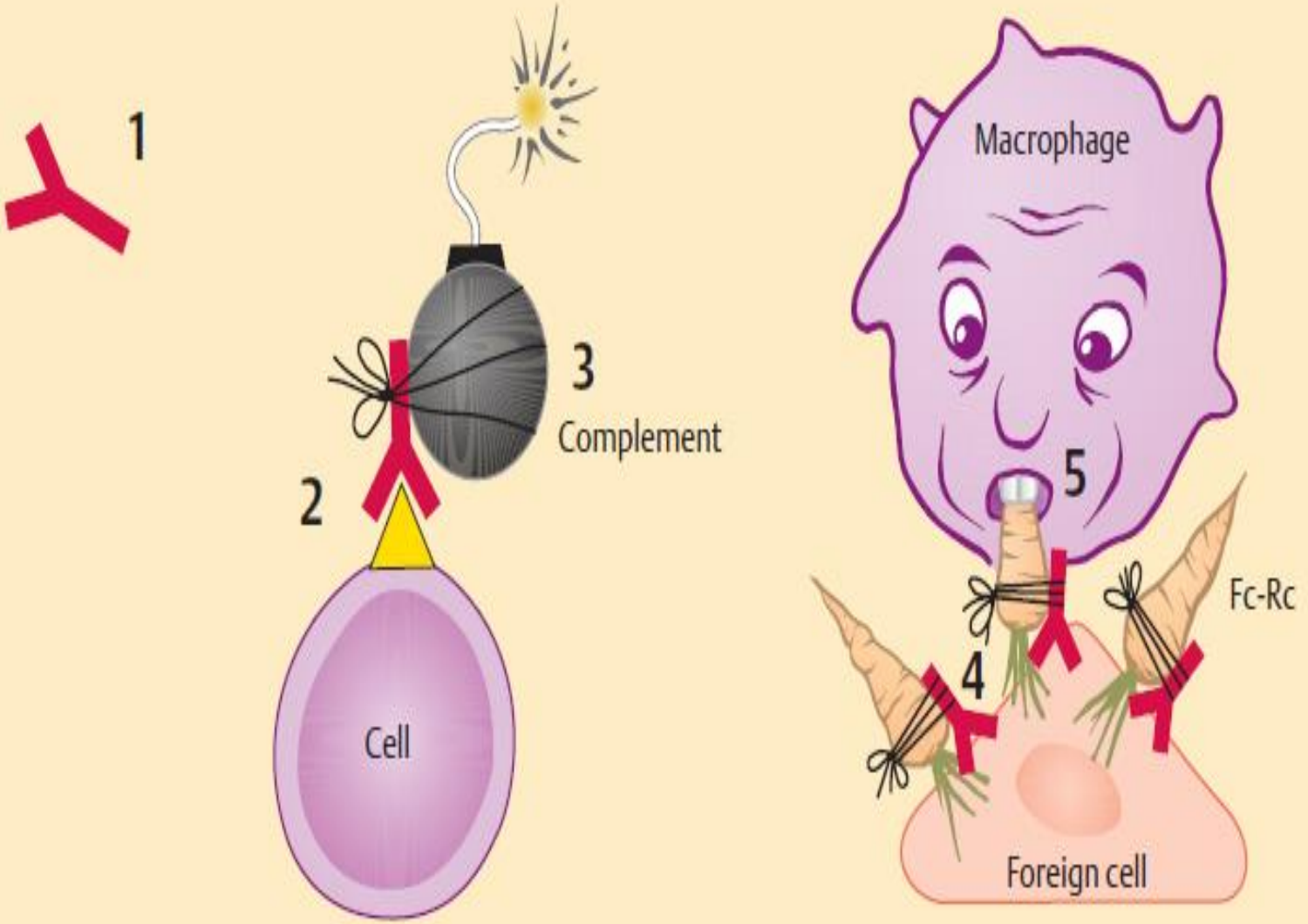
Transfusion reaction, autoimmune hemolytic anemia, autoimmune Thrombocytopenia and certain drug reaction

2-Type II hypersensitivity (ab-dependent)

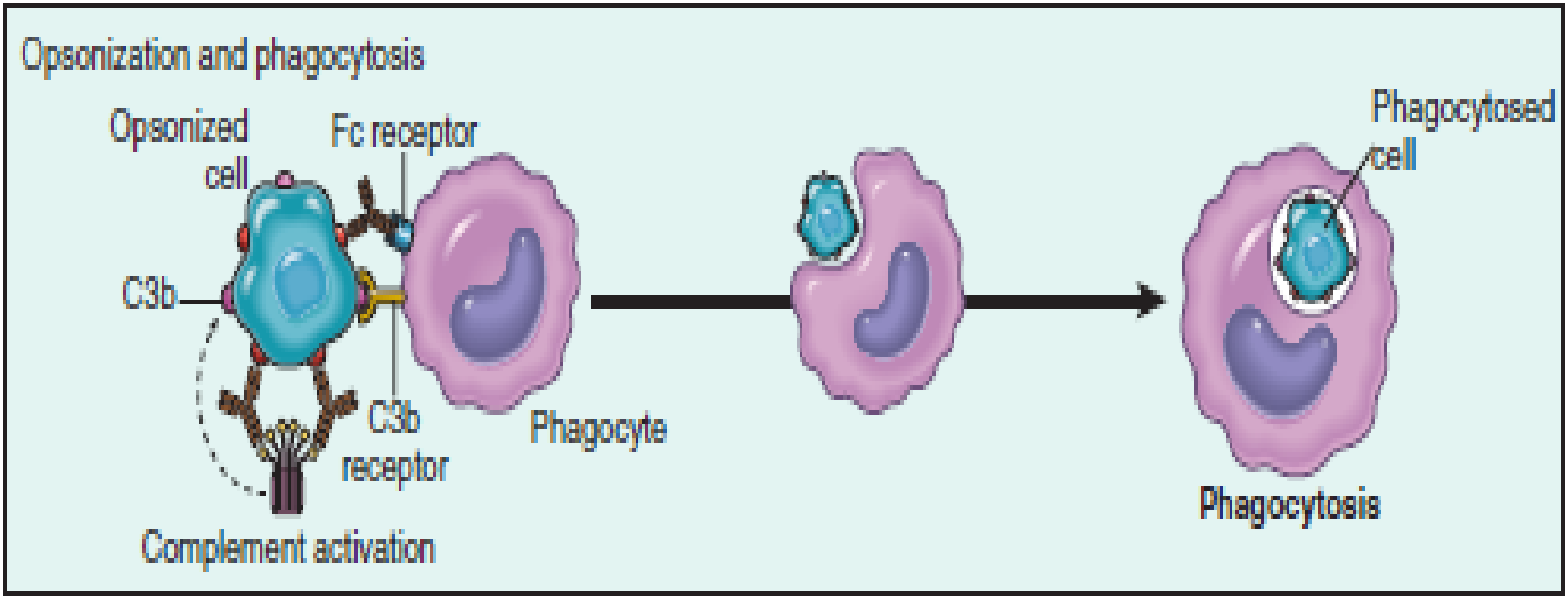
complement dependent reactions



A Cytotoxic reaction



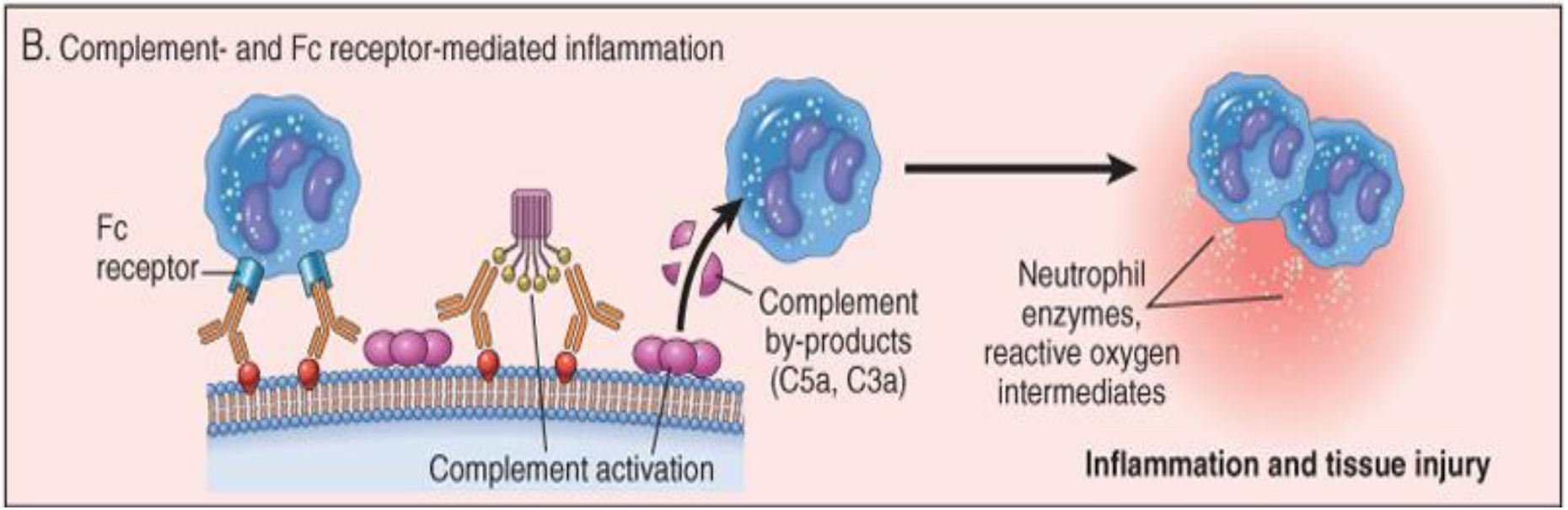
i.Opsonization and phagocytosis



- opsonization and phagocytosis. When circulating cells, such as erythrocytes or platelets, are coated (opsonized) with autoantibodies, with or without complement proteins, the cells become targets for phagocytosis by neutrophils and macrophages .
- These phagocytes express receptors for the Fc tails of IgG antibodies and for breakdown products of the C3 complement protein, and use these receptors to bind and ingest opsonized particles. Opsonized cells are usually eliminated in the spleen, and this is why splenectomy is of some benefit in autoimmune thrombocytopenia and hemolytic anemia.

- **2. *Inflammation***
- Antibodies(Ab) bind to antigens in tissues leading to complement activation, *recruitment of leukocytes* and tissue injury,
- E.g. some forms of glomerulonephritis and vascular rejection of transplanted organs occur by this mechanism .

Antibody-Mediated Diseases (Type II Hypersensitivity



- ***Inflammation .***Antibodies bound to cellular or tissue antigens activate the complement system by the "classical" pathway
- Products of complement activation recruit neutrophils and monocytes, triggering inflammation in tissues, opsonize cells for phagocytosis, and lyse cells, especially erythrocytes.
- Leukocytes may also be activated by engagement of Fc receptors, which recognize the bound antibodies

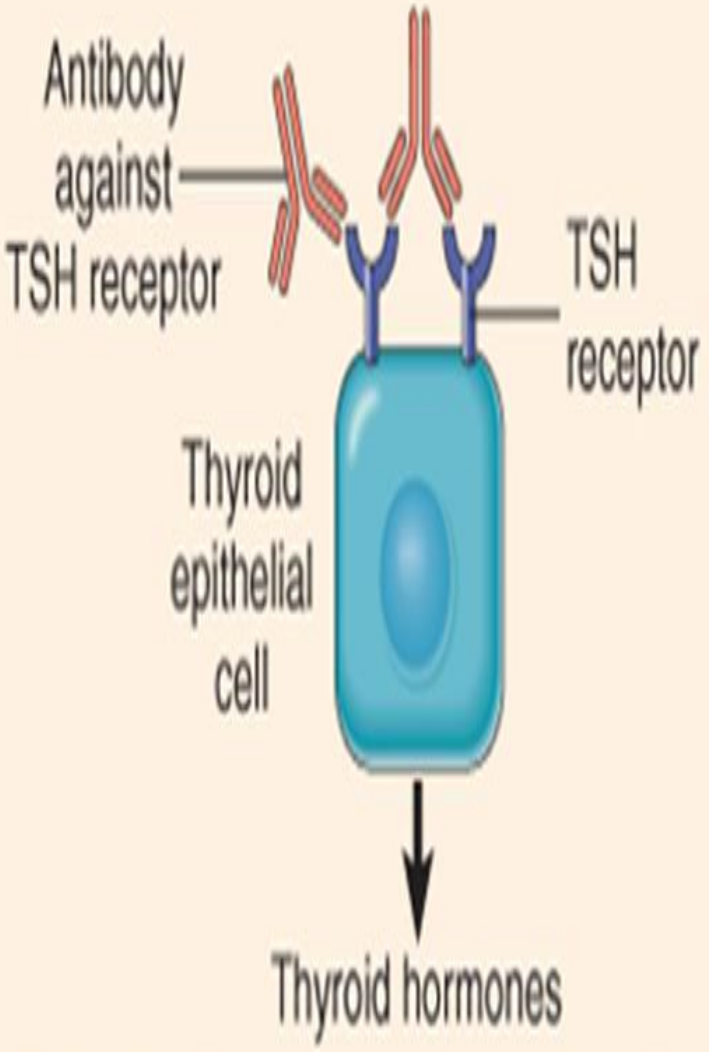
3. Antibody-mediated cellular dysfunction.

Antibodies can bind to cell surface receptors or essential molecules, and cause functional derangements either inhibition(e.g Myasthenia Gravis), or unregulated activation(e.g. Graves disease .

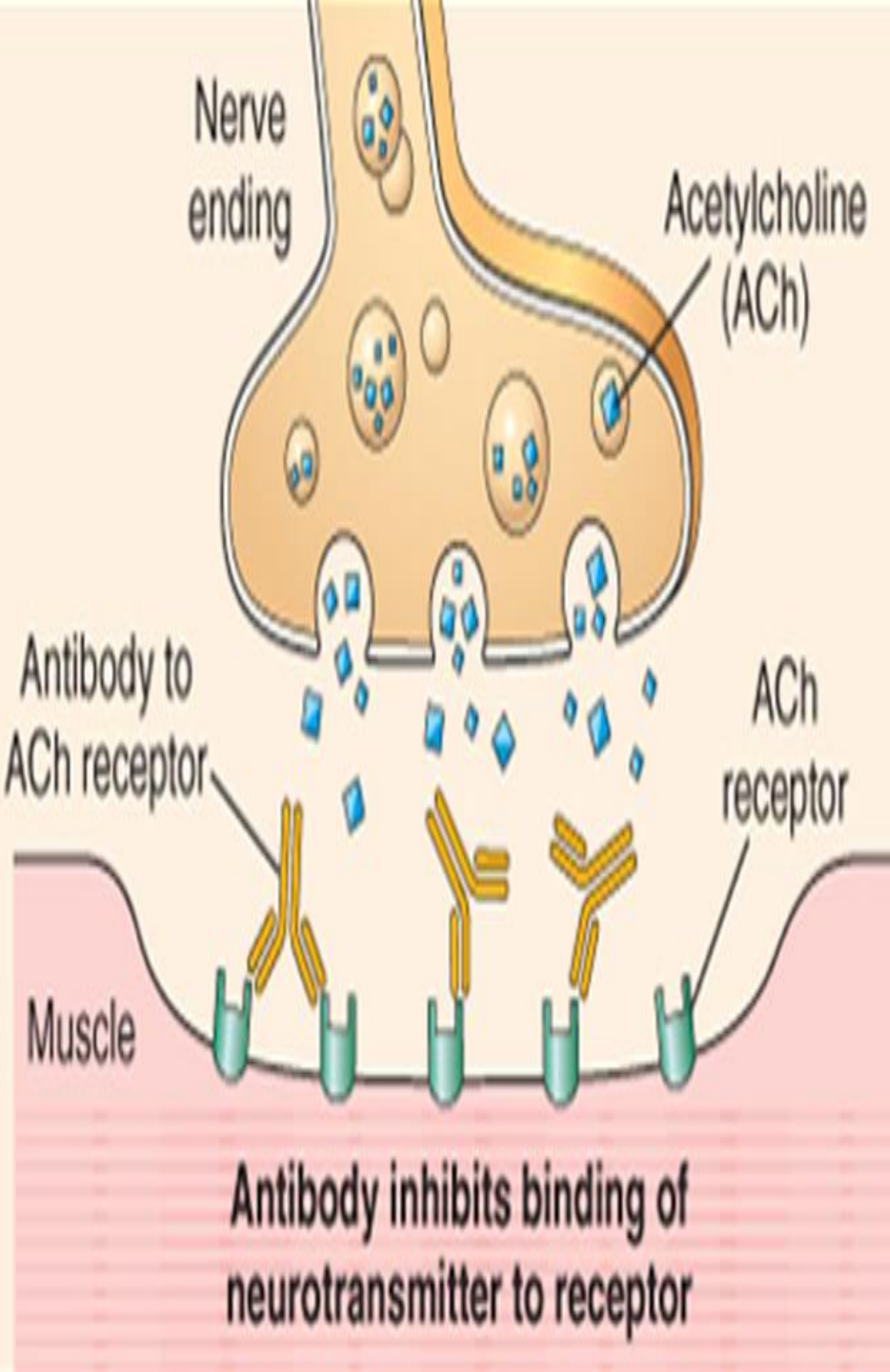
NO inflammation or prominent tissue destruction seen by this mechanism

- **myasthenia gravis** a disease characterized by muscle weakness, antibodies target acetylcholine receptors in the motor end plates of skeletal muscles… **block** neuromuscular transmission and therefore cause muscle weakness.
- The converse (i.e., antibody-mediated **stimulation** of cell function) is the basis In **Graves disease ,** In this disorder, antibodies against the thyroid-stimulating hormone receptor(TSH receptors) on thyroid epithelial cells stimulate the cells, resulting in hyperthyroidism.

C. Antibody-mediated cellular dysfunction



Antibody stimulates receptor without hormone

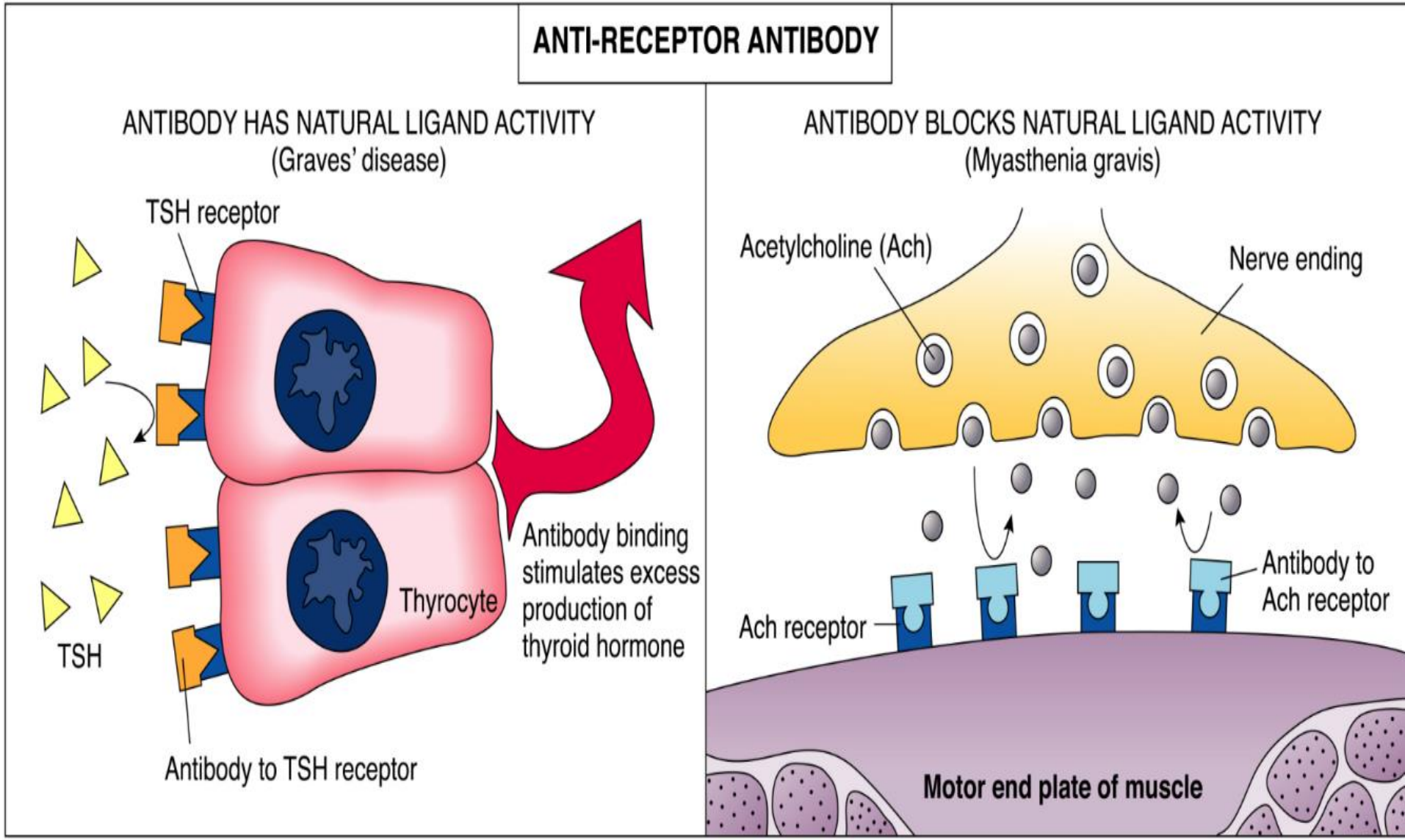


Antibody inhibits binding of neurotransmitter to receptor

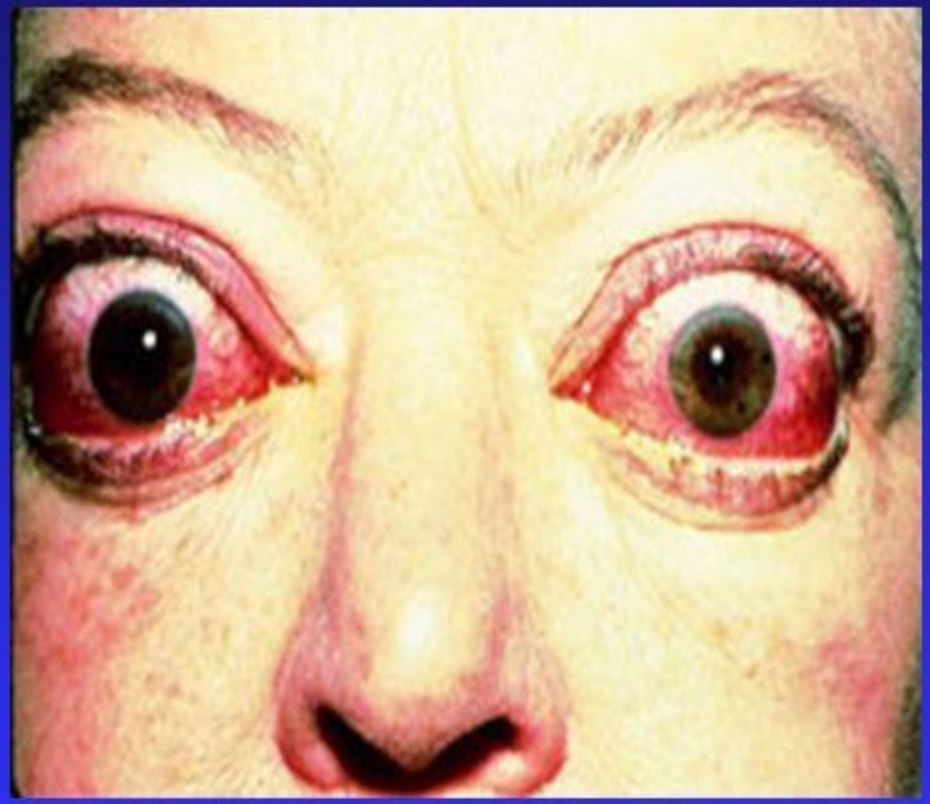
AB mediated cellular dysfunctions

Myasthenia gravis

Graves disease (ab against TSH receptor of thyroid epithelial cells lead to hyperthyroidism) .

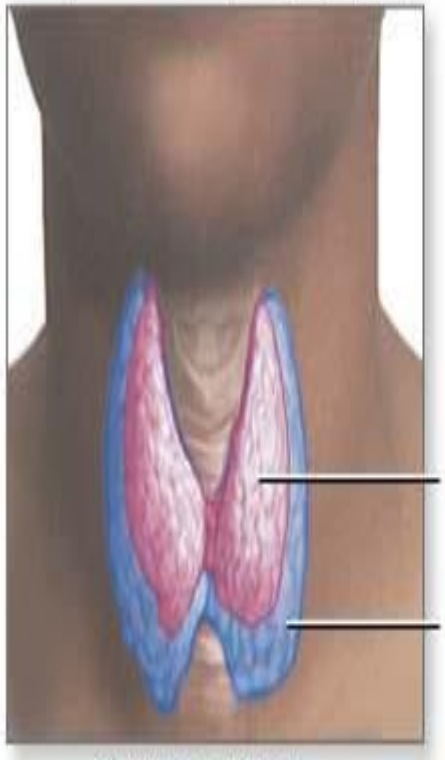


Grave's Disease



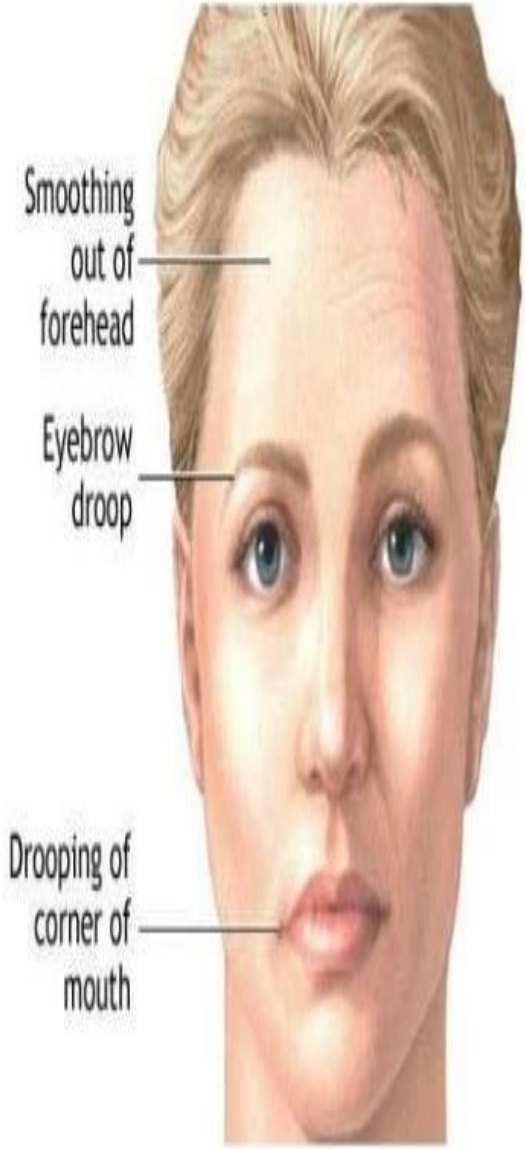
Myasthenia Gravis

Exophthalmos (bulging eyes)



Diffuse goiter

Graves' disease is a common cause of hyperthyroidism, an over-production of thyroid hormone, which causes enlargement of the thyroid and other symptoms such as exophthalmos, heat intolerance and anxiety



SYMPTOMS:

- The first noticeable symptom is weakness of the **eye muscles**, difficulty in swallowing and slurred speech may also be the first signs.
- Muscles that control eye and eyelid movement, facial expressions, **chewing, talking and swallowing** becomes weaker.
- The muscles that control **breathing** and neck and limb movements can also be affected.

Examples for Ab mediated diseases(type II hypersensitivity)

disease	Target antigen	Mechanism of disease	Clinical presentation
Autoimmune hemolytic anemia	Red blood cell membrane proteins	Opsonization and phagocytosis of red	Hemolysis and anemia
Autoimmune thrombocytopenic purpura	Platelet membrane proteins (Gpllb : Illa integrin)	Opsonization and phagocytosis of platelets	Bleeding
Goodpasture syndrome	Protein in basement membranes of kidney glomeruli and lung alveoli	Complement- and Fc receptor–mediated inflammation	Nephritis, lung hemorrhage
Acute rheumatic fever	Streptococcal cell wall antigen; antibody cross-reacts with myocardial antigen	Inflammation, macrophage activation	Myocarditis, arthritis
Myasthenia gravis	Acetylcholine receptor	Antibody inhibits acetylcholine binding, down-modulates receptors	Muscle weakness, paralysis
Graves disease	TSH receptors	Ab mediated stimulation oh TSH receptors	Hyperthyroidism
Insulin resistant diabetes	Insulin receptors	Ab inhibits binding of insulin	Hyperglycemia , ketoacidosis
Pernicious anemia	IF of gastric parietal cells	Neutralization of IF, decreased absorption of vit B12	Anemia, abnormal erythropoiesis

3.Immune Complex Diseases (**Type III Hypersensitivity):**

are caused by antibodies binding to antigens to form complexes that circulate and deposit in vascular beds and stimulate inflammation, typically as a consequence of complement activation.

- Complexes form either in the circulation or when antibodies bind to previously (planted) antigens in tissues (in situ immune complex)
- Antigens could be either:
- external (microbial or drug molecules) or
- endogenous (self-antigens) leading to autoimmune reactions

- **Type III hypersensitivity (immune complex mediated):**

- **There are 2 types :**

- **systemic (serum sickness)**
- **local (Arthus reaction)**

- **A. Systemic immune-complex disease:** complexes are formed in the circulation and are deposited in several organs.
- **The pathogenesis of systemic immune complex disease can be divided into three phases:**
- **1-formation of immune complexes:** after introduction of the foreign antigen, immune response is triggered and after about 1 week antibodies form and released into the circulation
- **2-deposition of complexes: in various tissues.** The deposition tend to be systemic but preferentially involve kidney leading to chronic glomerular diseases or in joints (arthritis) or small blood vessels (vasculitis)
- **3-acute inflammation:** due to complement activation or direct leukocytes activation.
- this phase occur around 10 days after antigen introduction with fever, joint pain and proteinuria
- -The antibody classes that induce such lesions are **complement-fixing antibodies** (i.e., **IgG and IgM**)
- The principal morphologic(histopathological) manifestation of type III reaction is **small vessel vasculitis** with fibrinoid necrosis of vessels walls and neutrophils infiltration

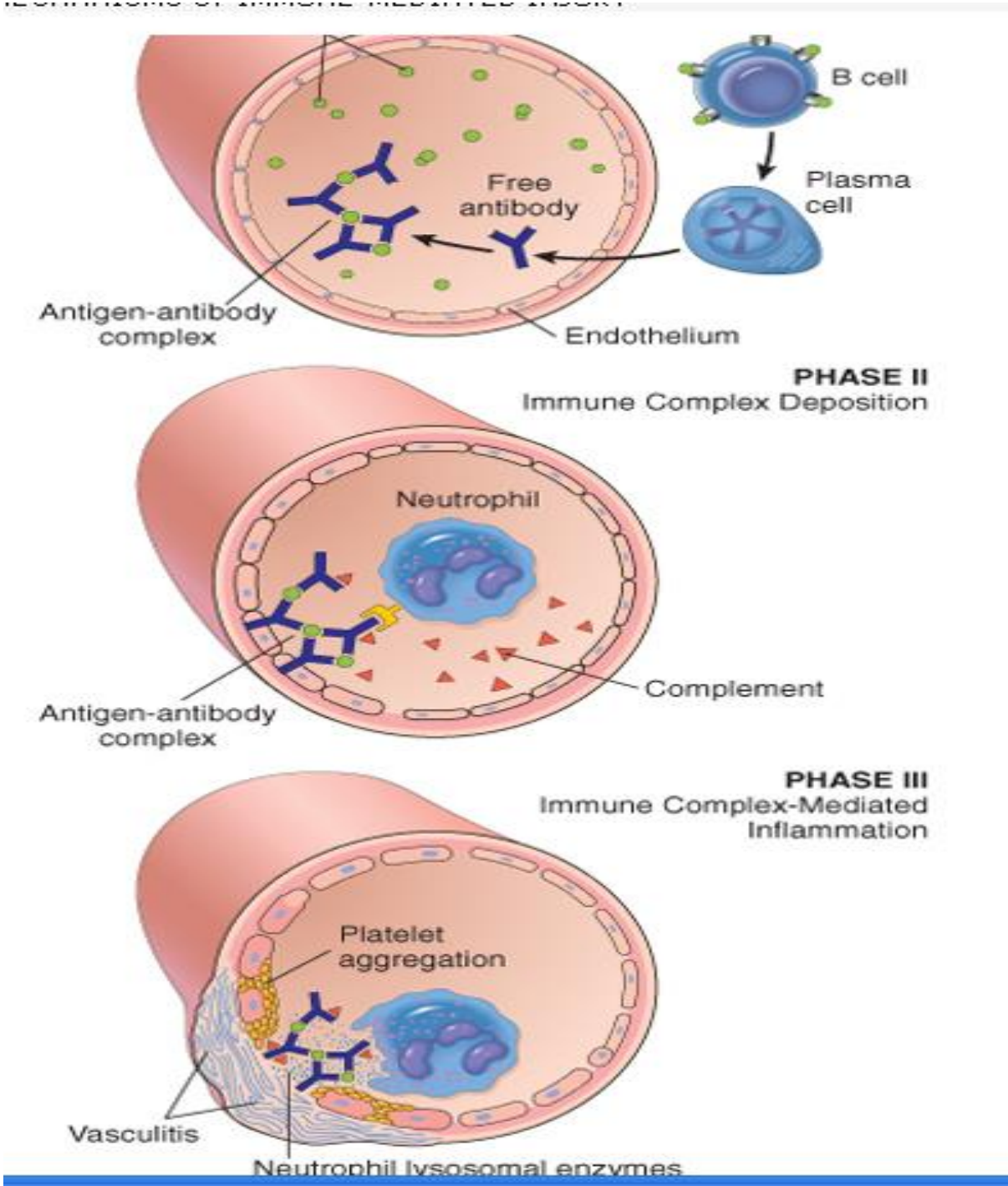
Types of systemic immune complex:

- **1-Acute type**: results from inoculation to a single large volume to exogenous antigen, the lesions tend to resolve (self limited) because the antigen is eliminated, and catabolism of the immune complexes.
- **A-Acute serum sickness** : It was first described in human when foreign serum was administered for passive immunization (e.g. horse anti tetanus serum). Now it is uncommon and seen infrequently.
- B- poststreptococcal glomerulonephritis

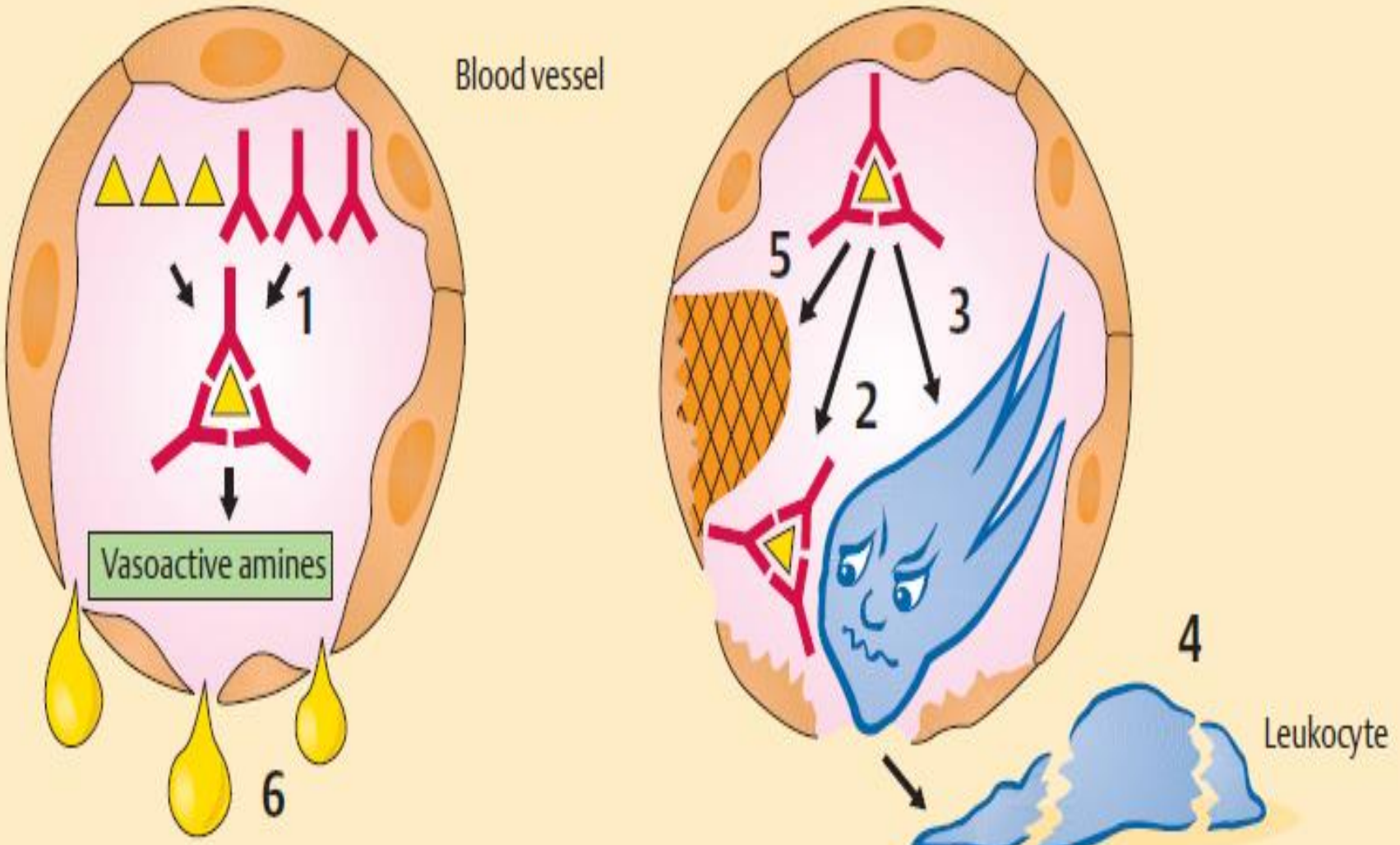
- -2-**chronic type**: **(chronic serum sickness)** : results from repeated or prolonged and recurrent exposure to an antigen e.g. Systemic lupus erythematosus.

Systemic Immune Complex Disease

The pathogenesis of systemic immune complex disease can be divided into three phases:
(1) formation of antigen-antibody complexes in the circulation and
(2) deposition of the immune complexes in various tissues, thus initiating
(3) an inflammatory reaction in various sites throughout the body



B Pathogenesis of immune complex diseases



B. Local Immune Complex Disease:

- In this type , the complexes are formed and deposited in a specific site.
- It is characterized by a localized tissue vasculitis and necrosis.

A model of local immune complex diseases is the :

Arthus Reaction :

It is a localized area of tissue necrosis resulting from **acute localized immune complex vasculitis.**

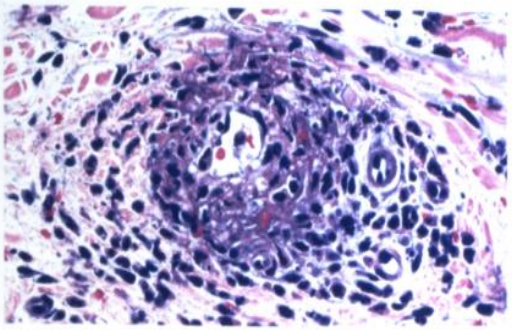
This reaction occurs after injection of an antigen into the skin of a previously immunized individual (antibodies to that antigen are already present in the circulation),

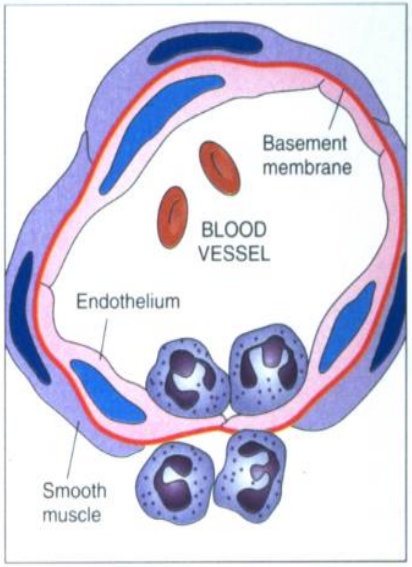
As the antigen diffuses into the vascular wall, it binds the preformed antibody, and large immune complexes are formed locally.

These complexes precipitate in the vessel walls and cause fibrinoid necrosis, and superimposed **thrombosis** worsens the **ischemic injury**.

Histopathologic Lesions: Inflammation, necrotizing vasculitis (fibrinoid necrosis).

Local Immune Complex Disease (Arthus reaction)





- **The** pathogenesis of Local immune complex disease can be divided into 4 phases:
  (**1**) Deposition of the **immune complexes** in vascular wall.
  (2) **Complement** activation.
  (3) Chemotactic attration & activation of **PMNs.**
  (4) an inflammatory reaction in the site.
- Arthus reaction. Various foreign protein ..**cutaneous vasculitis**

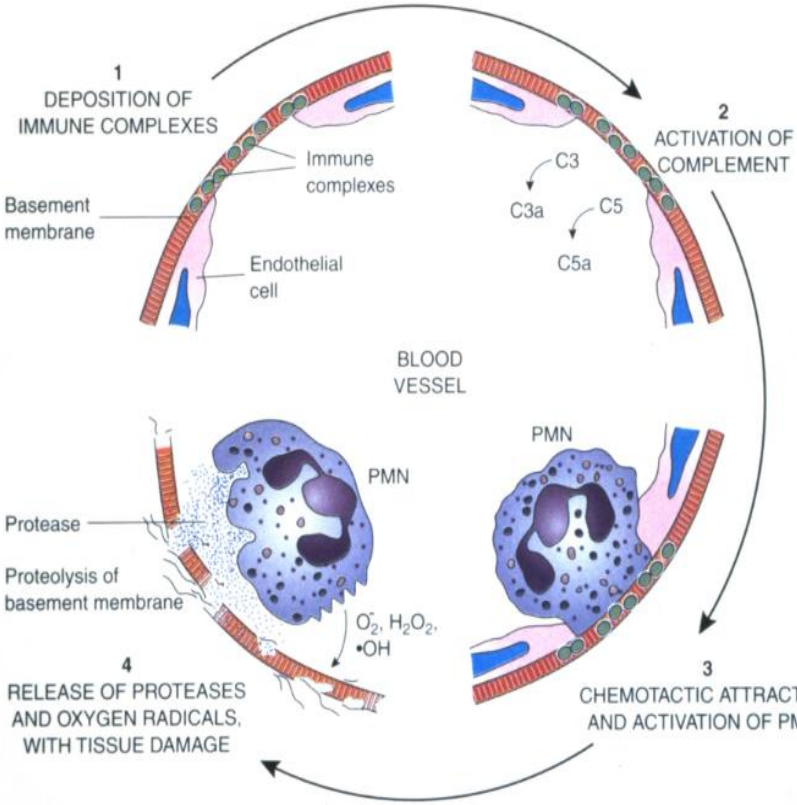


Table2: Examples of immune-complex mediated diseases

disease	Antigen involved	Cliniocpathologic manifestations
Systemic lupus erythematosus	Nuclear antigens (circulating or "planted" in kidney)	Nephritis, skin lesions, arthritis, others
Poststreptococcal glomerulonephritis	Streptococcal cell wall antigen(s); may be "planted" in glomerular basement membrane	Nephritis
Serum sickness	Various proteins (e.g., foreign serum protein)	Arthritis, vasculitis, nephritis
Polyarteritis nodosa	Hepatitis B virus antigens in some cases	Systemic vasculitis

- **4 . Cell–Mediated (Type IV) Hypersensitivity**

- **Definition:** The cell-mediated type of hypersensitivity is initiated by specifically sensitized **T lymphocytes**(**without antibodies**)
- Types:
- It includes 2 types:
- 1- CD4+ Cell-Mediated hypersensitivity reaction: Cytokines produced by the T cells induce inflammation that may be chronic and destructive. The classic example is :delayed type hypersensitivity reactions(DTH)
- 2-CD8+ T Cell-Mediated Cytotoxicity: direct cell cytotoxicity type: mediated by CD8+T cell.

Delayed type hypersensitivity(DTH)

Classically seen in:

1-granulomatous inflammation .

2-Tuberculin reaction .

3-contact dermatitis .

4-drug reaction.

5-some autoimmune diseases

Granulomatous inflammation :

occurs when persistent or nondegradable antigens (e.g., foreign bodies) lead to chronic macrophage activation manifesting as large epithelioid cells;

nodules of these activated cells are called granulomas.

Granuloma(Latin): "small corn"

A nodular arrangement of inflammatory cells

Pathogenesis of granulomatous inflammation:

The sequence of events in DTH begins with the:

- **first exposure** of the individual to tubercle bacilli. CD4+ lymphocytes recognize peptide antigen of tubercle bacilli in association with class II MHC on the surface of dendritic cells (APC).

Once CD4+ T lymphocytes recognize the antigen, it become sensitized with formation of TH1 type lymphocytes that develop **memory cells** and remain in the circulation for years.

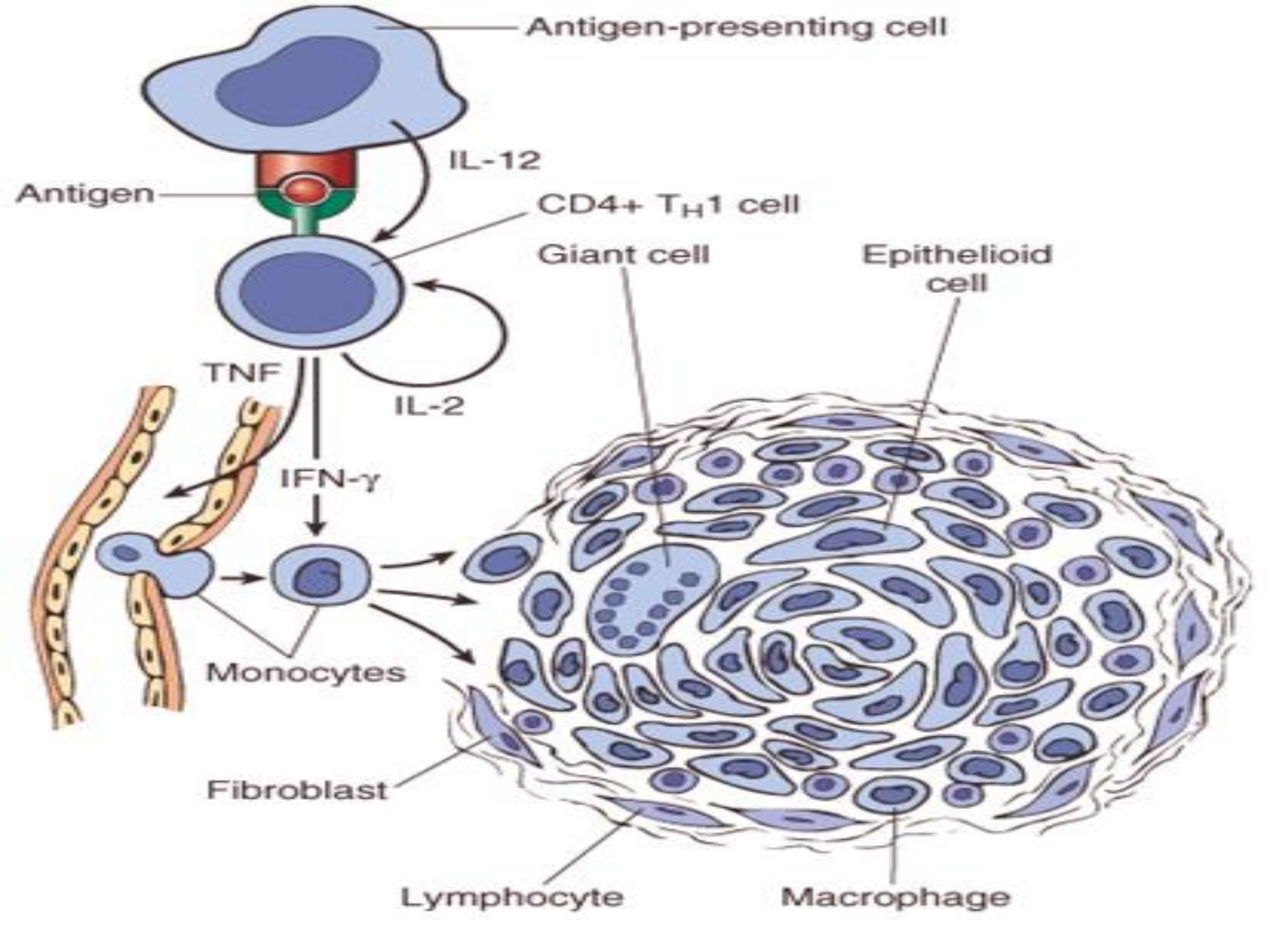
- **On subsequent exposure** to the same antigen, memory cells respond to the presented antigen on APC and become activated and secrete cytokines mainly **TNF, IL-2 and IFN-ɣ .**

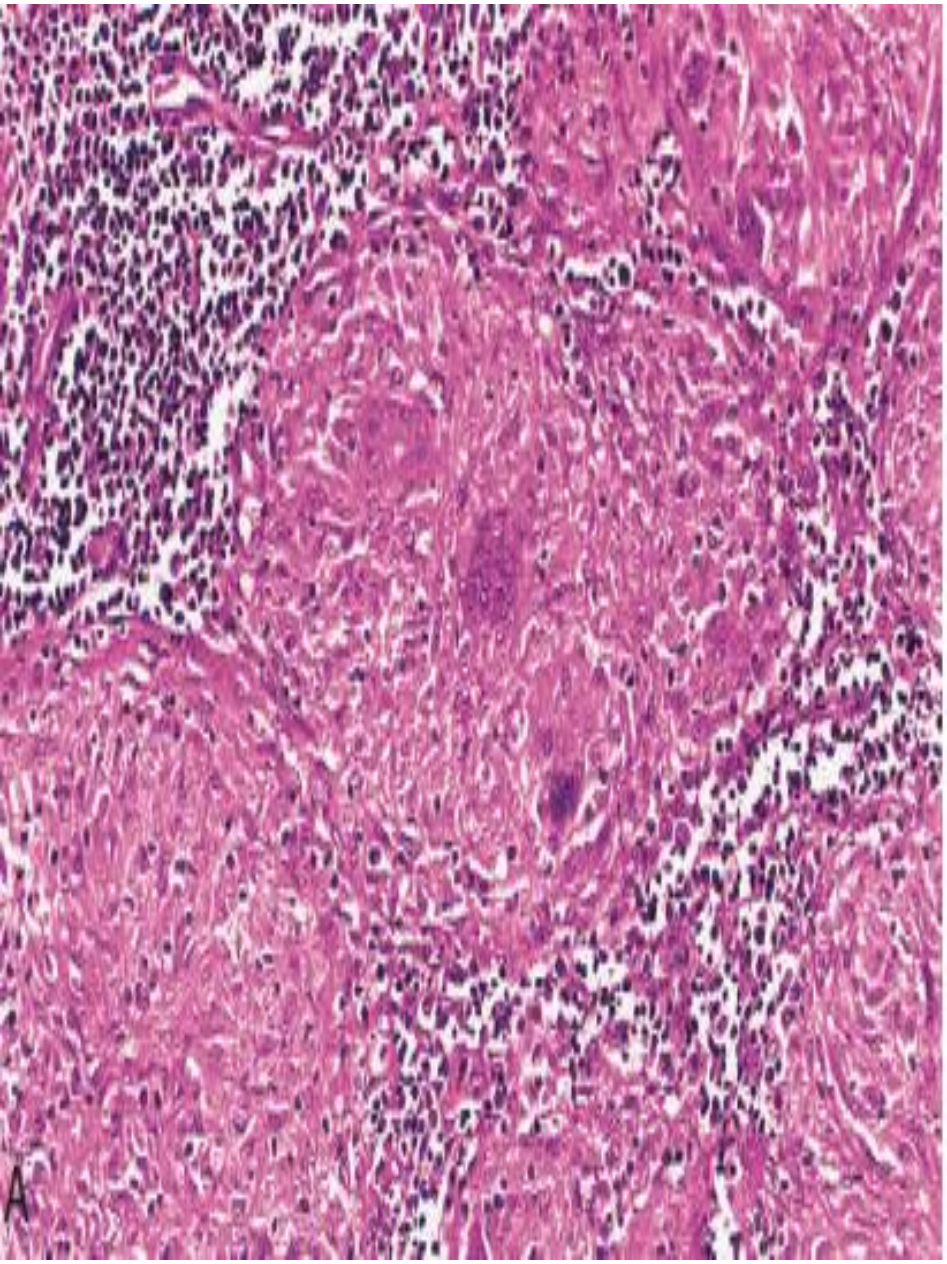
IL-2 causes proliferation of T cells that have accumulated at the site of delayed type reaction

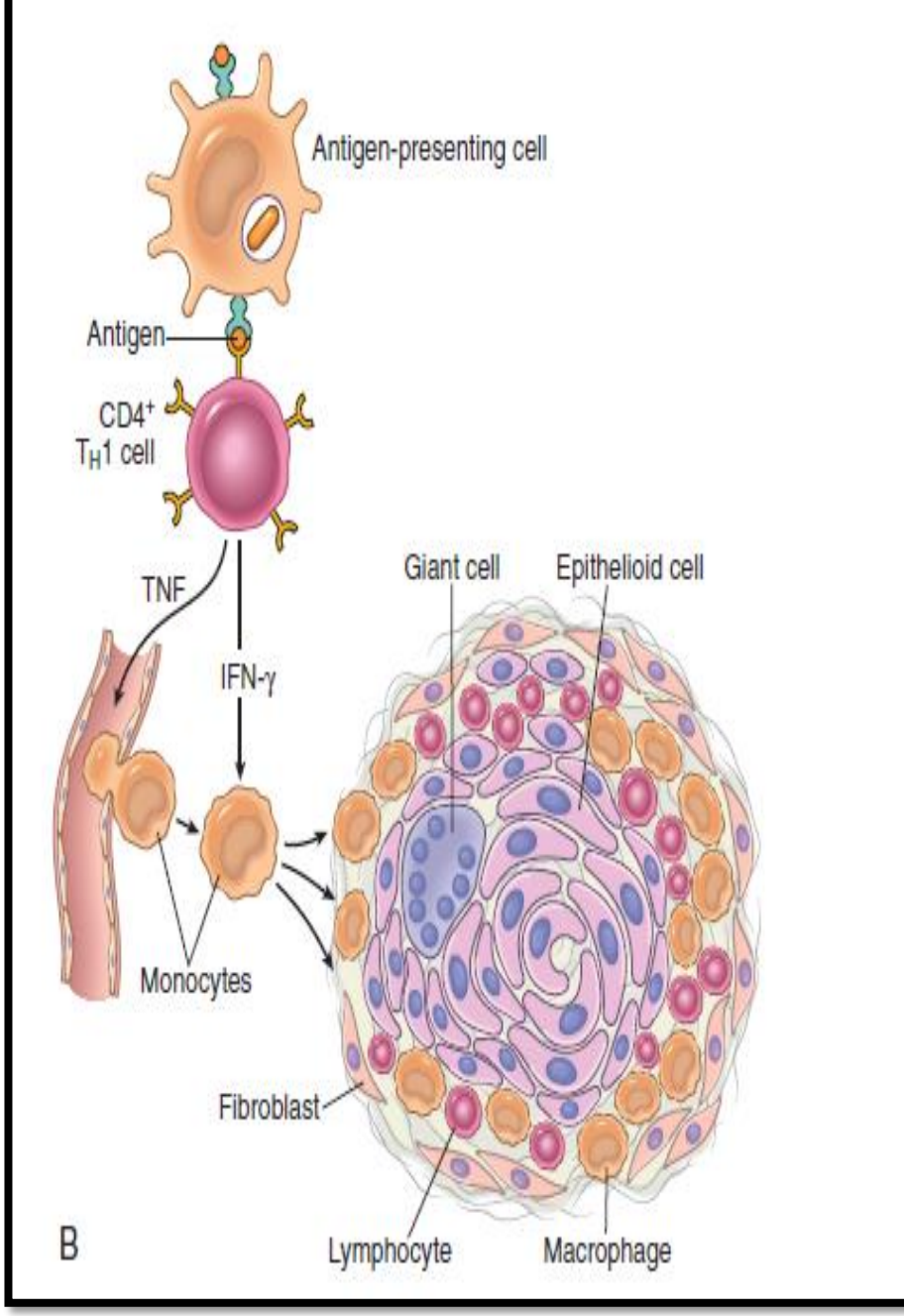
INF-ɣ is a potent **activator of macrophages**, it attract macrophages at the site of reaction from blood monocytes. **Activated macrophages become large, flat and eosinophilic** (called epithelioid cells) , some of these epithelioid cells under the influence of INF-ɣ fuse and form multinucleated giant cells. Epithelioid cells become surrounded by a collar of lymphocytes and fibroblasts and called granuloma and the pattern is called granulomatous inflammation.

Epithelioid cells produce potent products (proteases and oxide radicals) that are able to kill or neutralize mycobacteria and prevent dissemination of bacilli.

Loss of CD4+ T cells due to e.g. HIV infection, the ability of individual to respond against intracellular pathogens like mycobacteria is markedly impaired so mycobacteria are engulfed by macrophages but are not killed or inactivated and granuloma do not form leading to dissemination of tubercle bacilli

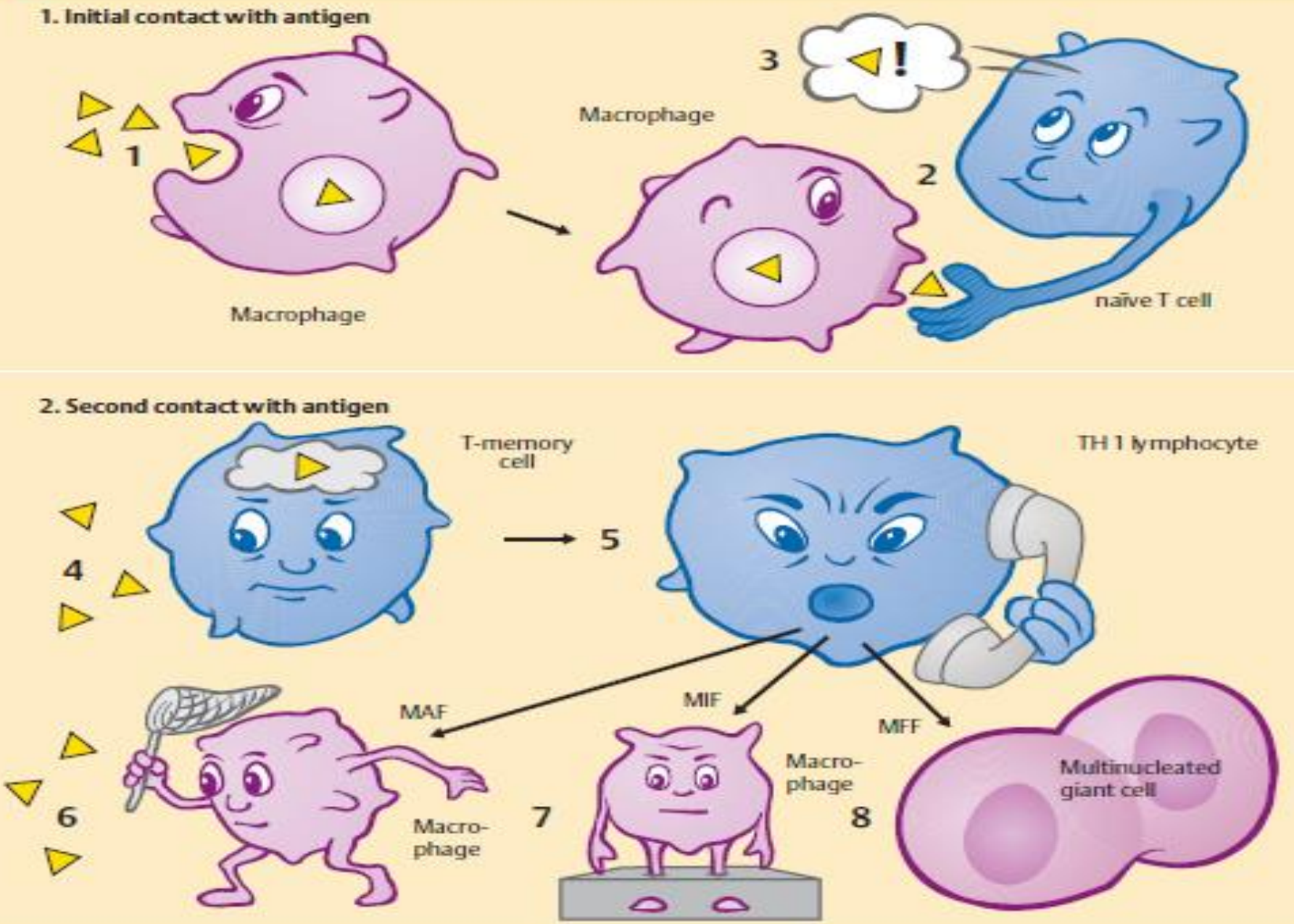

Antigen-presenting cell
IL-12
Antigen
CD4+ T_H1 cell
Giant cell
Epithelioid cell
TNF
IL-2
IFN-γ
Monocytes
Fibroblast
Lymphocyte
Macrophage



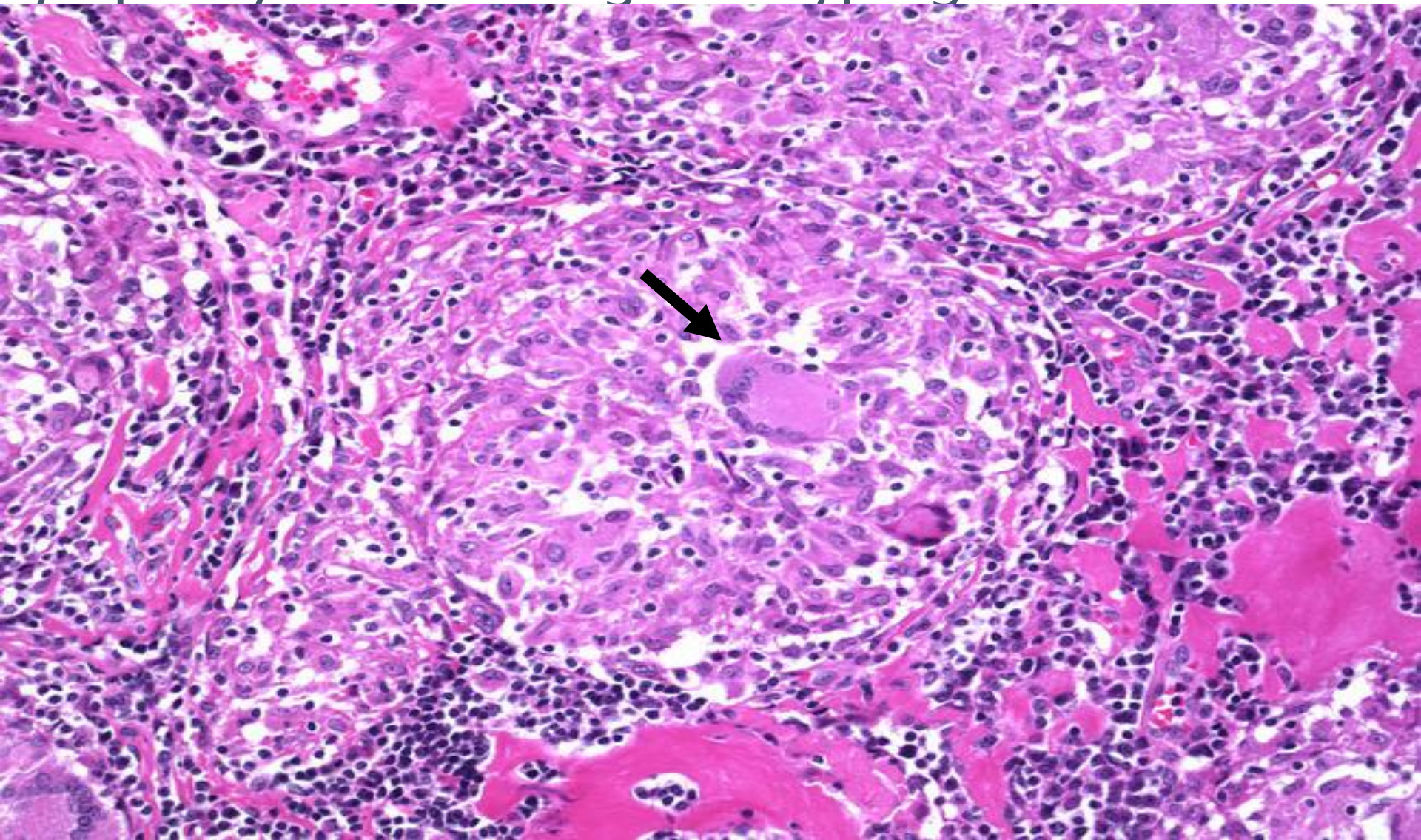


Granulomatous inflammation: an example of Delayed type hypersensitivity

Cell-mediated hypersensitivity reaction



The granuloma is composed of localized collection of epithelioid cells surrounded by lymphocytes with langhans type giant cell.



Tuberculin Reaction:

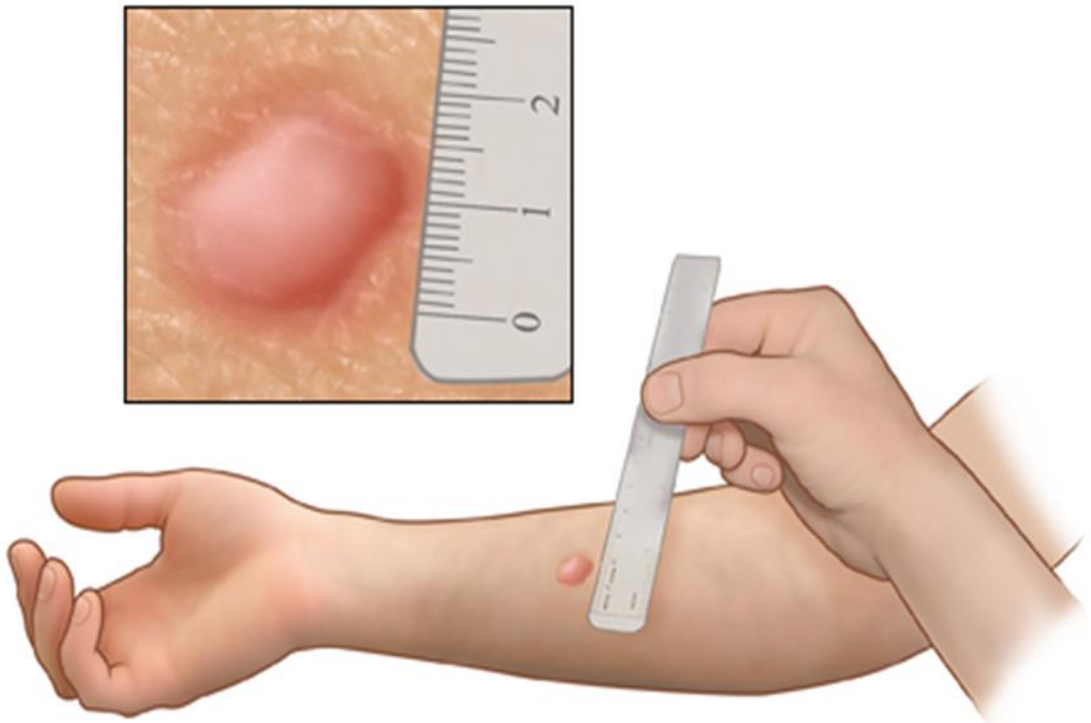
This reaction is found in individuals already sensitized to tubercle bacilli by a previous infection (a previous exposure of individual to tubercle bacilli with formation of sensitized CD4+ T lymphocytes and memory cells).

Tuberculin is a protein extract of tubercle bacilli and within 8-12 hours of subcutaneous injection of tuberculin, a local area of erythema develops reaching its peak of 1-2 cm within 24-48 hours and then subsides gradually.

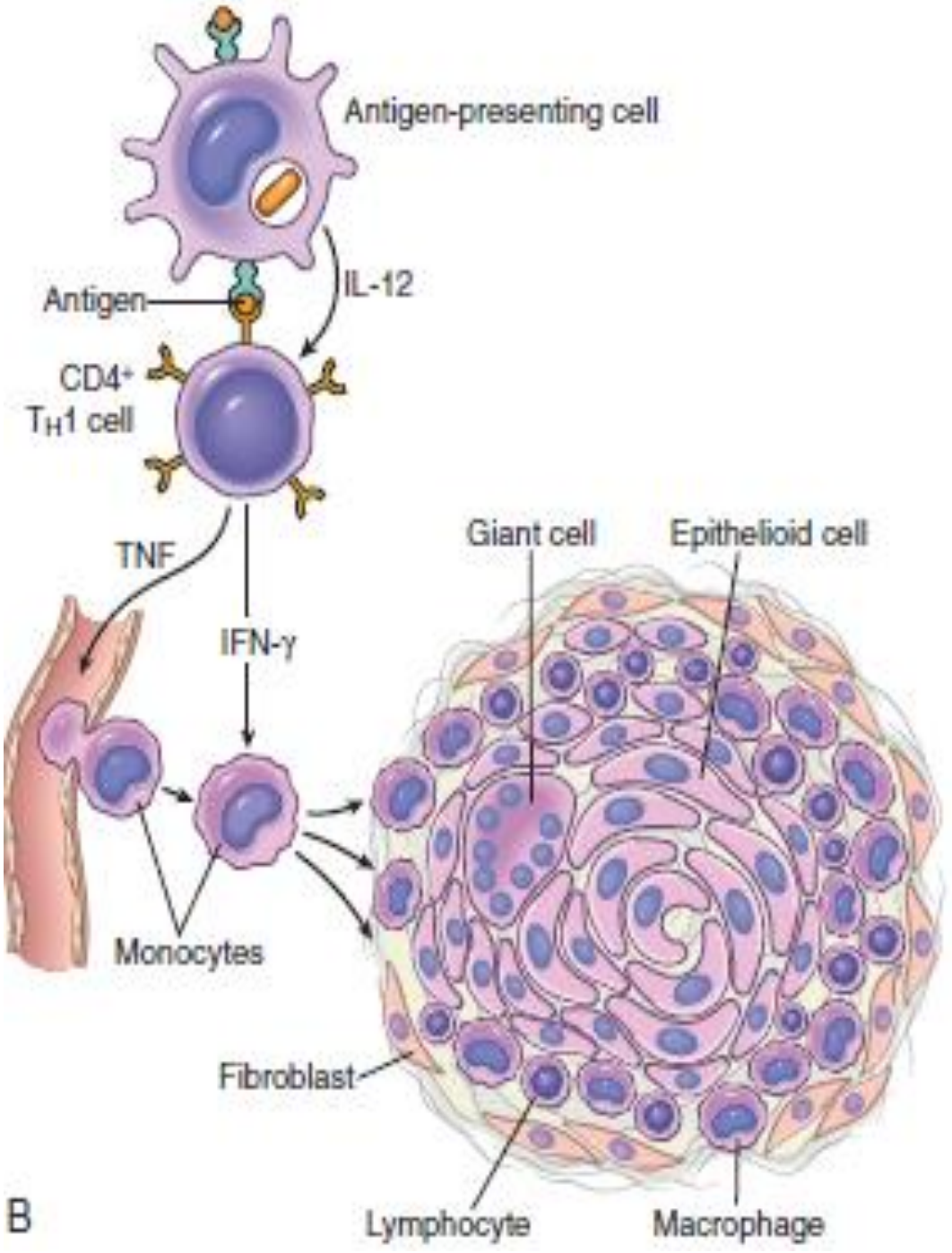
In this reaction, memory cells recognize tuberculin on surface of antigen presenting cells and secrete cytokines like IL-2 and INF-ɣ and causes accumulation of lymphocytes and macrophages in the perivascular area with local increase in vascular permeability leading to tissue indurations and local edema.

- Tuberculin reaction is used to:
- screen population for individuals who have prior exposure to tuberculosis and therefore have circulating memory cells,
- so immunosuppression or loss of CD4+ T lymphocyte e.g., due to HIV infection leads to negative tuberculin test even in the presence of severe infection.

- **Tuberculin reaction**: redness and induration in the skin after 8-12 hours and peaks at 24-72 hours with accumulation of T-helper cells and macrophages in the affected tissues around blood vessels
- local increase in vascular permeability leading to tissue indurations and local edema



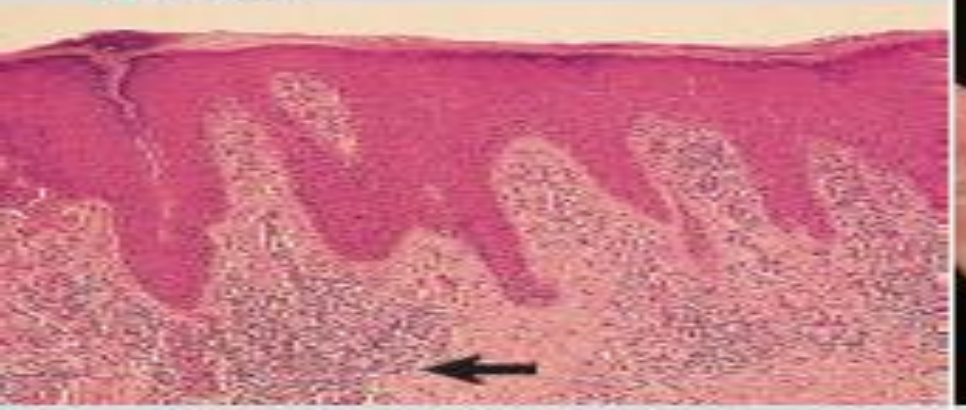
- **Steps involved in type IV reaction include**
- **A.** First the individual is exposed to an antigen for example to the tubercle bacilli where surface monocytes or epidermal dendritic cells engulf the bacilli and present it to naïve CD4+ T-cells through MHC type II antigens found on surfaces of antigen presenting cells (APC),
- **B.** The initial macrophage (APC) and lymphocytes interactions result in differentiation of CD4+TH type 1cells
- **C**. Some of these activated cells so formed enter into the circulation and remain in the memory pool of T cells for long period of time.
- D. An intracutanous injection of the tuberculin for example to a person previously exposed individual to the tubercle bacilli , the memory TH1 cells interact with the Ag on the surface of APC and are activated with formation of granulomatous Reactions

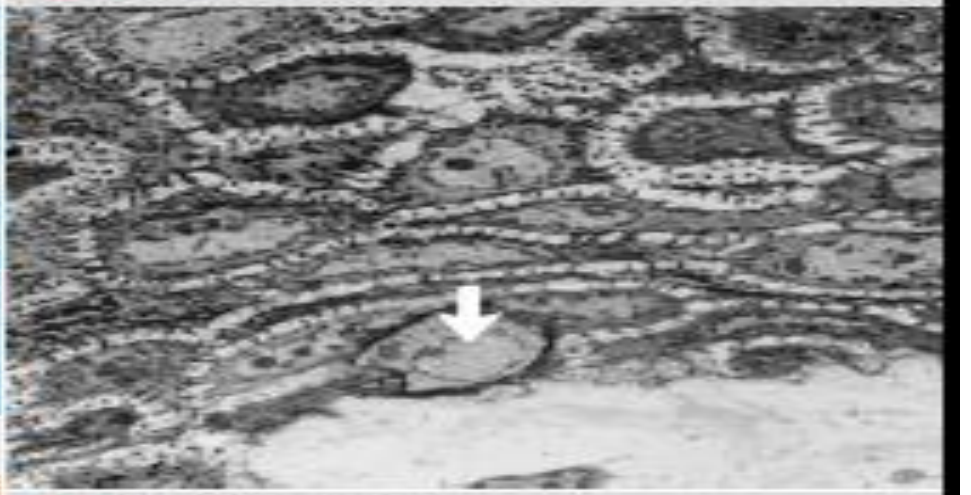


- **3-Contact dermatitis** is another example of DTH by contact with certain chemicals (Nickle, latex, fragrance, cosmetics and hair dyes).. modify self-proteins or HLA molecules,…. These modified proteins will stimulate T-helper response that regard them as foreign antigen…leading to inflammatory reaction.
- **4-Drug reactions** also involve modification of self-proteins by reactive chemicals leading to new-antigens and T-helper response with skin rash.
- **5-Systemic autoimmune disease** like rheumatoid arthritis and systemic sclerosis involve DTH against self-antigens

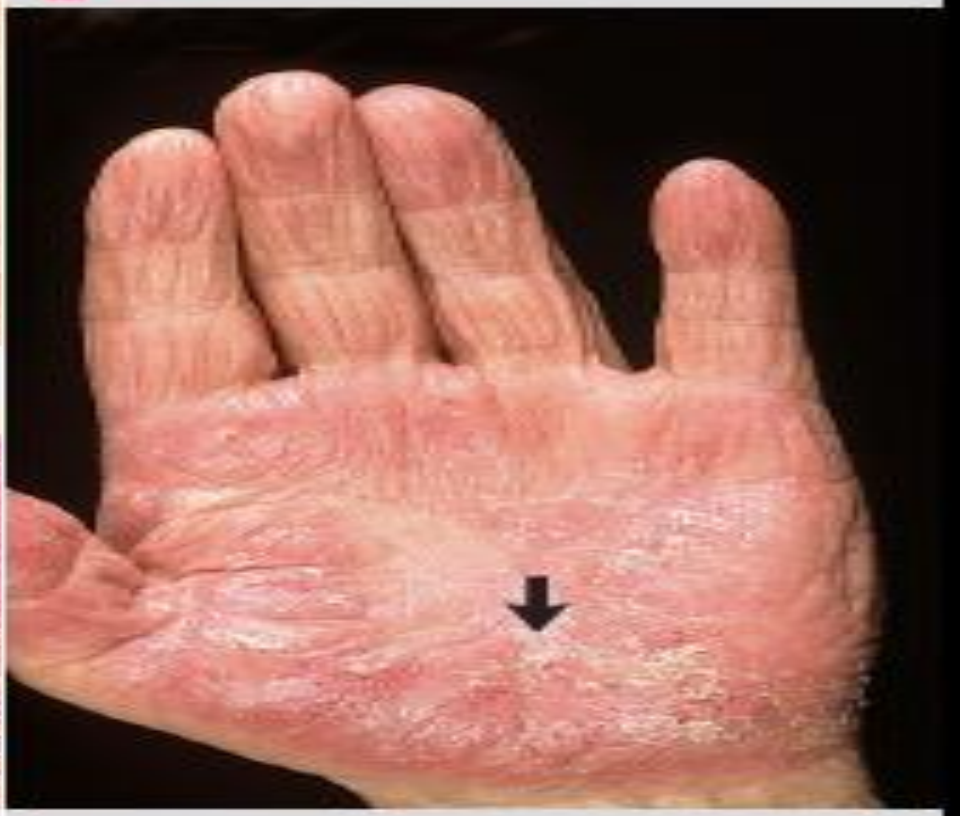
C Contact eczema

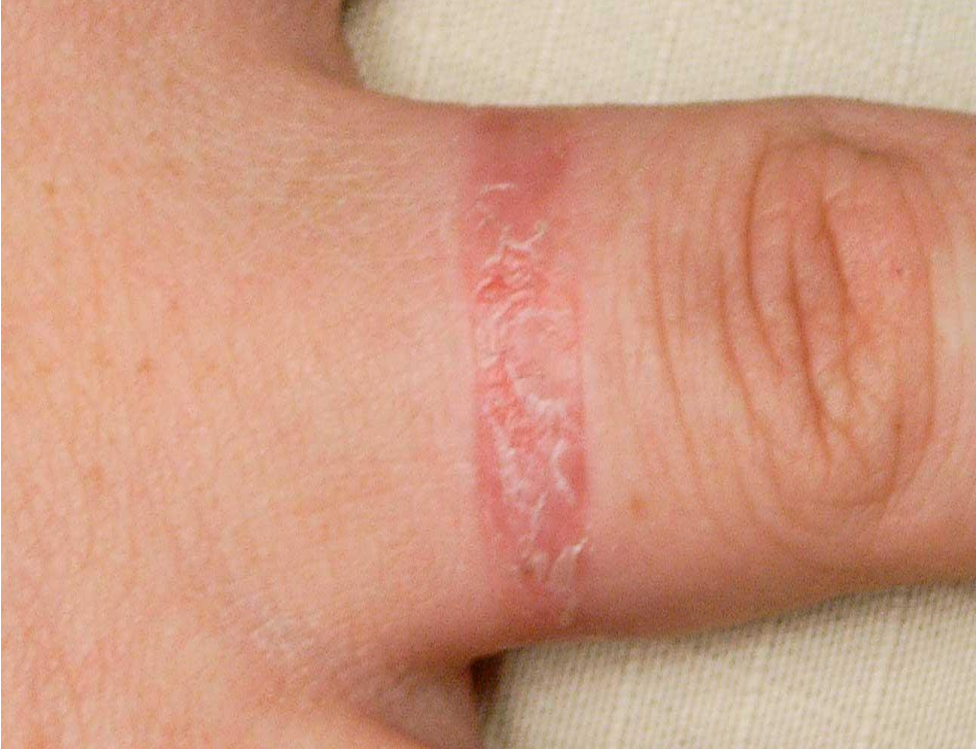
D Contact dermatitis (HE) x 50

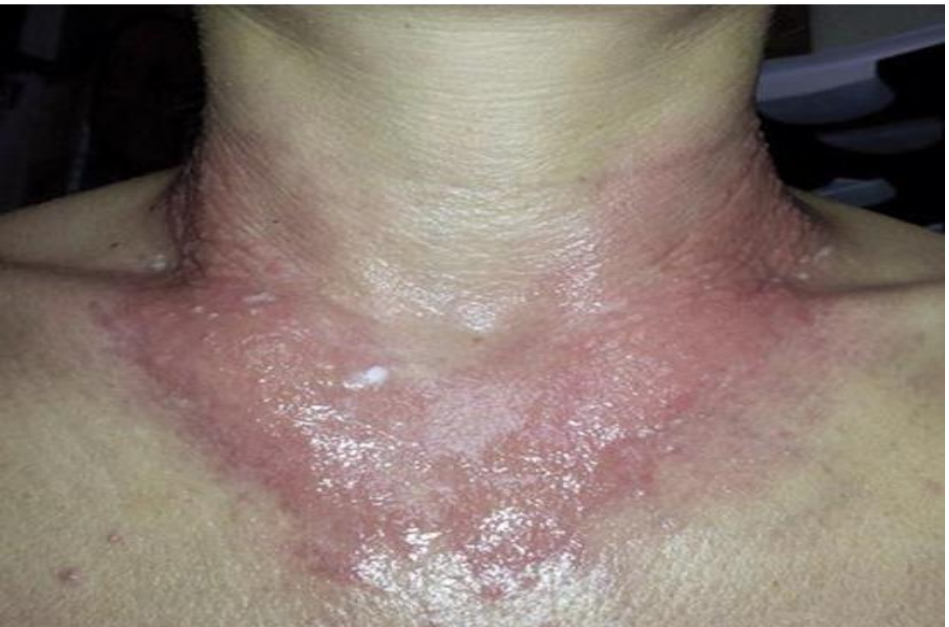


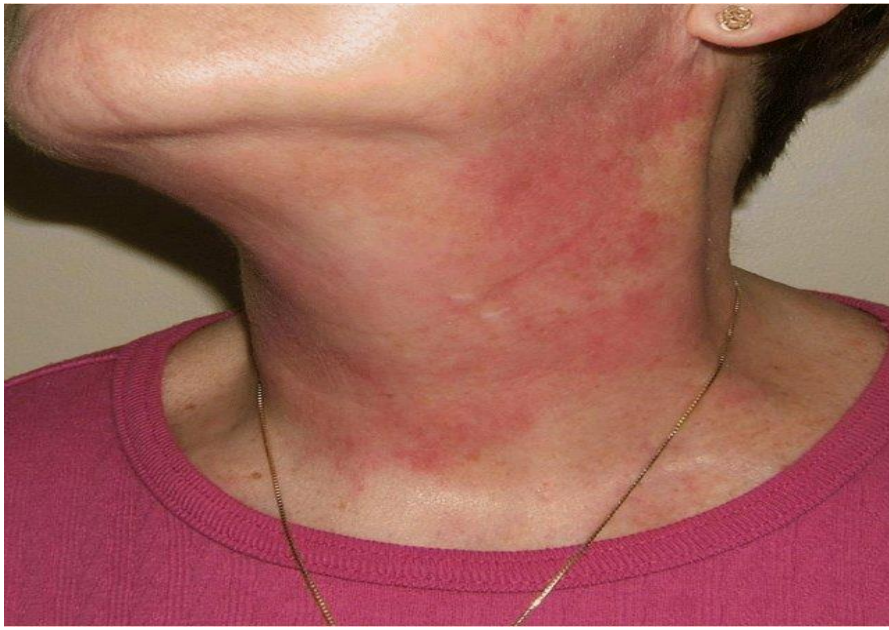


E Seborrheic eczema









- Q: Is the Allergic dermatitis is the same to contact dermatitis?

- Waiting your answers next lecture

•T-cell mediated cytotoxicity

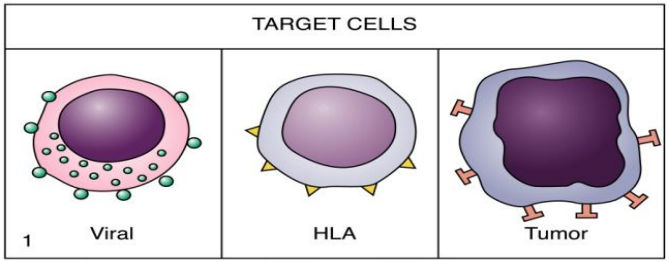
- In this variant of type IV reaction, sensitized **CD8+T cells** kill antigen-expressing target cells.
- T-cells in this reaction recognize foreign peptides in complex with MHC class I.
- These cells are main defensive mechanism against:
- **1-viral infection**: CD8+ kill viral infected cells which leads to elimination of the infected cells but this could also be the source of significant morbidity like in viral hepatitis
- **2-tumor cells** .
- **3-transplant rejection**.

- **Two mechanisms by which CTLs cause T cell damage are:**
- **Preforin-Granzyme** : dependent killing where perforin drill a hole into the cell membrane with resultant osmotic lysis and granzyme activates apoptosis of the target cells
- .**FAS-FAS ligand :** dependant killing which induce apoptosis of the target cells.

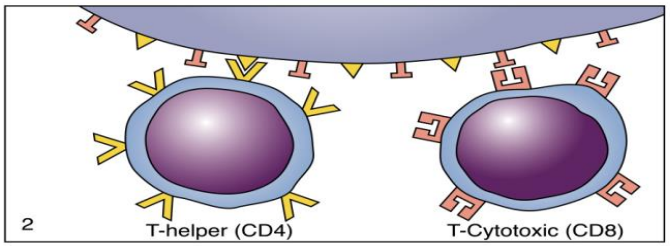
B. T-cell-mediated cytotoxcity

sensitized CD8-T cell kill antigen bearing target cells :

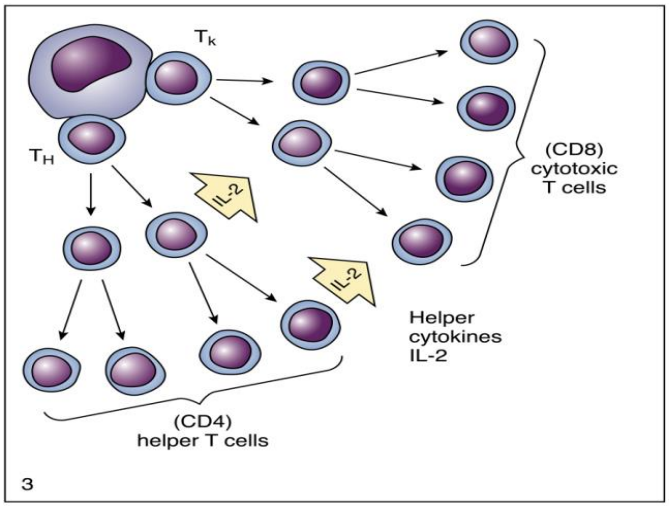
1. graft rejection
2. virus infection
3. tumor immunity



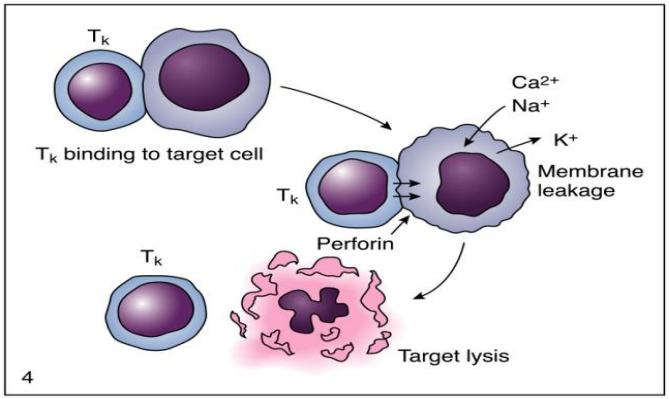
TARGET ANTIGENS
- Virally-coded membrane antigen
- Foreign or modified histocompatibility antigen
- Tumor-specific membrane antigens



RECOGNITION OF ANTIGEN BY T CELLS
- T-helper cells recognize antigen plus class II molecules
- T-cytotoxic/killer cells recognize antigen plus class I molecules



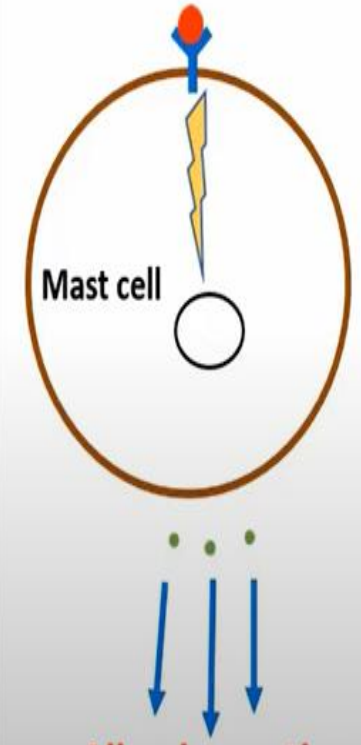
ACTIVATION AND AMPLIFICATION
- T-helper cells activate and proliferate, releasing helper molecules (e.g., IL-2)
- T-cytotoxic/killer cells proliferate in response to helper molecules



TARGET CELL KILLING
- T-cytotoxic/killer cells bind to target cell
- Killing signals perforin release and target cell loses membrane integrity
- Target cell undergoes lysis

Type I hypersensitivity

Antigen
IgE
Histamine



Allergic reactions

Type II hypersensitivity

Antigen
IgG
IgM

Activation

Complement system

NK cells

Macrophages

Type III hypersensitivity

Soluble antigen
IgG

Accumulation

Joints

Glomeruli

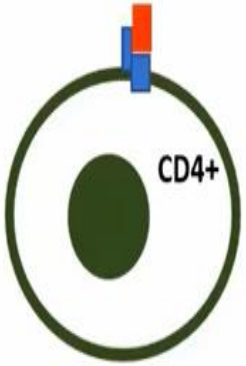
Blood vessels

activation

Complement system

Type IV hypersensitivity

Antigen
Cytokines



Type I	Type II	Type III	Type III
Antibody mediated immunity			Cell mediated immunity
IgE	IgG, IgM	IgG, IgM	T helper cells (Th1)
Fast response (minutes)	Intermediate	Intermediate	Late response (48-72 hours)
Allergic Reactions	Body cells directly attacked by antibodies	Complex accumulation and destruction	Cell mediated cytotoxicity
Asthma Allergic rhinitis	Rheumatic heart disease Autoimmune haemolytic anaemia	Rheumatoid arthritis Poststreptococcal glomerulonephritis	Transplant rejection Contact dermatitis


AUTOIMMUNE
DISEASE

AUTOIMMUNE DISEASES

Autoimmunity: Immune reactions to self (auto) antigens

Immunologic tolerance:

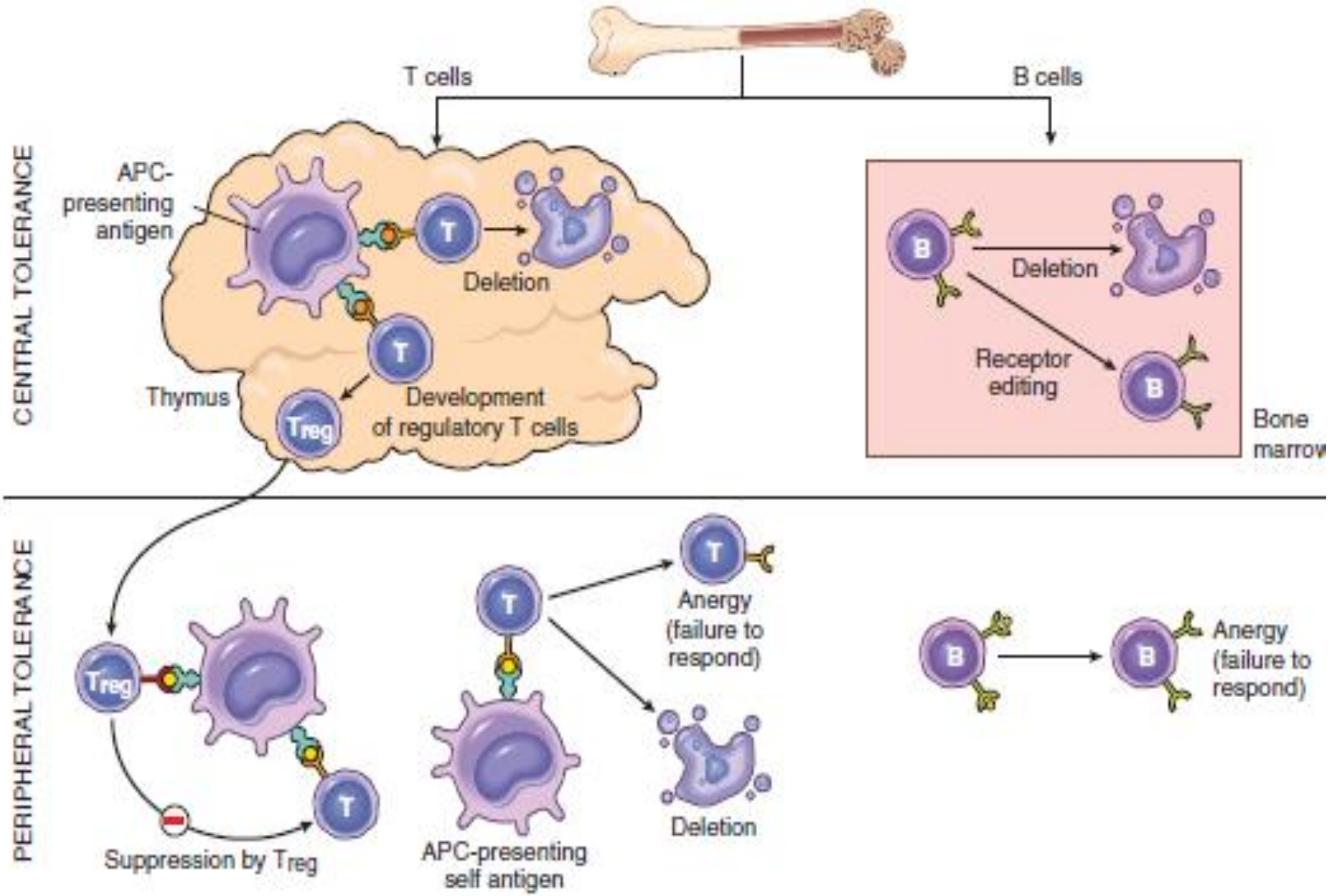
Normal persons are unresponsive (tolerant) to their own (self) antigens, and autoimmunity results from a failure of self-tolerance.

- **Self tolerance:**

lack of immune responsiveness one's own tissue antigens.

- The mechanisms of self-tolerance can be broadly classified into two groups:
- central tolerance
- peripheral tolerance

Immunologic tolerance



Central Tolerance :

Def.: it is the process by which T and B cells that recognize self antigens are either killed (negative selection) or rendered harmless during their maturation in central lymphoid organs (i.e., in the thymus for T cells and in the bone marrow for B cells).

- **If immature T-lymphocytes engaged with a self-antigen in complex with MHC molecules … transform into regulatory T-cell or apoptosis.**
- **If immature B-cell engaged with self-antigen in the bone marrow it will undergo either:**
- **receptor editing (some of the self-reactive lymphocytes switch to new antigen receptors that are not self-reactive) or**
- **If receptor editing does not occur, the self reactive cells) undergo apoptosis.**

Central tolerance is not perfect because not all self-antigens present in thymus or bone marrow and self-reactive lymphocytes escape into peripheral tissue

Peripheral Tolerance

Self reactive cells that escape central regulatory mechanisms can be removed or inactivated in the periphery through one of the following pathways:

1. **Deletion by apoptosis. T cells that recognize self-antigens may receive signals that promote their death.**

2- Anergy: This term refers to functional inactivation (rather than death) of lymphocytes induced by encounter with antigens under certain conditions.

Each T-cell need two signals to be activated:

- **first from the antigen bound to MHC molecules**
- **second from co-stimulatory receptors (which are found in low levels in normal circumstances) such as CD 28 must bind to their ligand called CD80 or CD86(also known as B7-1 and B7- 2)on APC and if the Ag is presented by cell that do not bear CD 28 ligand (i.e B7-1 or B7-2) a negative signal is delivered and the cell becomes anergic.**

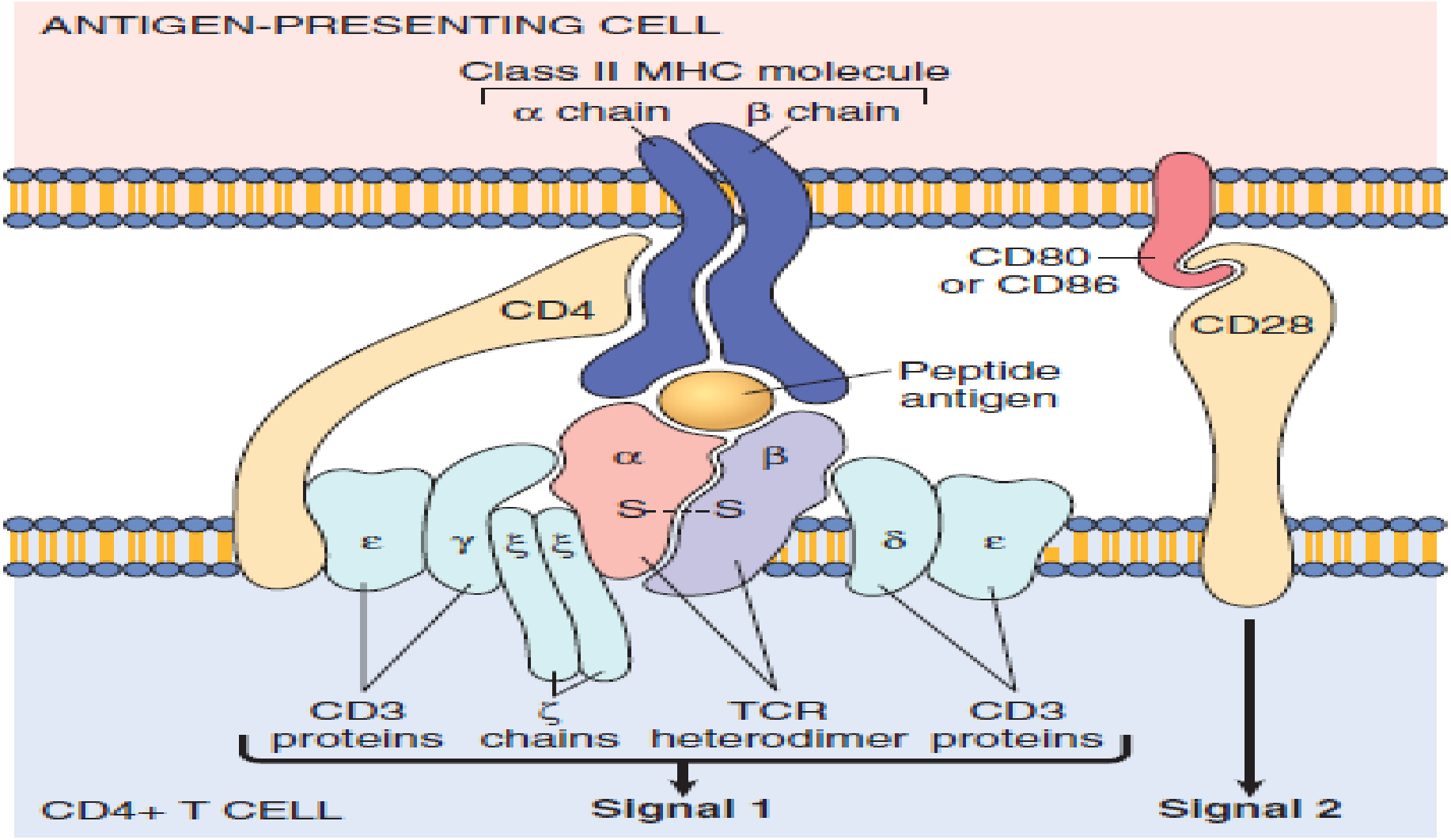
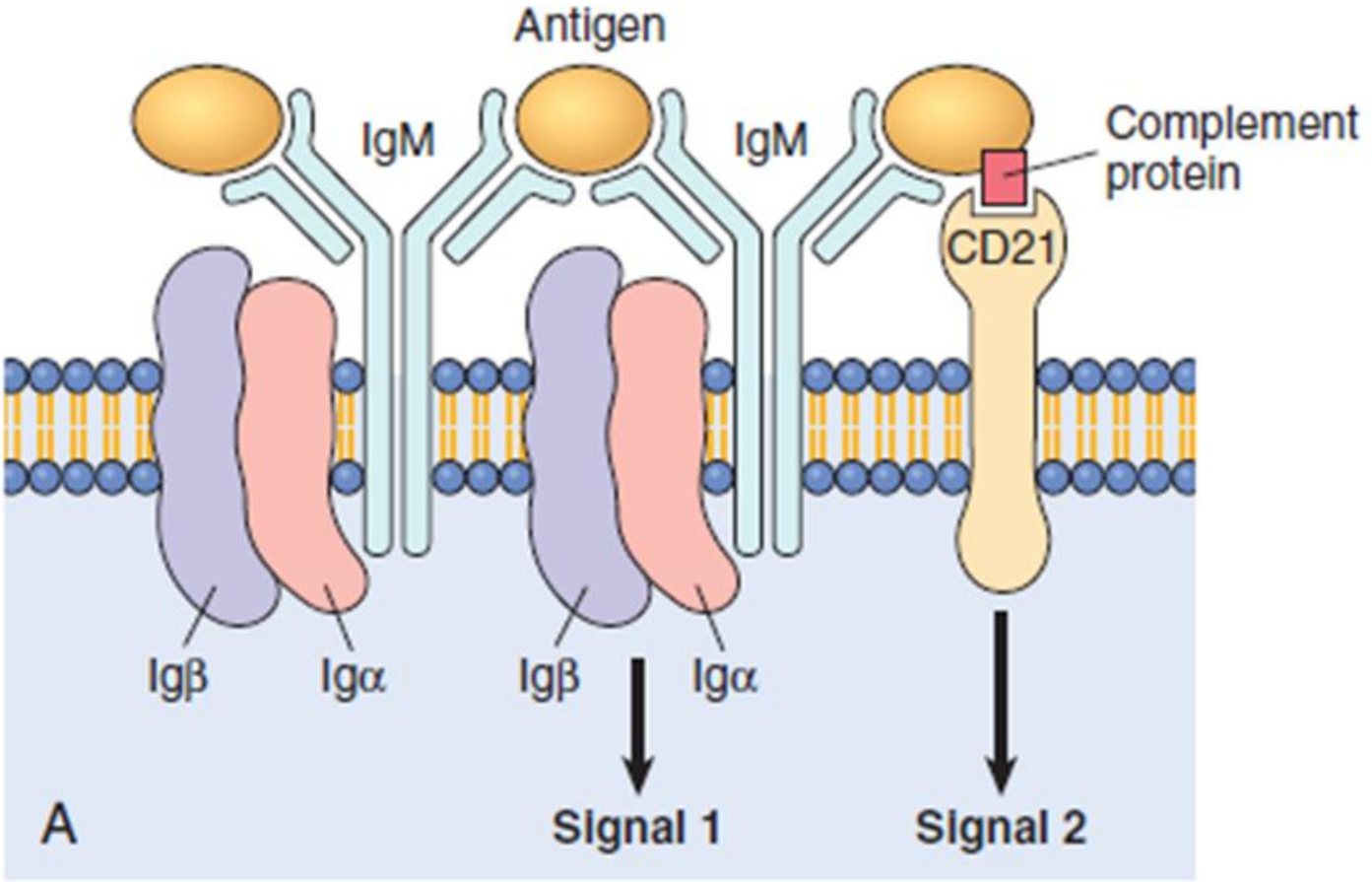


Fig. 5.5 The T-cell receptor (TCR) complex and other molecules involved in T-cell activation. The TCR heterodimer, consisting of an α chain and a β chain, recognizes antigen (in the form of peptide-MHC complexes expressed on antigen-presenting cells), and the linked CD3 complex and ζ chains initiate activating signals. CD4 and CD28 are also involved in T-cell activation. (Note that some T cells express CD8 and not CD4; these molecules serve analogous roles.) The sizes of the molecules are not drawn to scale. *MHC*, Major histocompatibility complex.

B-cell receptor complex(BCR)

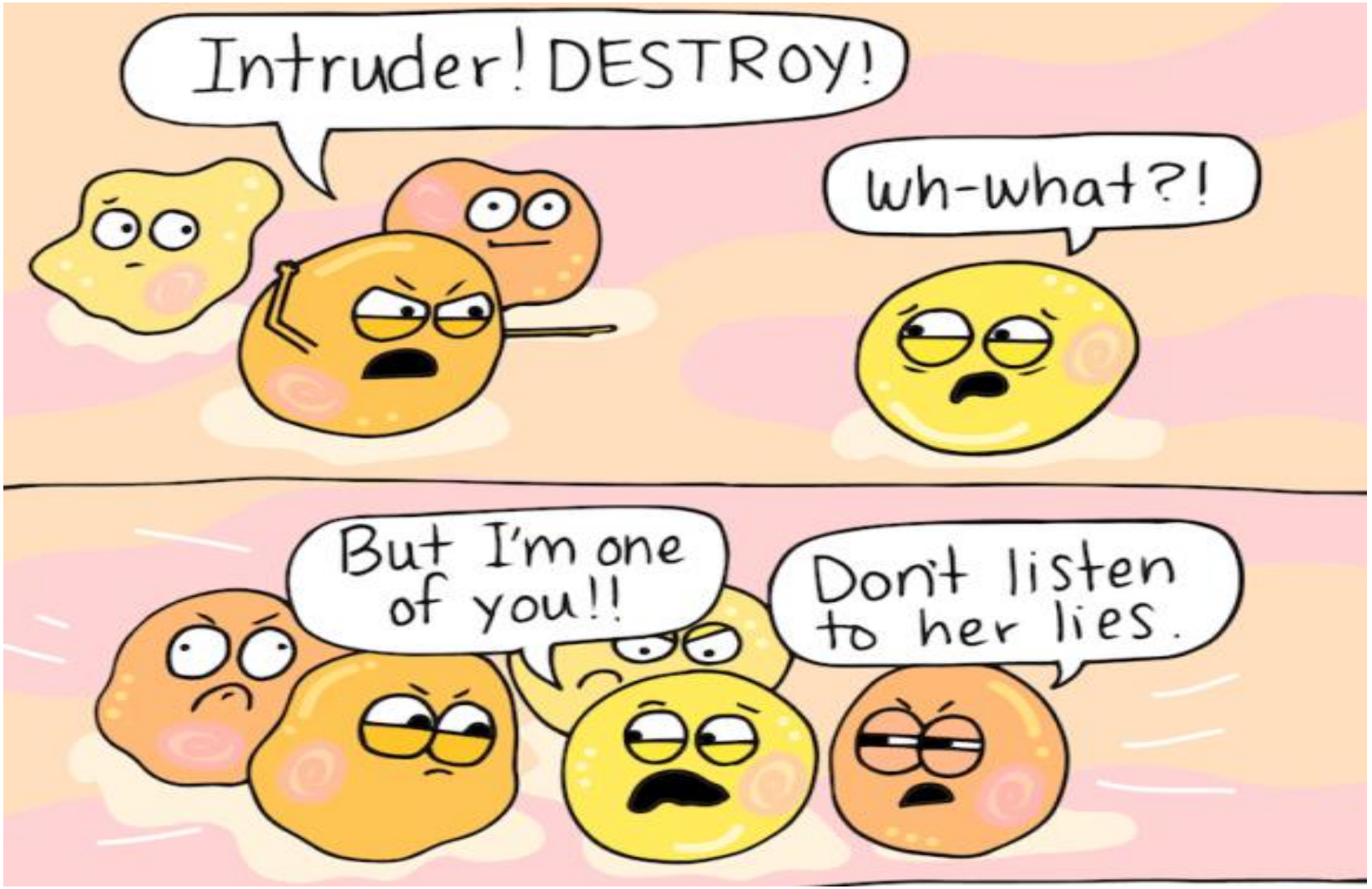


- Anergy also affects mature B cells in peripheral tissues.
- if B cells encounter self antigen in peripheral tissues, especially in the absence of specific helper T cells, the B cells become unable to respond to subsequent antigenic stimulation .

3-suppression by regulatory T lymphocytes(T reg. these cells develop mainly in the thymus and help control and inactivate self-reactive T-cells).

4-hidden (sequestered) self-antigens, from the immune system, e.g antigens in the testis, eye, and brain are relatively shielded from immune system, after trauma or infection they may induce prolonged inflammation like post-traumatic orchitis

- **When normal tolerance of the self antigens by the immune system fails, autoimmune diseases result**.



General pathogenesis of autoimmune diseases

- A normal body does not react against its own tissues.
- However, several mechanisms can compromise this self tolerance, causing endogenous tissue to act as a pathogen. These include:

1— No central immune tolerance .

2— Interruption of clonal Anergy of autoreactive T cells .

3-Immortalization of activated T cells

4— **Imbalance of suppressor- Helper T-cell function:**

- loss of suppressor T cell function or
- excessive helper T cell function result in B cell activation

5— Formation of **cross-reactive antibodies** with specificity against pathogenic and endogenous HLA (molecular mimicry and antigen mimicry).

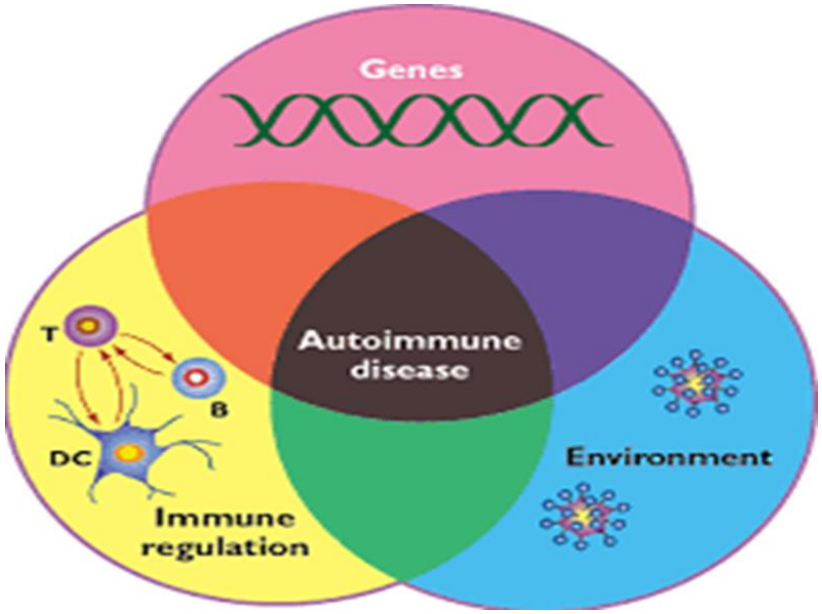
6— **Emergence of hidden(sequestered) antigens**: Some antigen are anatomically segregated from the developing immune system. special clonal deletion or anergy fails to occur, if they release into circulation from tissue destruction by trauma or infection, they induced an immune response

7- modification of molecule: if self antigen is modified as due to drugs or microorganisms, this recognized by T cells as a foreign antigen so cooperate with B cells leading to formation of autoantibodies as in autoimmune hemolytic anemia

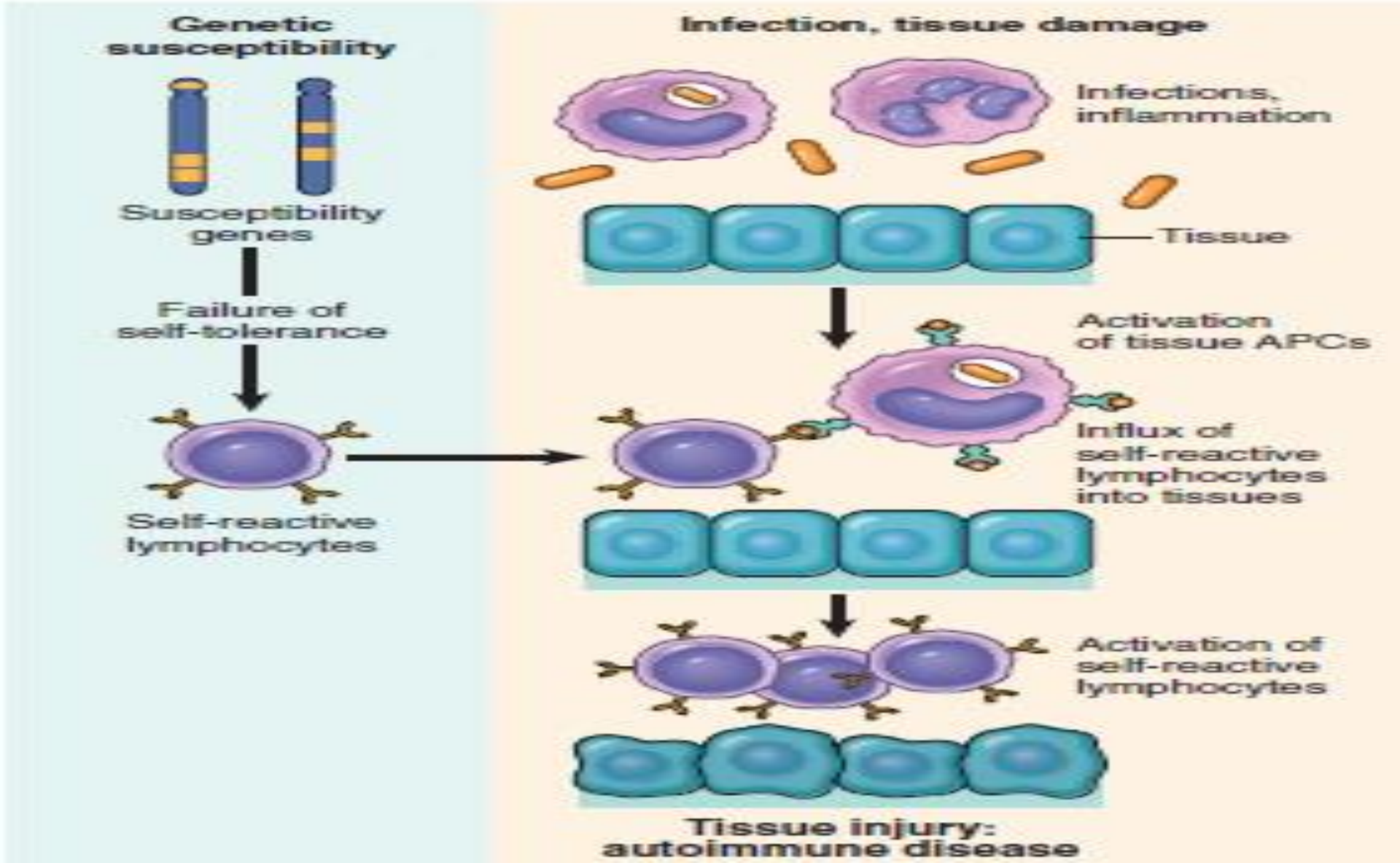
Mechanisms of Autoimmunity:

It is believed that the breakdown of self-tolerance and development of autoimmunity result from a combination of :

- **inherited susceptibility genes, which influence lymphocyte tolerance,**
- **and environmental factors, such as infections or tissue injury, that alter the display of self antigens**



Pathogenesis of autoimmune diseases



1.Genetic Factors in Autoimmunity :

1-**Autoimmune diseases have a tendency to run in families.**

2-Several autoimmune diseases are linked with the HLA locus, especially class II alleles (HLA-DR, -DQ) e.g.

- Rheumatoid arthritis and HLA –DRB 1

-Ankylosing spondylitis and HLA- B 27

3-many genetic polymorphisms in (non - HLA Genes) are associated with different autoimmune diseases.

e.g. PTPN-22 gene and type I diabetes and rheumatoid arthritis.

Polymorphisms in the gene for NOD2 are associated with Crohn disease

2. *Role of Infections and Tissue Injury*

Microbes may induce autoimmune reactions by several mechanisms:

1-Viruses and other microbes may share cross-reacting epitopes with self antigens, This phenomenon is called molecular mimicry.

Some microbes may express antigens that have the same amino acid sequences as self antigens. Immune responses against the microbial antigens may result in the activation of self reactive lymphocytes. This phenomenon is called **molecular mimicry**. E.g rheumatic heart disease, in which antibodies against streptococcal proteins cross-react with myocardial proteins and cause myocarditis

2-Microbial infections with resultant tissue necrosis and inflammation can expose self-antigens and activate APCs and lymphocytes in the tissues.

General Features of Autoimmune Diseases

- Diseases caused by autoimmunity have some important general features.

1-Autoimmune diseases tend to be chronic, sometimes with relapses and remissions, and the damage is often progressive.

2-Autoimmune diseases are **more common in women** than in men. perhaps due to **hormones** and **other factors.**

3-The clinical and pathologic manifestations of an autoimmune disease are determined by the **nature of the underlying immune response**.

- Some of these diseases are caused by **autoantibodies,**
- Most chronic inflammatory diseases are caused by **abnormal and excessive T helper** responses e.g psoriasis, multiple sclerosis, and some types of inflammatory bowel disease.
- **CD8+ CTLs** contribute to killing of cells, such as islet -cells in type 1 diabetes.
- In some autoimmune diseases, such as rheumatoid arthritis, **both antibodies and T cell mediated** inflammation may be involved
- **4-**In many of the systemic diseases that are caused by immune complexes and autoantibodies, the lesions affect principally the connective tissue and blood vessels of the various organs involved.
- Therefore, these diseases are often referred to as "**collagen vascular**" or "**connective tissue" disorders**, even though the immunologic reactions are not specifically directed against constituents of connective tissue or blood vessels.
-

Types of autoimmune diseases:

1-organ-specific disease: **specific immune responses are directed against one particular organ** or tissue type and result in localized tissue damage,

2-systemic or generalized disease: multisystem diseases characterized by lesions in many organs and associated with multiple auto Abs or T cell–mediated reactions against numerous self antigens.

- **Why does some autoimmune disease affecting single organ while other are systemic?**

* They depend on the nature of Ag:

(1) If Ag restricted in its expression to single organ e.g., Grave's disease the autoimmune disease will be limited to the cells of that organ only.

(2) If more organs express the same Ag, so more wide spread diseases occur.

Table 6-6 Autoimmune Diseases

Organ-Specific	Systemic
Diseases Mediated by Antibodies	
Autoimmune hemolytic anemia	Systemic lupus erythematosus
Autoimmune thrombocytopenia	
Autoimmune atrophic gastritis of pernicious anemia	
Myasthenia gravis	
Graves disease	
Goodpasture syndrome	
Diseases Mediated by T Cells*	
Type 1 diabetes mellitus	Rheumatoid arthritis
Multiple sclerosis	Systemic sclerosis (scleroderma)† Sjögren syndrome†
Diseases Postulated to Be Autoimmune	
Inflammatory bowel diseases (Crohn disease, ulcerative colitis)‡	
Primary biliary cirrhosis†	Polyarteritis nodosa†
Autoimmune (chronic active) hepatitis	Inflammatory myopathies†

*A role for T cells has been demonstrated in these disorders, but antibodies may also be involved in tissue injury.
†An autoimmune basis of these disorders is suspected but the supporting evidence is not strong.
‡These disorders may result from excessive immune responses to commensal enteric microbes, autoimmunity, or a combination of the two.


Thank
you