# Unit III

# Immunology

# Chapter 8 : Role and components of the immune system

## Document 1 : HLA: a major self marker

### 1) An experimental study of body responses against cells deriving from different origin.

**Types of grafting:**

**1- Autograft:** Tissue graft between two different sites in the same individual. In this case the grafting is accepted.

**2- Isograft :** Tissue graft between two individuals of the same strain (Identical twins). In this case the grafting is accepted.

**3- Allograft:** Tissue graft between 2 non-sibling individuals of the same species. In this case the grafting is rejected after 15 days.

**4- Xenograft :** Tissue graft between two individuals that belong to different species. In this case the grafting is rejected after few days.

### 2) Organization and expression of MHC

In man, the MHC (Major Histo compatability complex) genes code for two classes of membrane glycoprotein that differ by their structure, distribution and role. MHC or HLA (Human leukocyte antigen) is classified into HLA classe I (HLAI) that includes A, B and C Loci and HLA class II (HLAII) that includes Dp. DQ and DR Loci .

The gene coding for HLA are highly polymorphic because:

1- There exists a large number of allelic forms.

2- The alleles taken from each parent are co-dom.

∴It is impossible to have two individuals having the same MHC except in identical twins.

Note: Immunological self: (HLA + peptide present in it)

How can you explain the rejection that takes place in the allograft?

This rejection is due to that the grafted cells are recognized as non self components due to their difference in MHC (HLA).

## Document 2 : Blood groups: another self marker

Nucleated cells are characterized by the presence of HLA markers on their surface. Do the anucleated cells present the same markers?

**ABO system**

Human blood groups are classified into four groups: A, B, AB and O.

The surface of RBC are made up of glycoprotein molecules (Oligo Saccarides) and to this surface agglutinogen molecules can be attached.

**What are agglutinogen, agglutinin and agglutination?**

**Agglutinogens :** Are protein molecules found on the surface of RBC and they are of two kinds: agglutinogen A and agglutinogen B.

**Agglutinin :** Are protein molecules that are circulated in the plasma of the blood and they are of two kinds agglutinin anti A and agglutinin anti B.

**Agglutination (Coagulation):** Agglutination is the process by which agglutinins agglutinate agglutinogens.

e.g: Agglutinin A coagulates agglutinogen A.

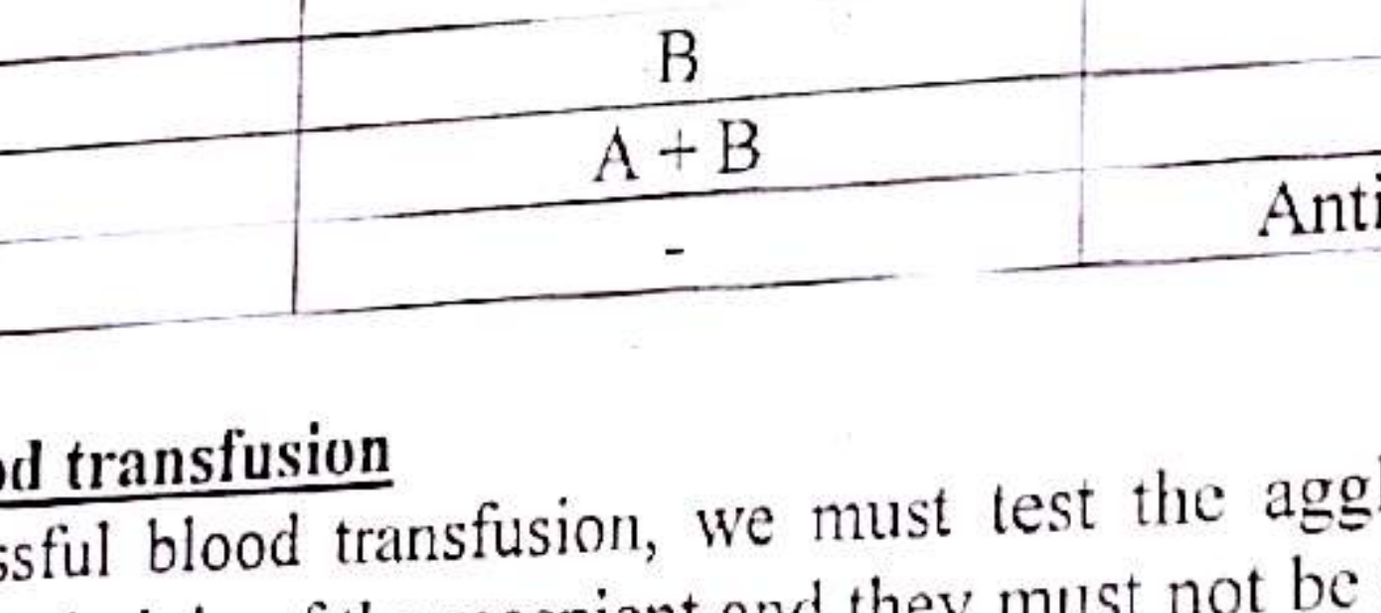
Agglutinin anti B coagulates agglutinogen B

**Distribution of agglutinogens and agglutinin in each of the blood groups**

| Blood groups | Agglutinogen | Agglutinin |
|---|---|---|
| A | A | Anti B |
| B | B | Anti A |
| AB | A + B | - |
| O | - | Anti A + Anti B |

**Successful blood transfusion**

To have successful blood transfusion, we must test the agglutinogen of the donor and the agglutinin of the recepient and they must not be of the same type like: Anti A and antigen A or Anti B and antigen B.



**Rhesus system:** Some RBC have additional proteins called Rhesus factor ($Rh^+$) and the absence of these proteins are known as ($Rh^-$) knowing that $Rh^+$ is not compatible with $Rh^-$ while $Rh^-$ is compatible with $Rh^+$ when they are given to each other by blood transfusion.

| Serums-tests | | | Blood Group |
|---|---|---|---|
| With agglutinine anti-A | With agglutinine anti-B | With agglutinine anti-A and anti-B | |
|  |  |  | ? |
|  |  |  | ? |
|  |  |  | ? |
|  |  |  | ? |
|  No agglutination |  Agglutination | | |

Give the blood group for each of the above serums-tests.

## Document 3 : The non-self

- **Pathogenic agents:**

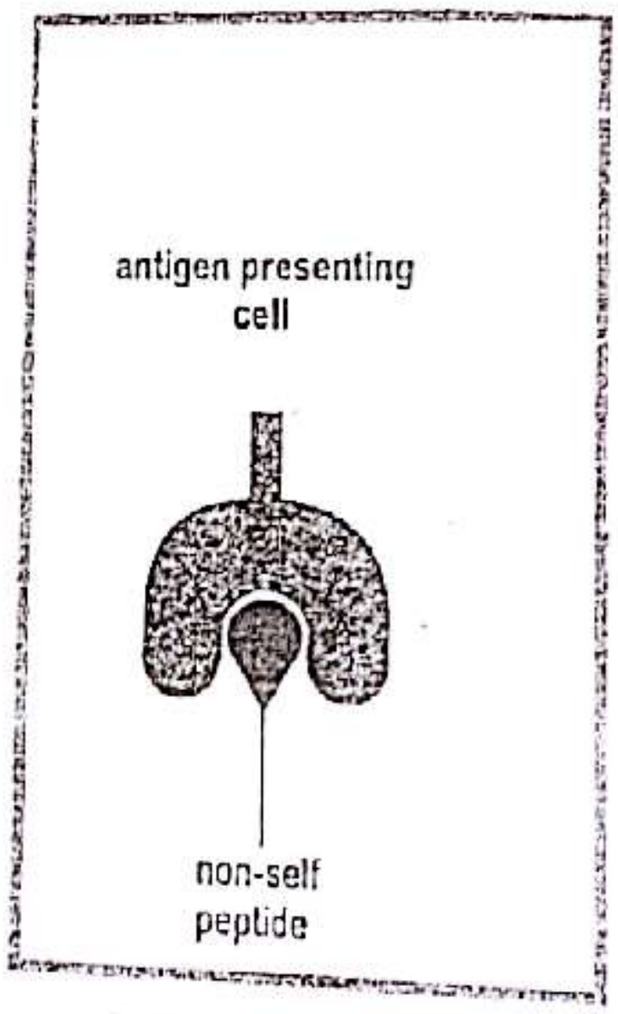
  Viruses, bacteria, fungi, protozoa and worms can cause diseases and known as pathogenic agents.

- **Elements of the "non self" or antigens.**

  The non-self elements or antigens that are recognized by our immune cells can be soluble like toxins, venome of snakes, or celluler like viruses, bacteria etc……

- **What is a modified cell?**

  The modified cell, like cancer cells, has within its HLA markers non-self peptide instead of self or useful peptide.




*The modified "self ".*

## Document 4 : Cells of the immune system

### Classification of leucocytes

The leukocytes are originated from the pluripotent stem cells in the bone marrow that are of two types: Myeloid and lymphoid stem cells.

I) **Myeloid stem cells:**

**A)** Granulocytes: Are characterized by:

1- Diameter 10 µm

2- They constitute 67% of the leukocyte population.

3- Lifespan: 2 to 3 days

4- Multilobed nucleus

5- They are of 3 kinds:

- Neutrophil: For phagocytosis and bacteria destruction
- Basophil : For amplification of allergic reactions.
- Eosinophil: For phagocytosis of antigen-antibody complex.

Granulocyte

Monocyte

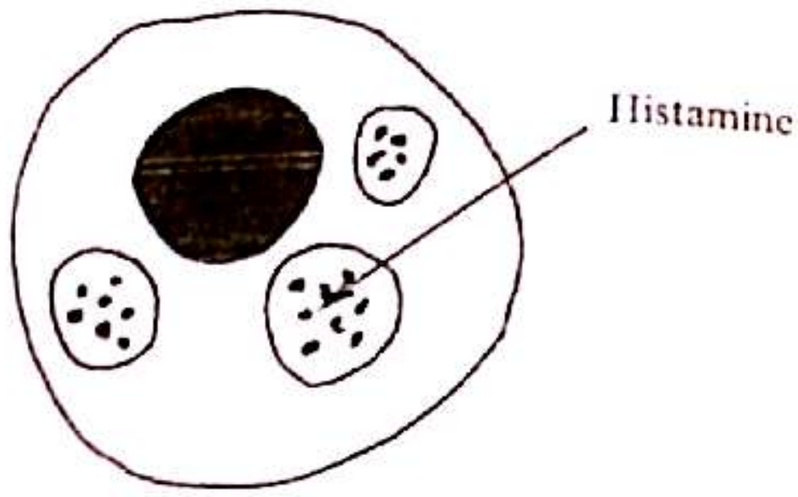
**B) Monocytes: Are characterized by:**

1) Diameter 10 to 18 µm.
2) Horse shoe shaped nucleus.
3) They constitute 6% of leucocyte population.
4) They become macrophage when migrate to the tissue to phagocytose viruses and bacteria.
5) Life span: From months to several years.

**C) Mast cells : Are characterized by:**

1) Round nucleus
2) Contain granules called histamine
3) They have receptors for antibody.

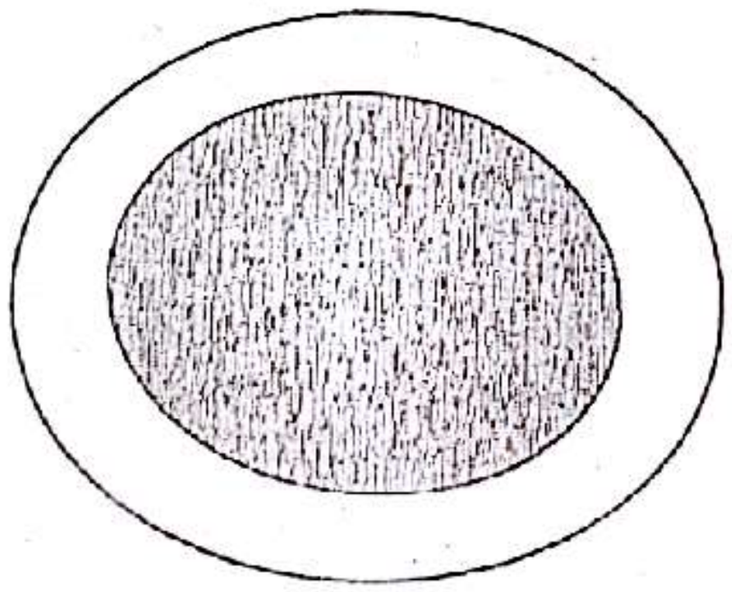
4) They are found in the connective tissue and mucosa.




Mast cell

II) **<u>Lymphoid cells:</u>** The leucocytes that derive from the lymphoid stem cell are of two types : B and T lymphocytes. They are characterized by:

1) Very big and round nucleus.
2) They constitute 25% of leukocyte population
3) Diameter : 7 µm.



Lymphocyte

- Characteristics of B lymphocyte: They are characterized by the presence of membrane receptor called antibody. Upon activation, the B lymphocytes become plasma cells or plasmocytes and can release antibodies into the plasma. (or immunoglobulins IG)
- Characteristics of T lymphocyte: Characterized by the presence of membrane receptor called TCR. T lymphocytes are of two kinds:

1) $T_C = T_{cytotoxic} = T_8 = T_{killer}$ = the receptor of such cell is $CD_8$.
   Role : They kill the infected and the modified self cells.
2) $T_H = T_{helper} = T_4$ : The receptor of such cell is $CD_4$.
   Role : They help the other Lymphocytes by activating them.

## Document 5 : Lymphoid organs

### Classification of lymphoid organs:

A) Lymphoid organs are classified into primary and secondary.

**Primary lymphoid organs:** Are classified into bone marrow and thymus.

1) Bone marrow :

| | | |
|---|---|---|
| Role | | Production of B and T lymphocytes |
| | | Maturation of B – Lymphocyte |

2) Thymus : Role : maturation of T lymphocyte

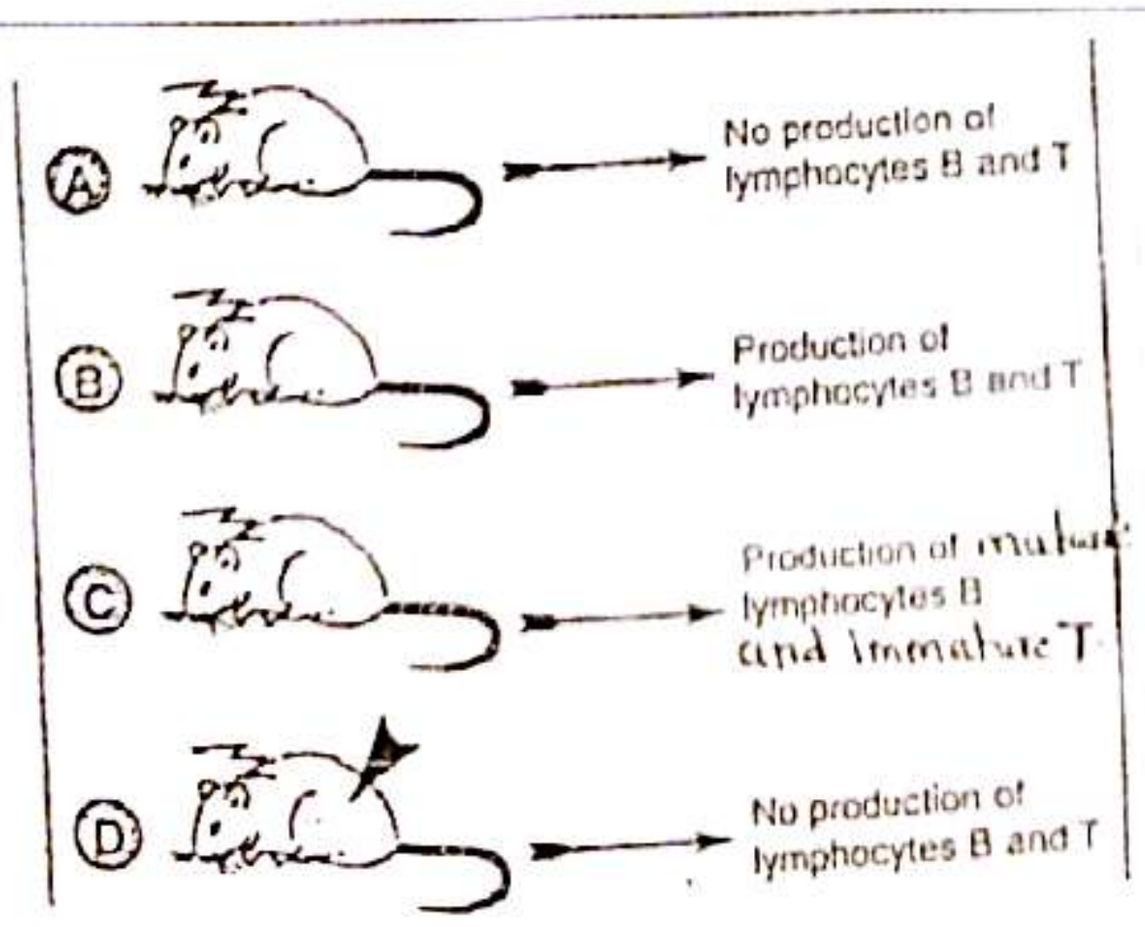
### Notions about the origin of lymphocytes B and T.

Document 1 shows the various experimental given (conditions ) applied to mice in order to determine the **source of lymphocytes.**

| | **Experimental conditions** |
|---|---|
| A | Irradiation. |
| B | 1- irradiation . 2- Grafting of bone marrow. |
| C | 1- Ablation of the thymus. 2- Irradiation. 3- Grafting of bone marrow |
| D | 1- Ablation of the thymus . 2- Irradiation. 3- Grafting of the thymus |

**Remark:**

Irradiation allows to kill bone marrow's cells which multiply quickly.



**Lymphocyte maturation**

Maturation is the mechanism by which the lymphocytes become immuno-competent (functional) and are able to fight non self-antigens. All the lymphocytes, before any encounter with antigens, have receptors against self and non self components. So, screening is necessary.

**Screening:**

- **In the bone marrow:** B Lymphocytes that have receptors against self component must be eliminated while the others are preserved.
- **In the thymus :** All the T lymphocytes that have receptors against self HLA and non self peptide within it must be preserved while the others that recognize self HLA and self peptide within it must be eliminated.

**B) Secondary lymphoid organs** : All the lymphocytes that were maturated in the bone marrow and the thymus migrate to the secondary lymphoid organs: spleen and lymph nodes to be stored there.

**Lymph nodes:** Lymph nodes are distributed around the lymphatic vessels that contain lymph which is a colorless liquid collected from between the cells.

**Role :** Lymph nodes fight the non-self components coming from infected tissues to the lymph.

**Spleen :** Is an organ connected to the blood vessels.

**Role:** Fight the non-self components circulated in the blood.

## Document 6 : Antigen recognition by B-Lymphocytes

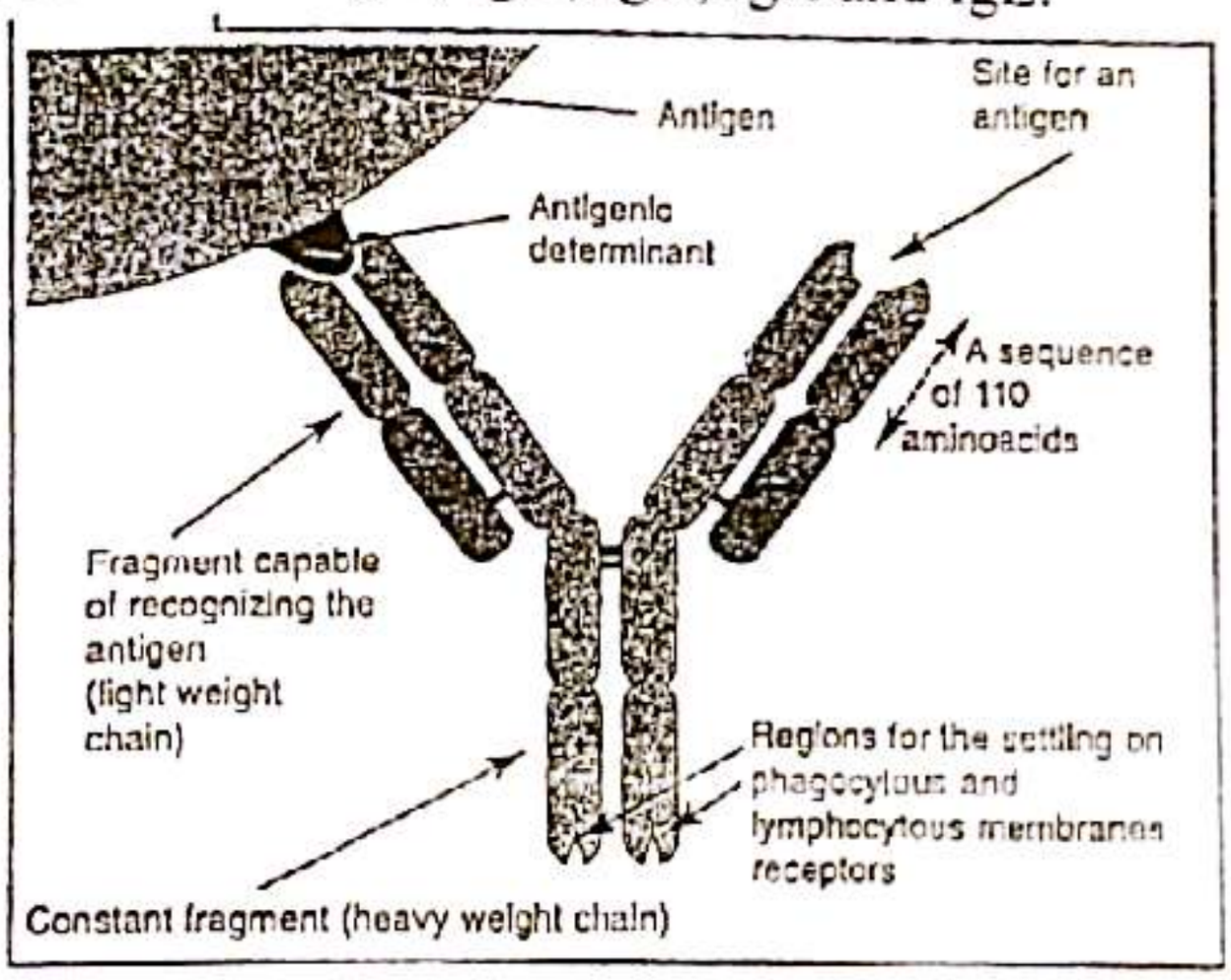
Antibodies can't recognize the antigens within HLA, they can recognize only the free antigens like viruses and bacteria.

### Structure of an antibody and its classes

The surface of B-Lymphocytes have specific receptors called immunoglobulins or antibodies.

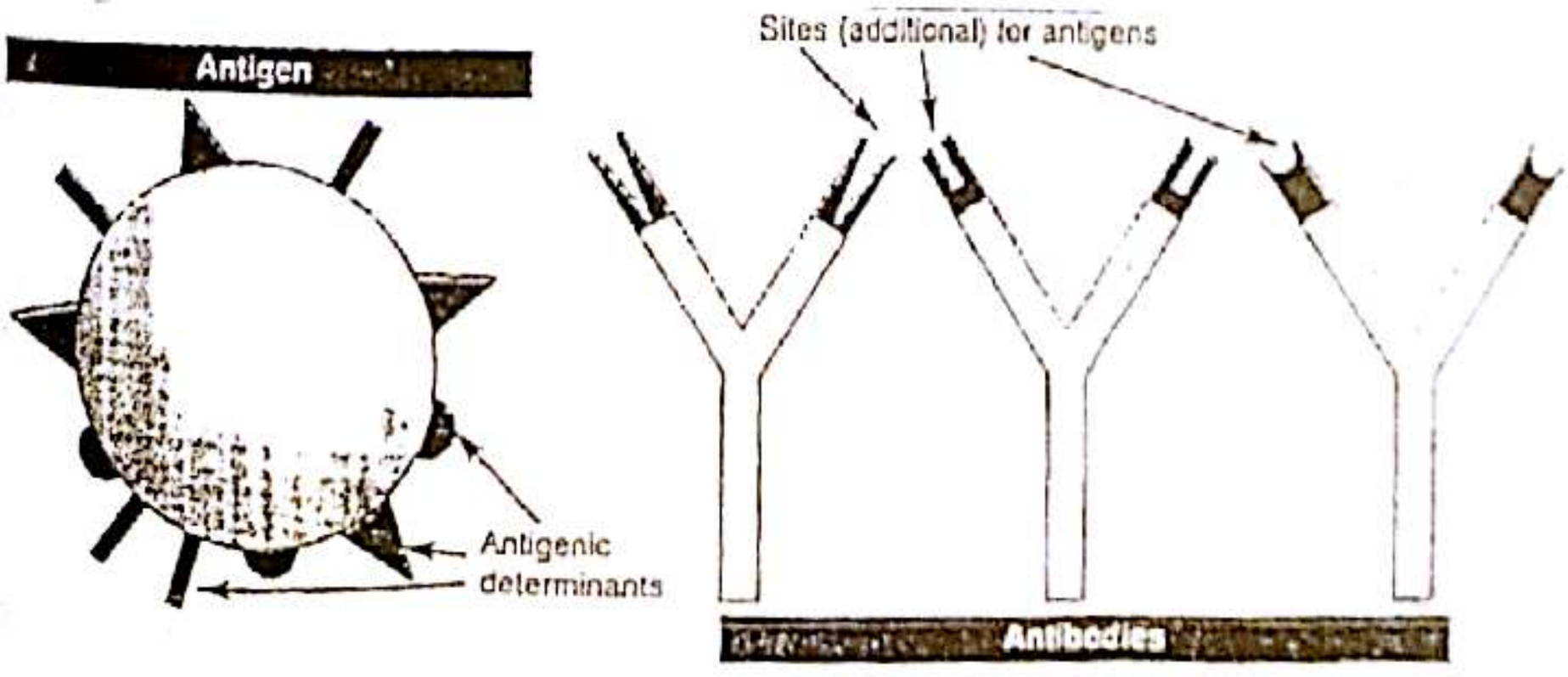
An antibody has the following characteristics:

1) It consists of four polypeptide chains: 2 heavy and 2 light.
2) It has an upper variable region and a constant (more or less) lower one.
3) The variable region differ from one antibody to recognize a specific antigen and binds to it.
4) It has two antigen binding sites.
5) The constant region has slight variations that determine the different classes of antibodies. IgM, IgD, IgG, IgA and IgE.




### Specificity :

The antibody can't recognize the whole body of the antigen but it recognizes only the epitope of it (antogenic determinant) : The antigen may have several epitopes, so it needs many antibodies to recognize it.

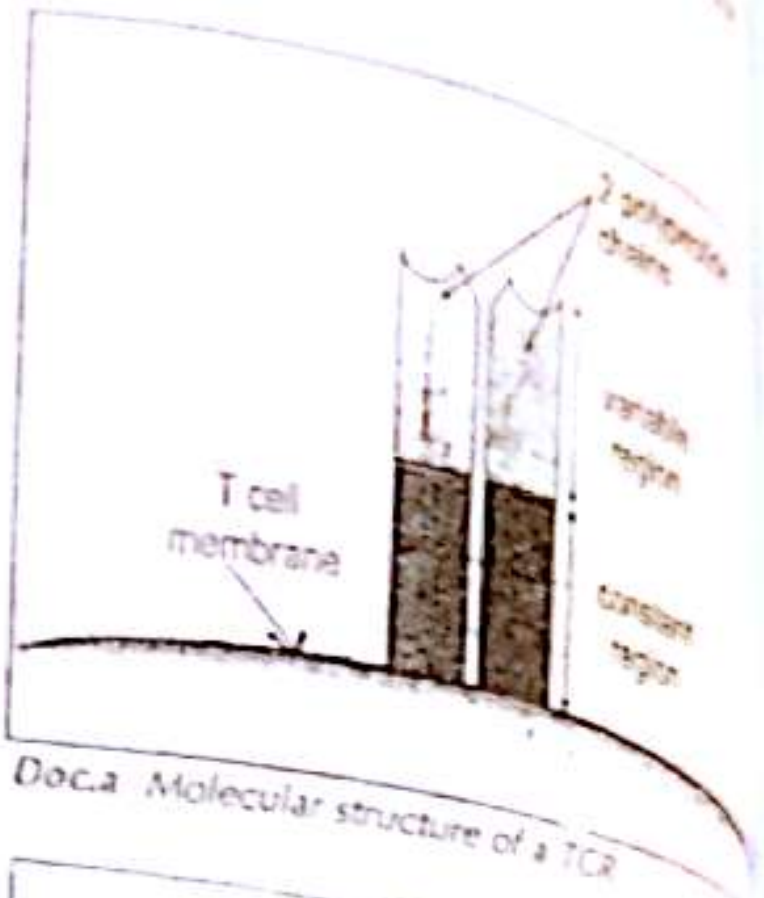


## Document 7 : Antigen recognition by T lymphocytes

T lymphocytes can't recognize the free antigens, they can recognize only the antigens present within HLA markers.

### Molecular structure of a TCR.

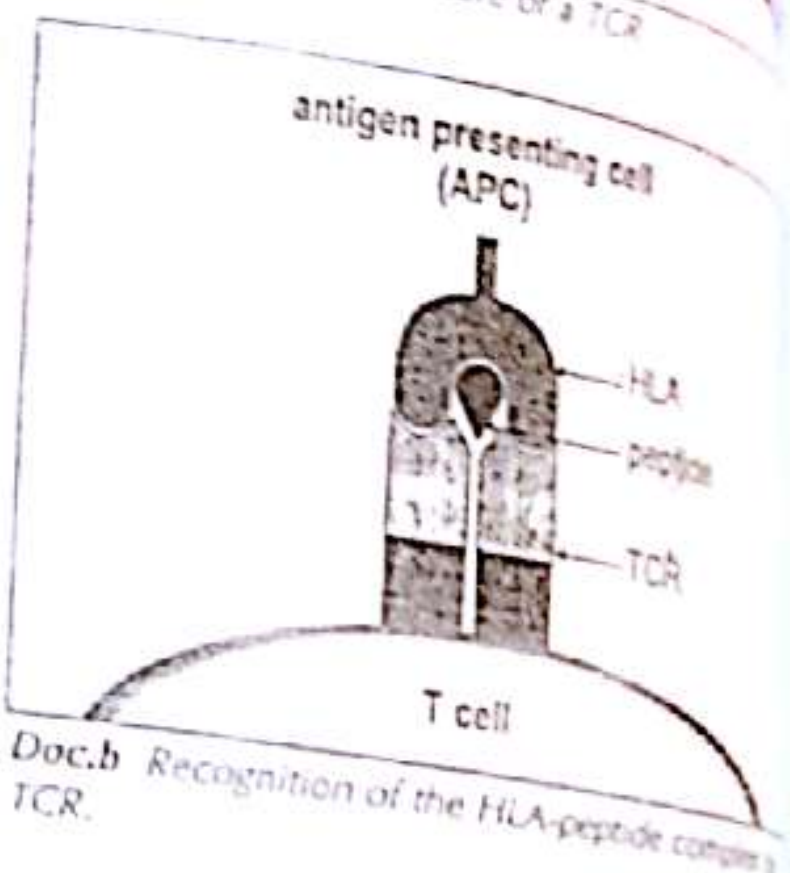
TCR consists of two polypeptide chains, the upper region is variable and the lower one is constant. The two chains together form a single antigen binding site.




Doc.a Molecular structure of a TCR

### Double recognition by TCR

Unlike an antibody, a TRC can't recognize a soluble or a free antigens, it can recognize only the antigen or the peptide present within HLA in a way that the TCR binds the HLA and the peptide present within it . This is known as double recognition.




Doc.b Recognition of the HLA-peptide complex by TCR.

### Peptide presentation to T Lymphocyte

- Any nucleated self cell has on its surface HLAI markers and self peptide within it, but there is no mature $T_c$ cells that can recognize and attack these cells.
- When a virus infects a self cell or in the case of modified self cells, they start (self cells), their secretion of viral or non self peptide instead of self peptide and present within HLAI on the surface. Such cells are recognized through double recognition by $T_c$ cells to destroy them.
- When a macrophage digests a bacterium, the remaining peptide of the digested bacterium are carried to the surface of the macrophage within HLAII to be recognized by $T_H$ cells through double recognition.

# Chapter 9 : The immune response

## Document 1 : Non – specific immune response

When a pathogen crosses a natural barrier and replicates in the tissues of the host, it trigger the host defense mechanism within only few hours. The first phase of defense after the natural barrier is called non specific immune response.

1) **Natural barrier:**

The natural barriers try to prevent the penetration of the pathogens into the body. These barriers are skin, acidity of the stomach, sweat, vaginal secretion, nasal mucus ..... etc.

2) **Manifestations of a non specific immune response**

- **Symptoms of inflammation :** reddens, swelling, hot and pain.
- **What happens in the inflamed wound?**

When microbes enter a tissue, the infected cells, the macrophage and other leukocytes release soluble molecules called cytokine which has a local function.

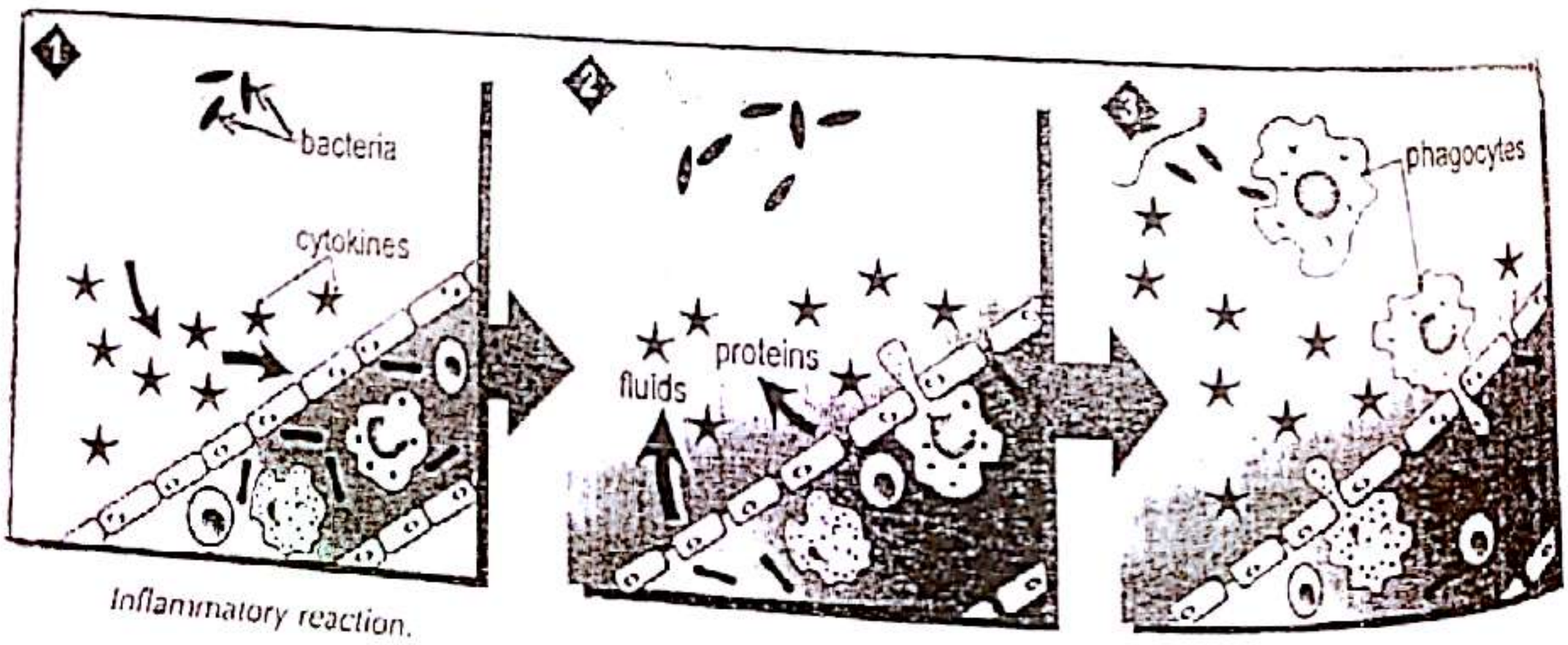
What is this function?

Cytokine :

1- It increases the diameter of the blood vessel to increase the flowing of blood into the infected area.

2- It increases the leakage of plasma from the blood vessels to the infected area.

3- It increases the squeezing of leukocytes from the blood vessels to the inflected area by diapdesis.




*Inflammatory reaction.*

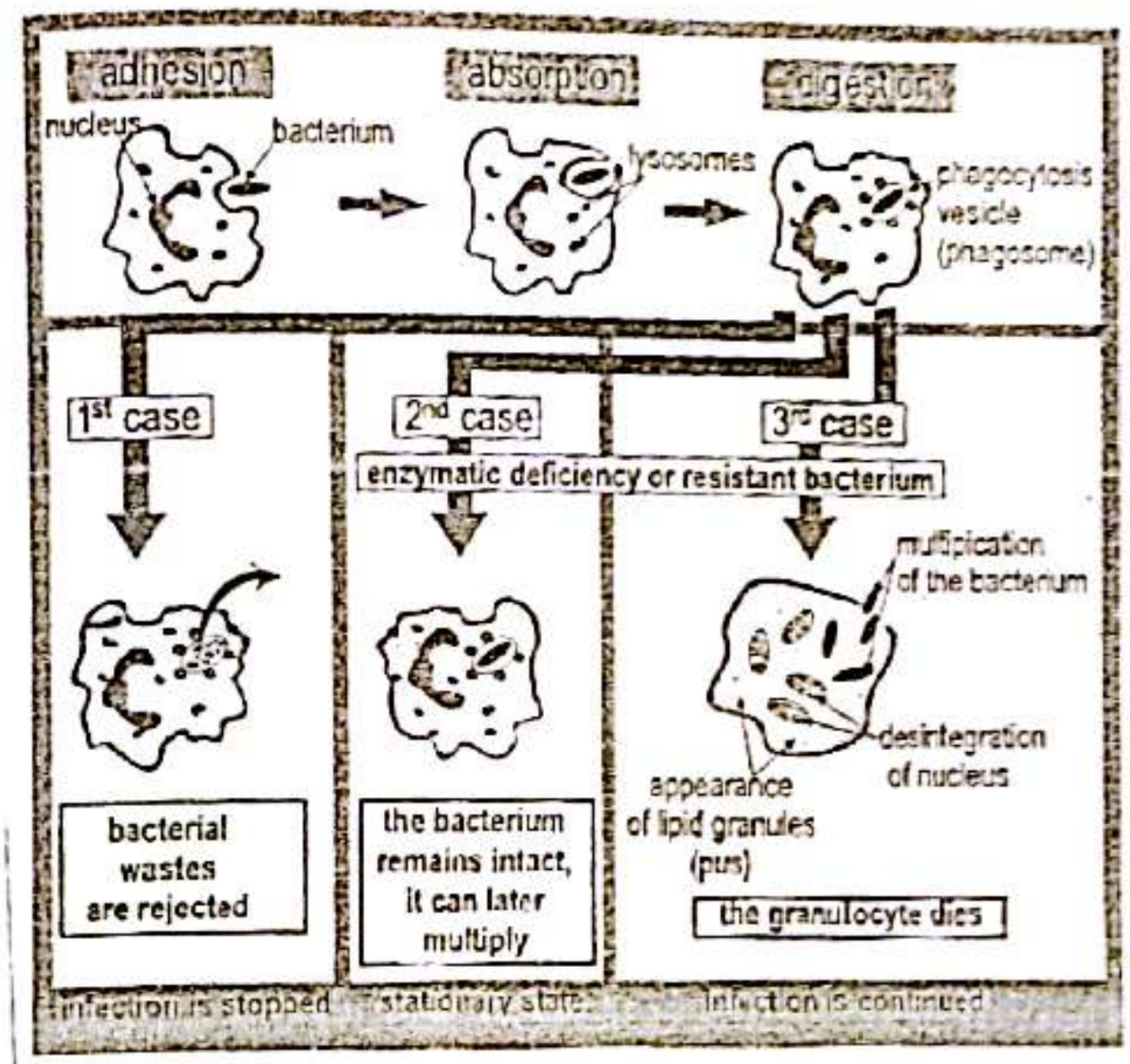
### 3) Phagocytosis:

Phagocytosis is an essential process which is able eliminate the intruders during non-specific immune response. It includes three steps:

1- **Adhesion** : The macrophage gets in contact with the intruder.

2- **Absorption** : The macrophage engulfs the intruder.

3- **Digestion** : The macrophage digests the intruder by lysosome enzymes.




*The steps of phagocytosis: adhesion, absorption, digestion.*

Note: The non-specific immune response is characterized by that there is no memory against the attacked cells since in such response there is no discrimination among the target cells and also there is no elapsed time or latency period to start the process of attacking.

## Document 2 : The specific immune response

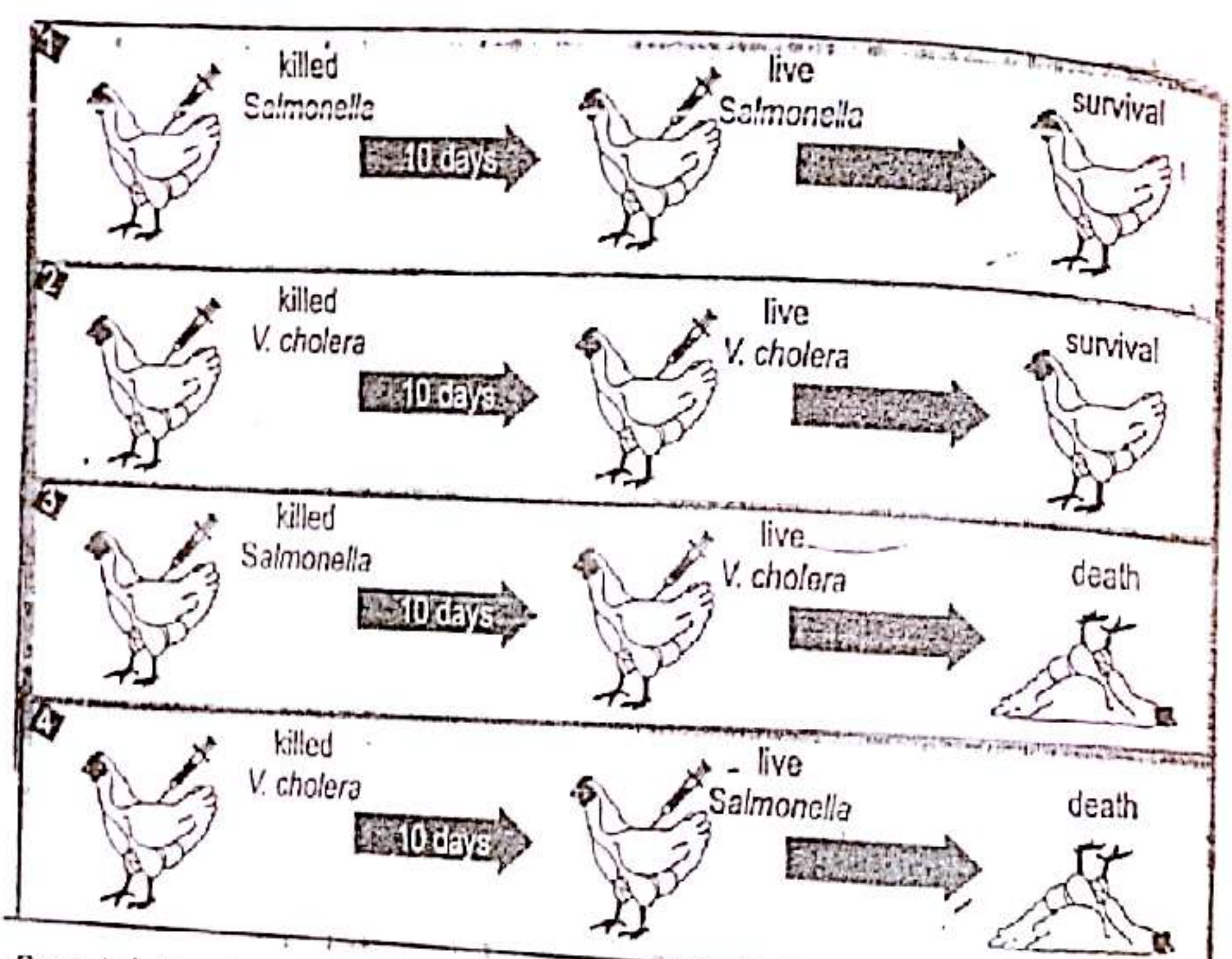
When the non-specific immune response fails to eliminate the intruder, a specific immune response becomes necessary.

What are the different types of the specific immune response and what are their characteristics?

**1- Experimental studies:** Induction of specific immune response.

**Document a** shows that any particular specific immune response is protective only against the agent that induce it.

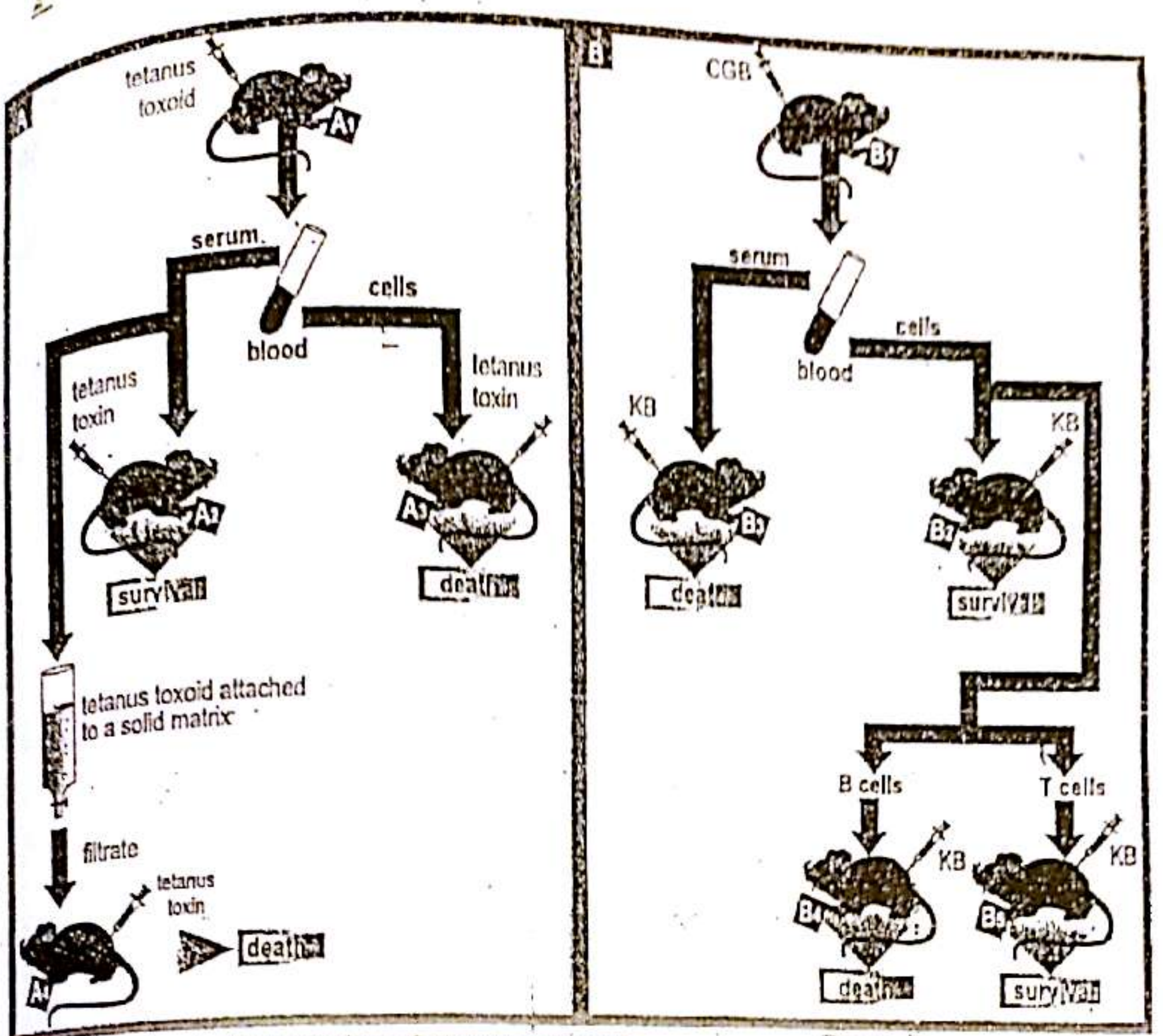
How do the experimental results of document a shows that the immune response, developed 10 days after the injection of salmonella or vibrio cholera is specific?




*Doc.a Induction of specific immune responses.*

The immune response observed 10 days after bacteria injection is specific since injection of killed salmonella leads to subsequent resistance against live salmonella but not against vibrio cholera. Similarly, injection of killed vibrio cholera leads to subsequent resistence against live vibrio cholera but not against salmonella.

## 2- Types of the specific immune response .




Humoral and cell-mediated specific immune responses. Doc b

There are two types of specific immune response:

1) **Humoral immune response** : The effectors of such type are chemicals (antibodies) present in the serum.

2) **Cell mediated specific immune response** : In this type the effectors are not chemical substances circulated in the plasma but it is a cellular response : T lymphocytes.

**Note:**

**What is meant by toxoid?**

Laboratory manipulations eliminate the harmful effects of the toxin without changing its antigenic determinants. The neutralized toxin is called a toxoid.

**What is meant by C.G.B?**

Calmette and Guerin bacillus (CGB) is a harmless bacterium that shares common antigenic determinants with KB (koch bacillus).

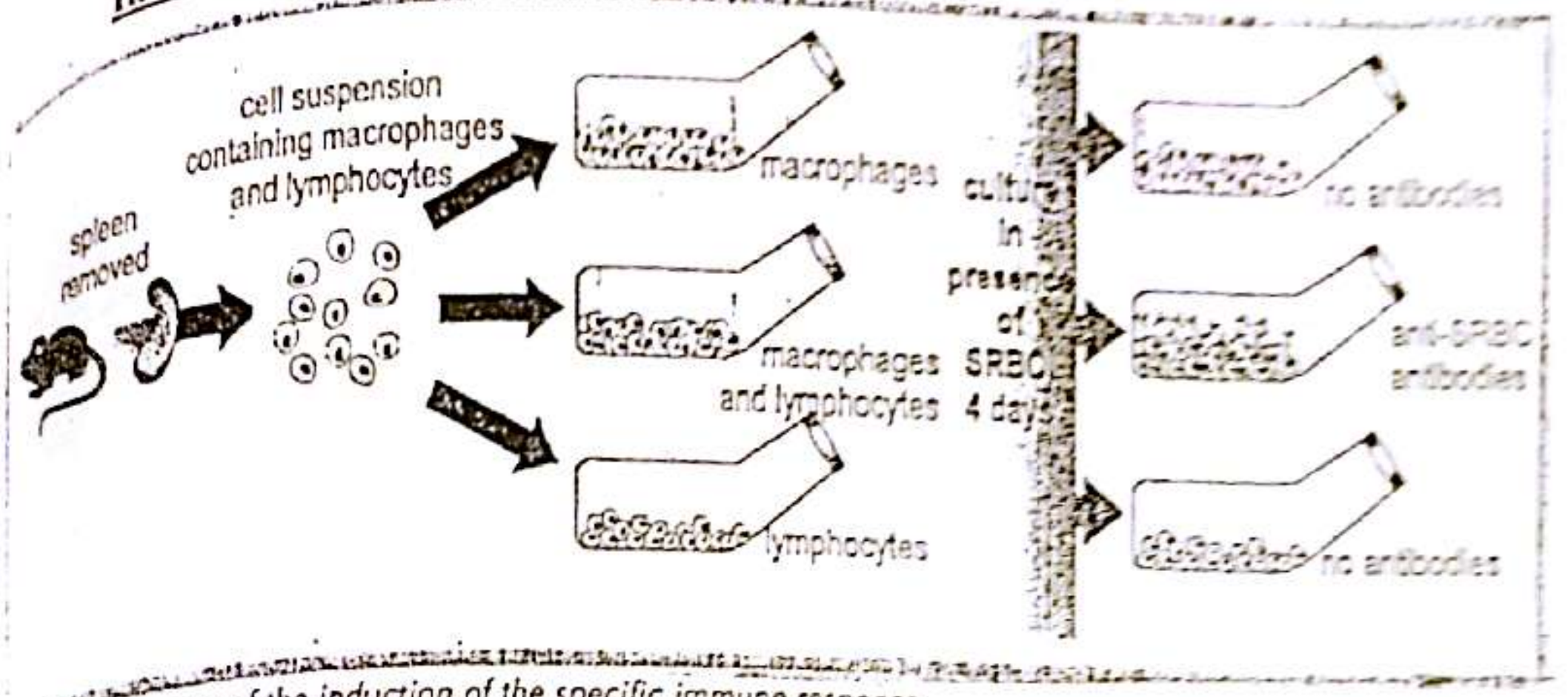
**Document b** shows that the types of immune response against tetanus is humoral since the serum can ensure immunization to a non immunized animal. This means that the serum has chemicals that can transmit the immunization while the type of immune response against KB is cell mediated since the serum can't transmit the immunization but the T cells can do this..

## Document 3 : Induction of the specific immune response

### 1- Mosier experiment

This experiment shows the importance of non specific immune response in the induction of specific immune response.

**Interpret document a. what do you conclude?**




*Doc a Demonstration of the induction of the specific immune response.*

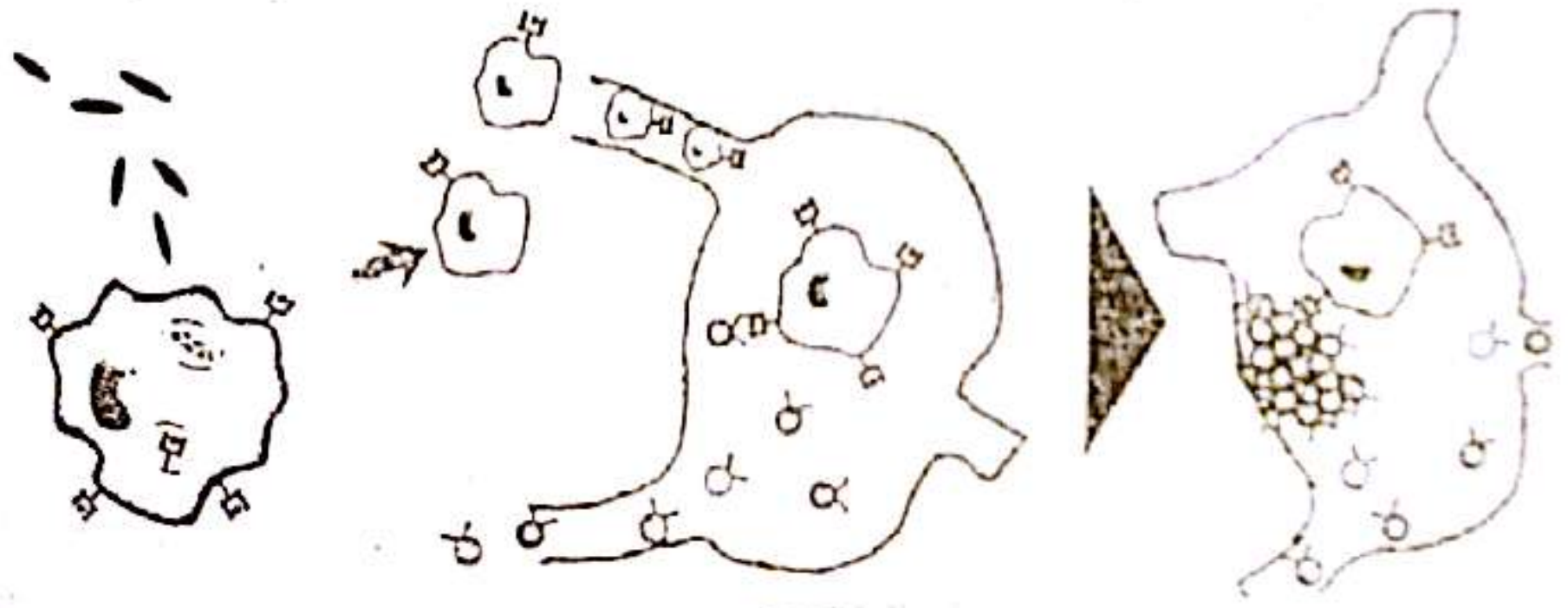
The experiment shows that there is no secretion of antibodies in a medium containing macrophages alone or lymphocytes alone, while there is a secretion of anti SRBC antibodies in the medium containing macrophage and lymphocyte at the same time. This shows that neither macrophage alone nor lymphocyte alone can ensure the secretion antibodies and that both are essential in this process.

∴ A cellular cooperation is needed to Produce antibodies .

### 2- Macrophagés role in the induction phase

When a macrophage digests an antigen, the remaining peptides are carried to the surface of the macrophage within HLA II then the macrophage migrates to the closest lymph node where it becomes APC (Antigen presenting cell)

In the lymph node $T_H$ cells recognize this APC by double recognition and start their activation.

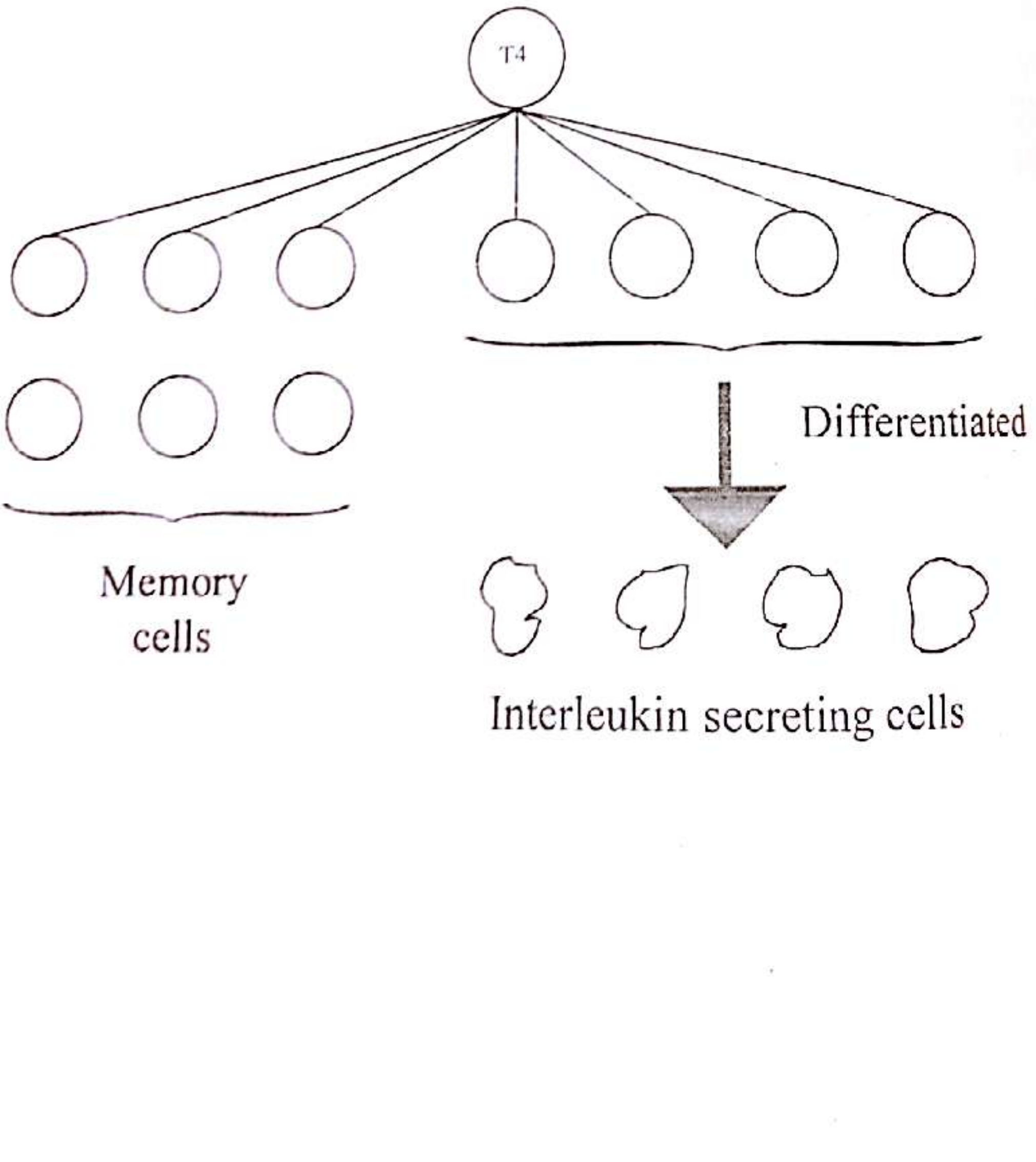


## 3- Fate of activated $T_H$ lymphocytes

After the recognition of $T_H$ to APC, it multiplies abundantly and gives rise to a cellular clone of a large number of daughter cells identical to the mother cell. (Clonal selection). The multiplied $T_H$ cells are classified into two groups:

**1st group :** Kept as memory cells and can live for many years.

**2nd group :** This group is differentiated to become interleukin secreting cells that can live for few days only and are able to secrete cytokines called interleukins.



## Document 4 : Role of $T_H$ cells in the specific immune response

What is the role of interleukins in immune cells activation?

### Characteristics of a nude mouse

A nude mouse is characterized by the absence of thymus which in turn leads to the absence of maturated $T_H$ lymphocytes and as a result the specific immune response will remain in active.

### Experiments to show the importance of $T_H$

**1st experiment :** $T_H$ lymphocytes are cultured in the presence of killed CGB and macrophages. A few days later the culture medium contains interleukin $IL_2$ secreted by activated $T_H$ cells. This interleukin is added to a mixture of B and $T_C$ lymphocytes but only $T_C$ lymphocytes start their multiplication.

Thus $IL_2$ activates only $T_C$ lymphocyte.

**2nd experiment :** $T_H$ lymphocytes are cultured in the presence of tetanus toxoid and macrophages. A few days later the culture medium contains $IL_4$ secreted by activated $T_H$ cells. This interleukin is added to a mixture of B amd $T_C$ lymphocytes but only B lymphocytes start their multiplication.

Thus $IL_4$ activates only B lymphocytes.

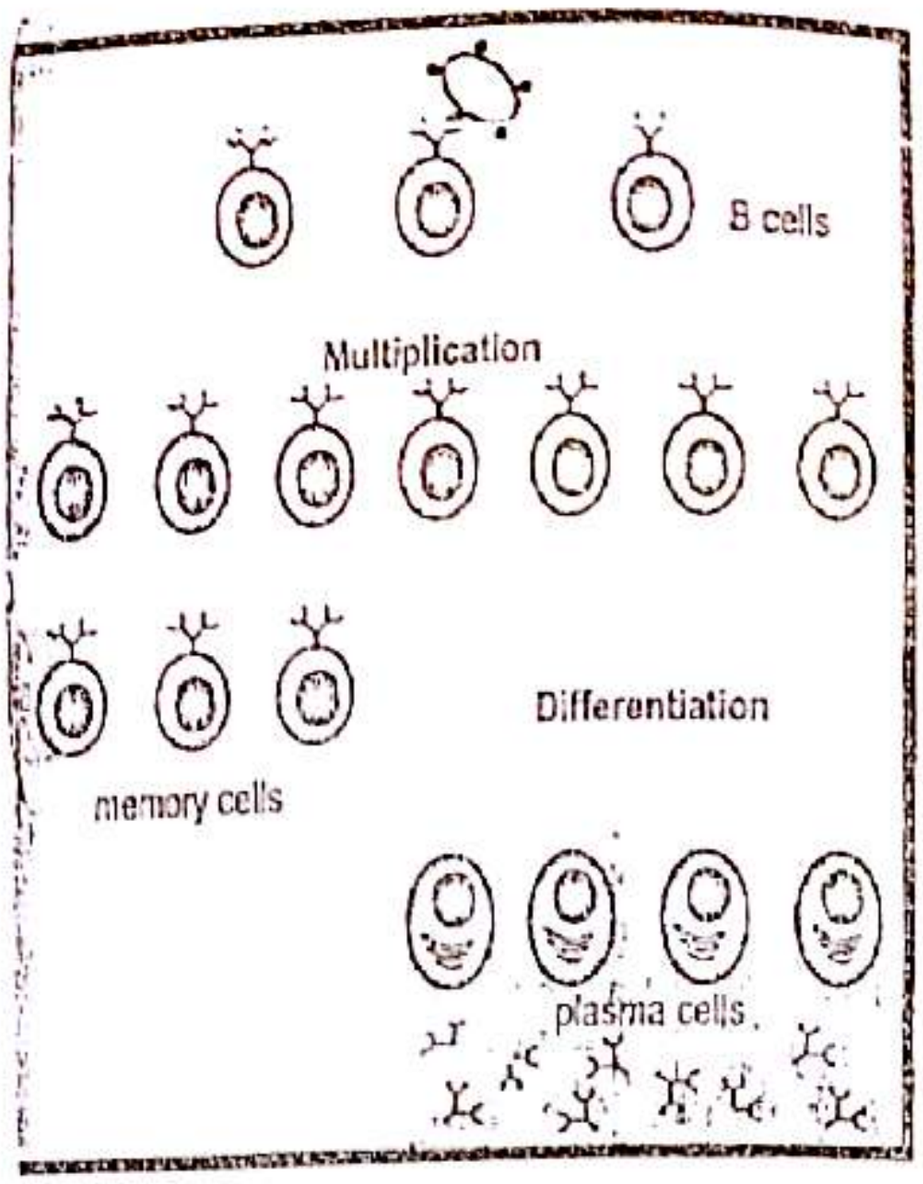
### Fate of activated B lymphocytes

Among billions of B cells expressing different antibodies, only those that are specific for the antigen undergo clonal selection.

$IL_4$ will activate B lymphocytes that will multiply. Then the multiplied cells are classified into two groups :

**1st group :** Kept as memory cells and can live for several years.

**2nd group :** Differentiated into plasmocytes to secrete antibodies. These cells can live for few days only.



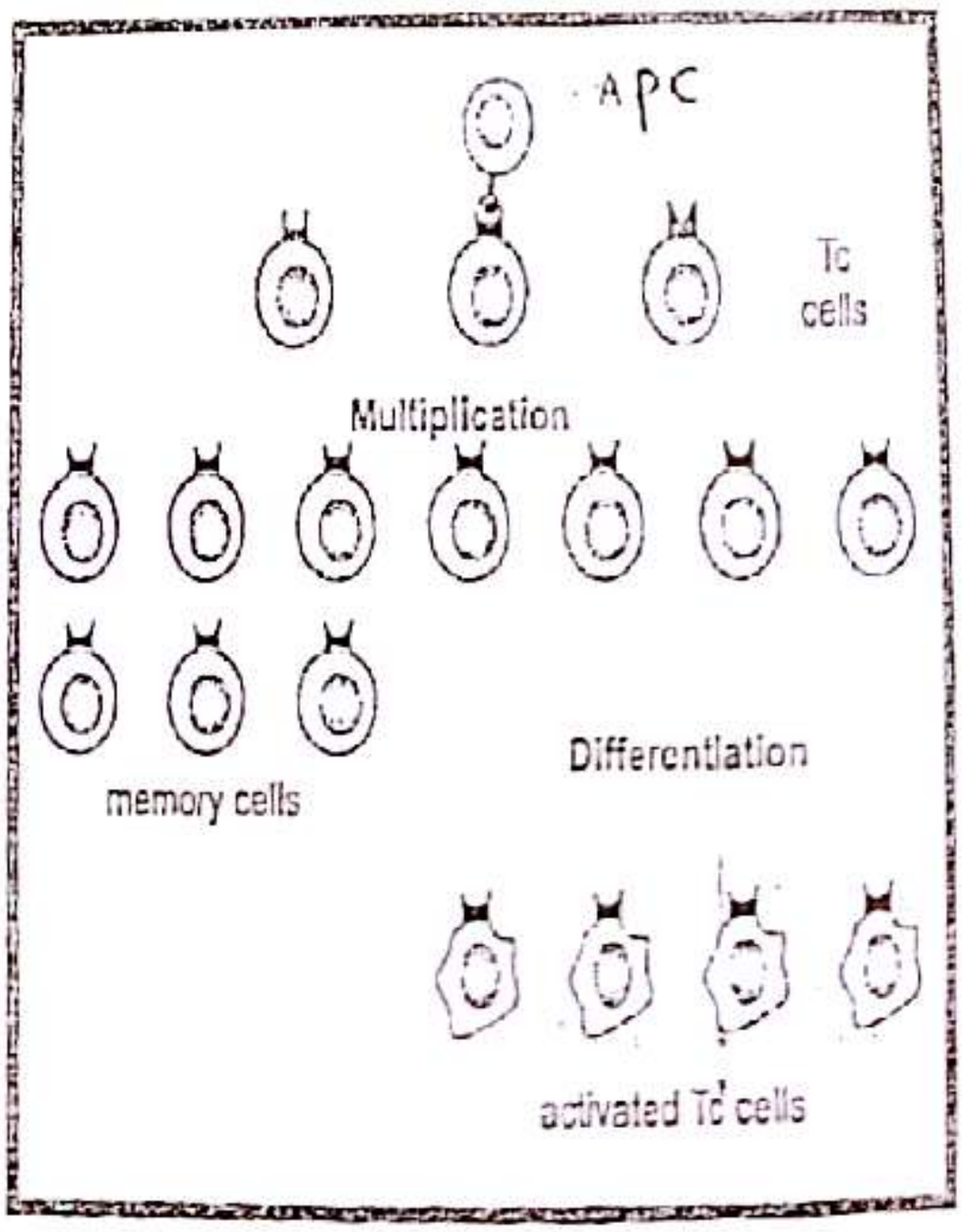

## Fate of activated $T_C$ lymphocytes

Among billions of $T_C$ cells expressing different TCR, only those that are specific for the antigen undergo clonal selection and are activated.

The selected $T_C$ cell proliferates under the action of $IL_2$ . The multiplied cells are classified into two groups:

**1st group :** Kept as memory cells and can live for several years.

**2nd group :** Differentiated into active $T_C$ that can live for few days only.



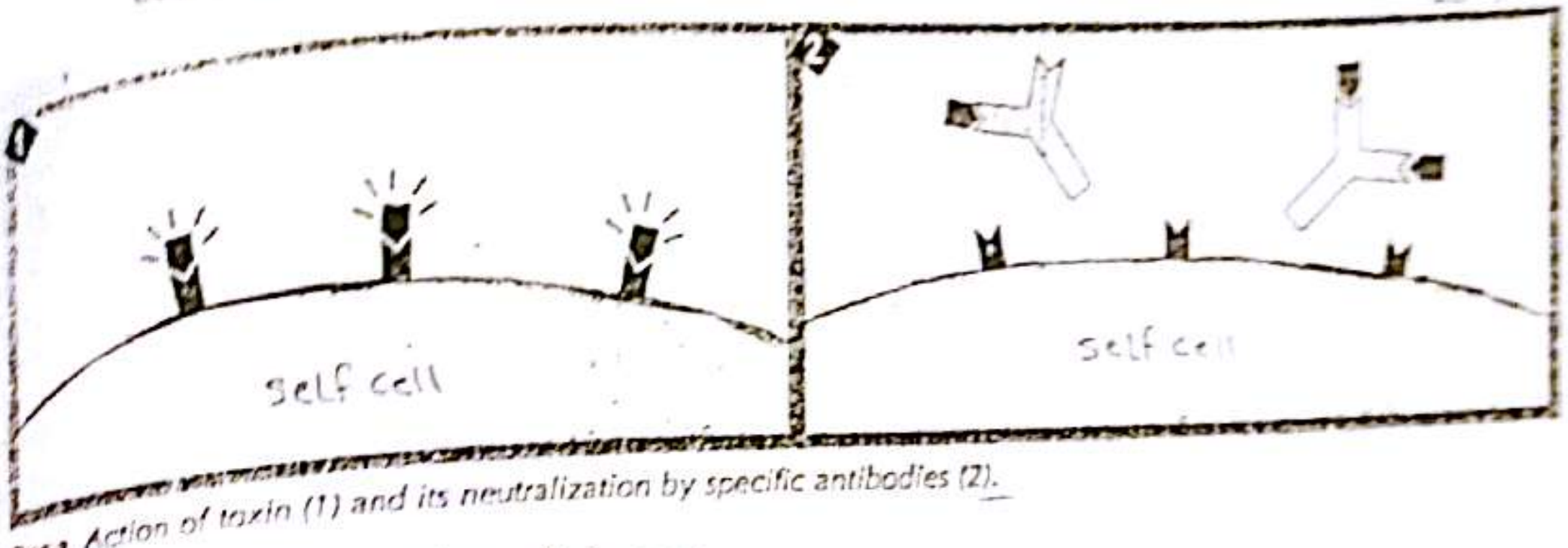
## Document 5 : Specific humoral immune response

*Antibodies which are secreted by the plasma cells go to the lymph and the blood where they circulate to eliminate the antigens. How?*

### 1) Neutralization of toxins and virus

#### a) Neutralization of toxin

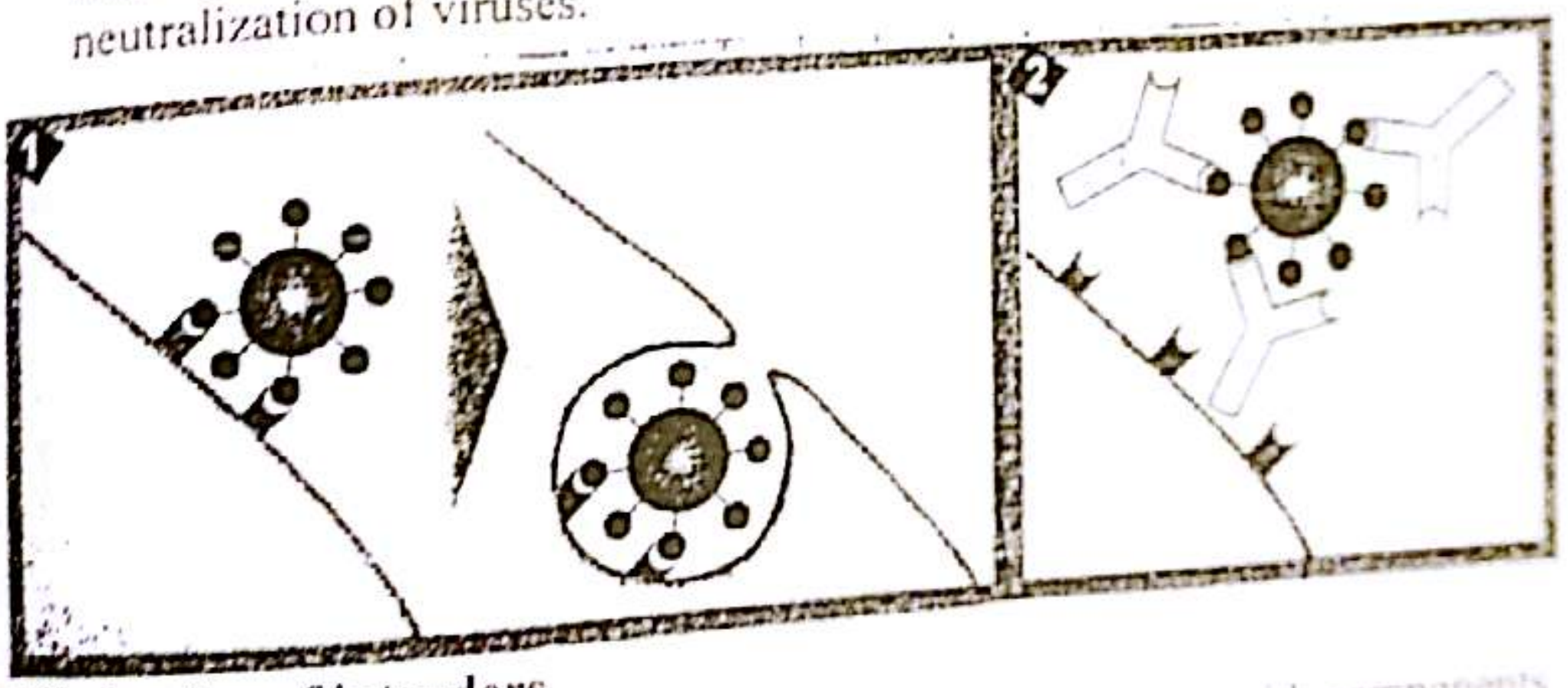
The toxins like venome of snakes have an aim which is the resting on the receptor of our self cells. The circulated antibodies can bind to these toxins through antigen binding sites preventing them from resting on the cells. This is known as neutralization of toxins.




*Doc.5 Action of toxin (1) and its neutralization by specific antibodies (2).*

#### b) Neutralization of viruses

Viruses and bacteria enter into the body trying to penetrate the target cells. The circulated antibodies can bind to these viruses through antigen binding site preventing them from invading the cells. This is known as neutralization of viruses.




### 2) Elimination of intruders

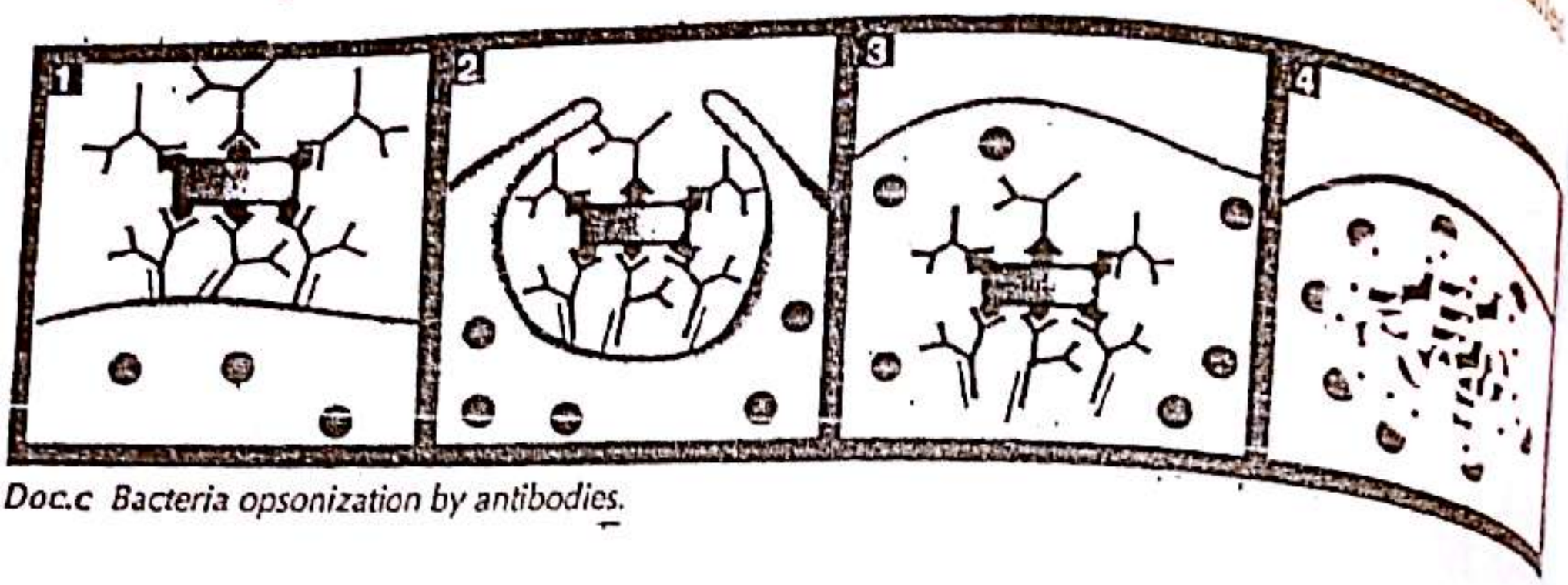
The antibody can't kill the virus directly, it must cooperate with components like macrophage and plasma proteins.

a) Cooperation between macrophage and antibodies (opsonization)

The antibody, after binding the antigen, can bind to the receptor of macrophage through its constant region making a bridge between the

macrophage and the antigen. Then the macrophage engulfs, ingest and digest the antibody and the virus carried by it.

Such cooperation between the macrophage and the antibody is called opsonization.



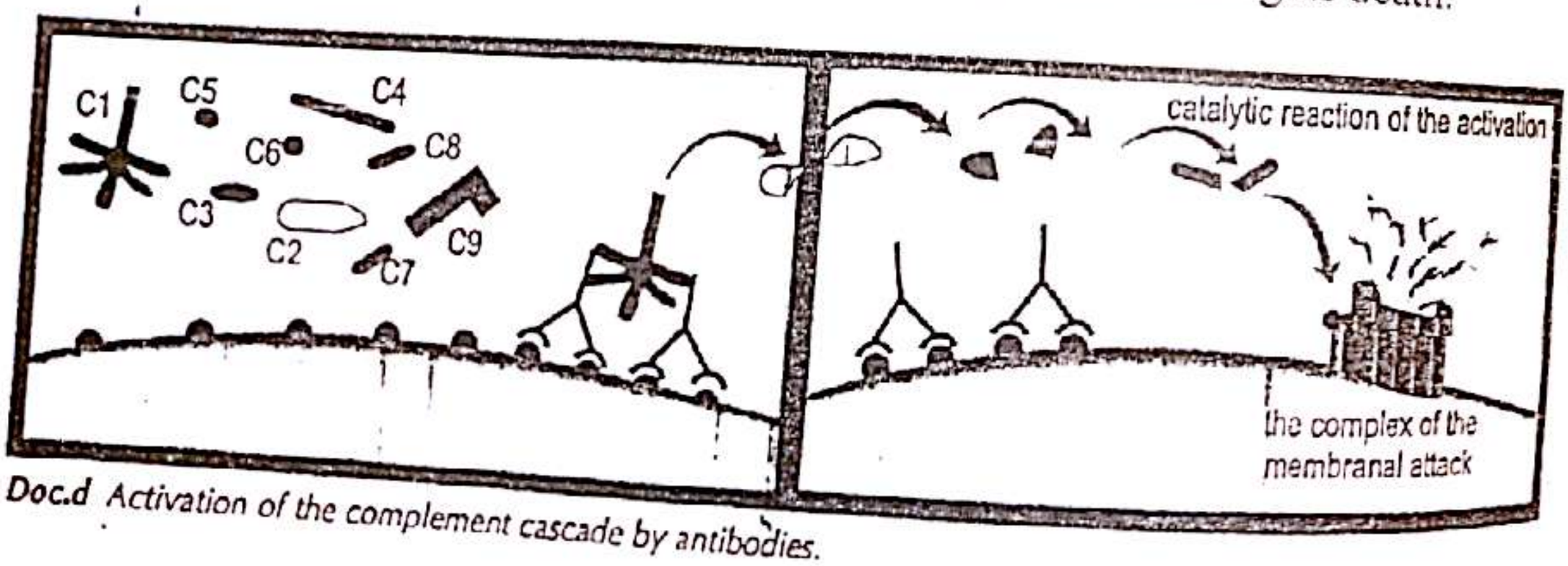

*Doc.c Bacteria opsonization by antibodies.*

b) Cooperation between an antibody and plasma protein (complement cascade).

The complement is a set of plasma proteins, most of which are enzymes that activate each other. The most important ones are $C_1$ to $C_9$.

Once antibodies have bound antigens on the surface of a target cell, their constant region may bind to one of the complement proteins called $C_1$. $C_1$ activates in turn other components of the complement. The chain activation of the complement proteins is called the complement cascade.

The cascade leads to the formation of a membrane attack complex that perforates the antibody – bound target cell causing its death.



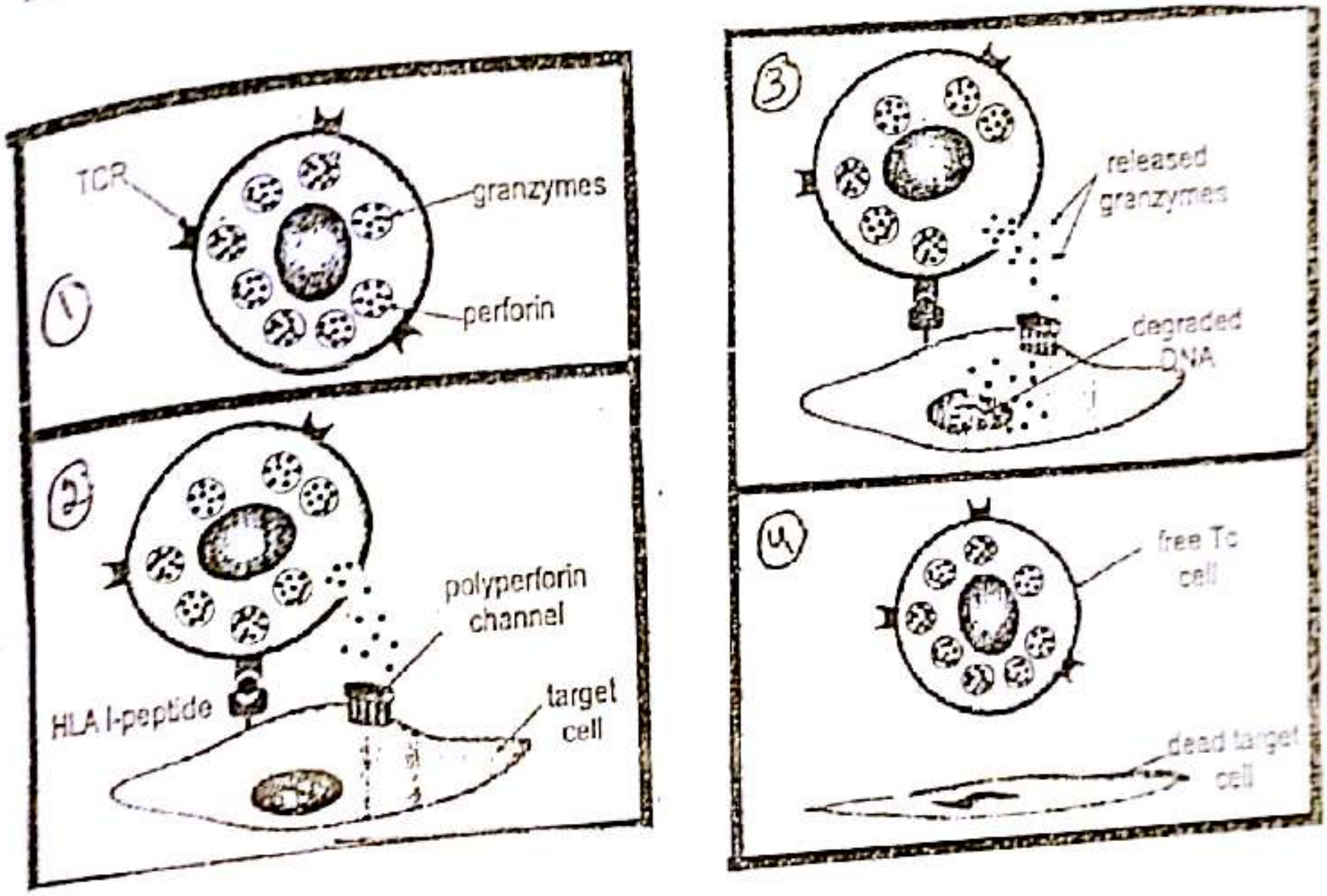

*Doc.d Activation of the complement cascade by antibodies.*

**Note:** $C_5$ after its activation, is a chemotactic molecule that attract phagocytes to the inflammation site.

## Document 6 : Specific cell mediated immune response

### 1) Elimination of infected host cells.

$T_c$ lymphocyte has toxic substances that can kill infected cells called perforin and granzymes. When a $T_c$ lymphocyte recognizes an infected cells by double recognition, it starts its releasing of perforin to make a hole in the membrane of infected cell, then granzyme is secreted into the infected cell to trigger a series of enzymatic reaction in order to destroy the DNA leading to the death of the infected cell.



## 2) *Cancer and immunity*

*The immune system can recognize in addition to inflected cells, modified cells like cancer. These cancer cells multiply abundantly more than the proliferation of $T_C$ cells for this reason cancer needs a certain therapy that includes:*

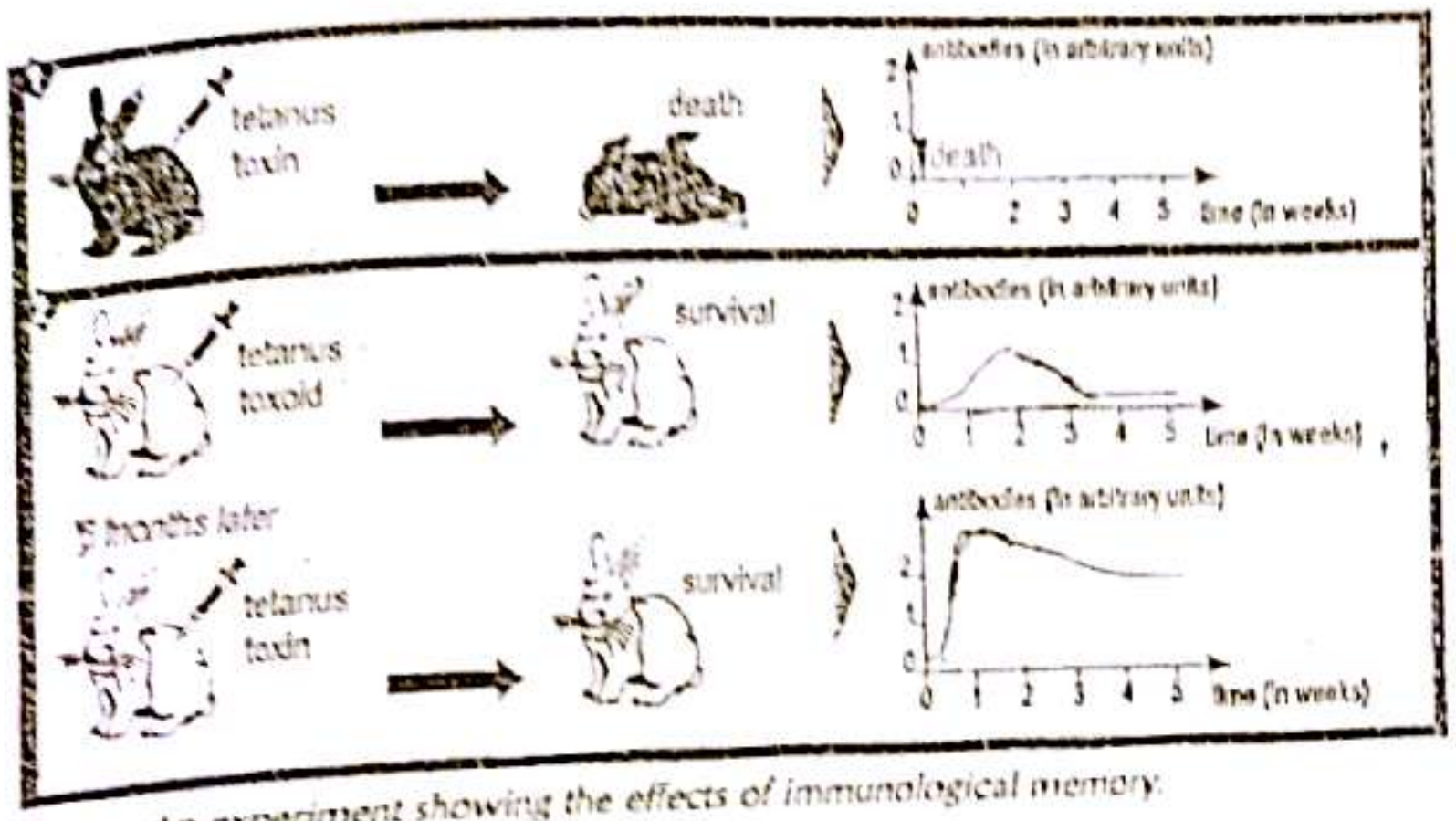
1. *Surgery*
2. *radiotherapy to block the mitotic division of the cells.*
3. *chemotherapy to block the mitotic division of the cancer cells but this will lead to anemia and immuno-deficiency .*

## Document 7 : Immunological memory

One of the most remarkable effects of specific immune response is the presence of memory cells from the first encounter.

1) **Characteristics of primary and secondary responses**

Interpret the results of **document** a and draw out the characteristics of the secondary response.




*Doc.a An experiment showing the effects of immunological memory.*

- **In experiment 1**, the injection of tetanus toxin has provoked the death of the rabbit. This shows that tetanus toxin is pathogenic due to the absence of antibodies.
- **In experiment 2** ,the injection of tetanus toxoid has kept the animal alive, the concentration of anti-tetanus antibodies did not appear until the 1st week. It reached 1.2 arbitrary unit within 2 weeks. This is the primary response. One week later, this concentration becomes nil.

The injection of tetanus toxin 6 months later also kept the animal alive but the level of Abs has reached 2.5 arbitrary unit within 3 days. It has slowly decreased while persisting for several weeks and reached 2 arbitrary units.

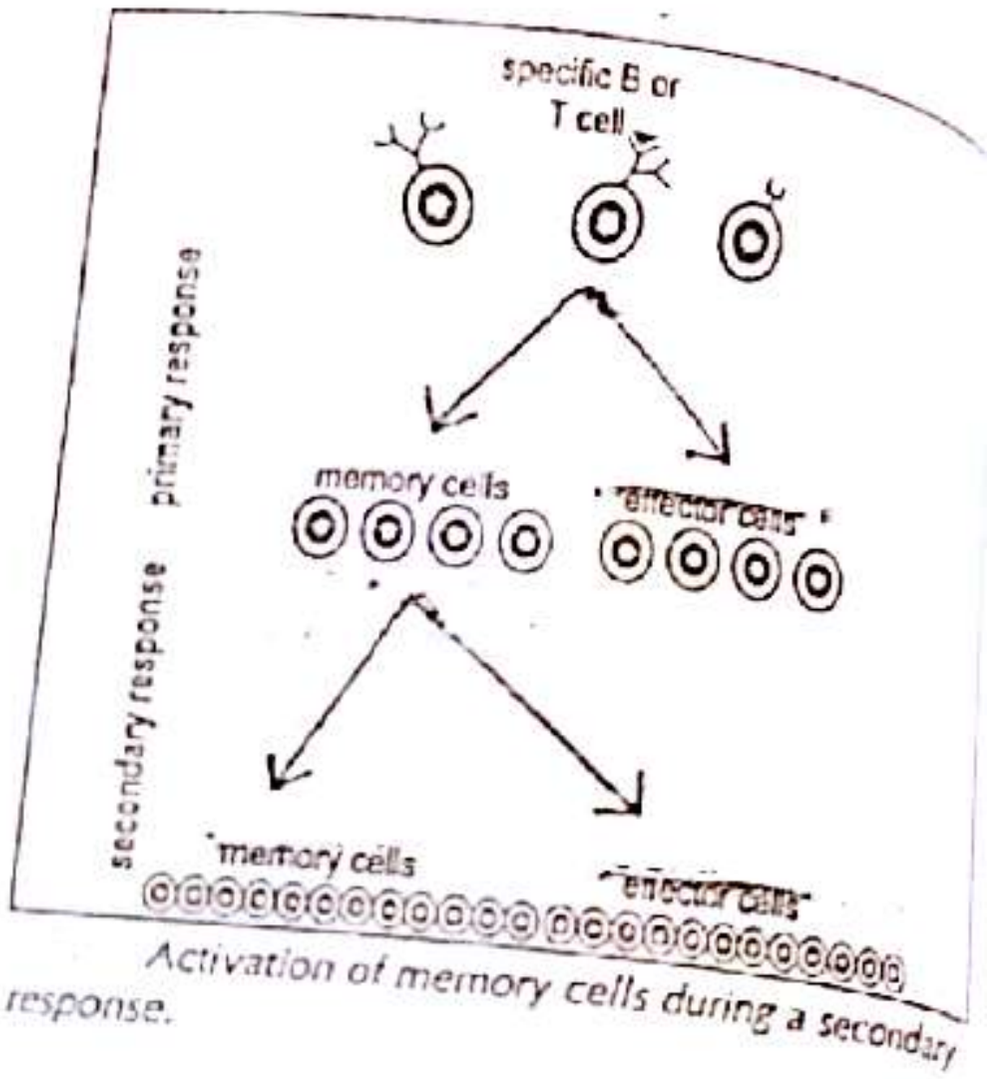
Thus the concentration of Abs is more ample and long lasting in the case of secondary response.

∴ The secondary response is rapid, amplified and long lasting.

## 2) *Bases of immunological memory*

*When an antigen is introduced in the body, it causes a clonal expansion of specific T and B cells. A clone gives rise, on one hand, to short-lived effector cells and on the other hand to long-lived memory cells.*

*The reintroduction of the same antigen in the body activates memory T and B cells. Since memory cells are more differentiated and more numerous than the cells stimulated in the primary response, the secondary response is comparatively faster, more amplified and more persistent.*




*Activation of memory cells during a secondary response.*

## Document 8 : diagnostic applications of antibody properties

### 1) Agglutination reactions

Each antibody has two antigen binding sites. When antibodies react with antigens expressed on cell surfaces, they form molecular bridges between the cells, causing their agglutination. The aggregates can be seen with the naked eye.

The diagnosis for typhoid, for example, relies on the screening for anti-salmonella antibodies in the serum of the patient. A suspension of killed, artificially colored salmonella is mixed with the test serum in a tube. After incubation, the suspension is observed:

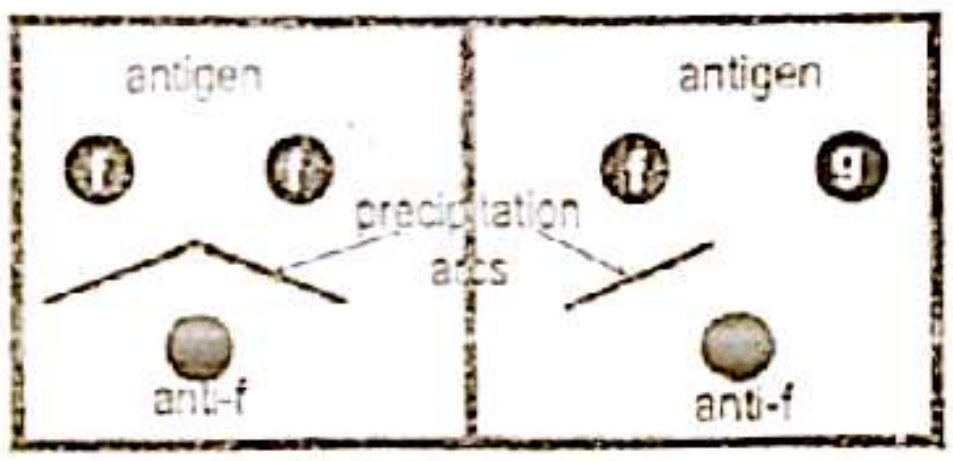
If the bacteria are agglutinated, it means that antibodies are present in the serum. Thus the diagnosis is confirmed.

If the bacteria remain free, it means that the serum does not contain anti-salmonella antibodies.

### 2) Immunodiffusion in gel

In an agar gel, antibodies and antigens are placed in hollowed wells. They can migrate in all directions in this humid medium.

The contact between an antibody and its specific antigen constitutes an immune complex that can be observed in the form of a gray arc (**document a**) specifically colored by poppy red stain.




*Double diffusion in agar gel.*

### 3) ELISA : Enzyme Linked Immuno Sorbant Assay

It is a technique used to test the presence of HIV.

**Steps:**

1- To a well whose bottom is covered with HIV, we add a serum taken from a person, in the serum there are many types of antibodies that can recognize specific antigens.

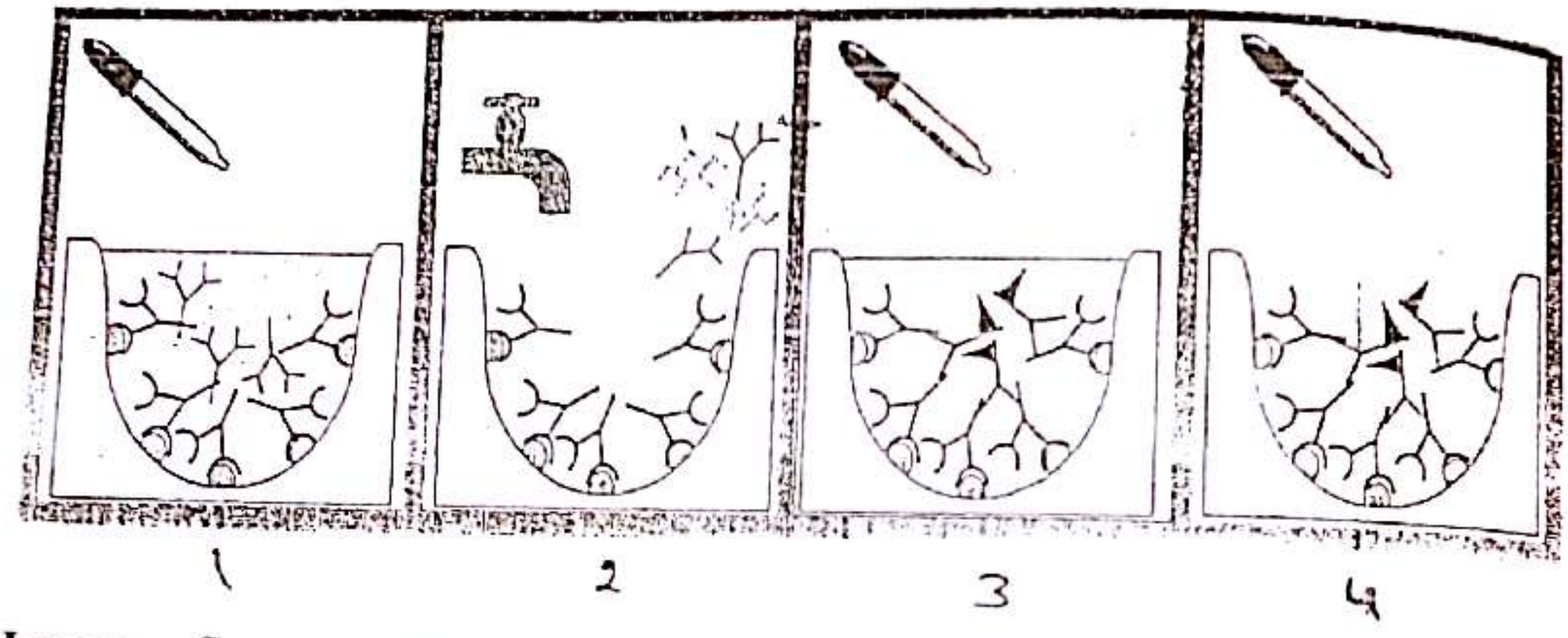
2- Wash well , then add an anti-antibody coupled to an enzyme.

3- Wash well , then add a colorless substrate.

**Result :** There are two possible results:

1- If the substrate becomes colored means that the serum has anti-Hiv antibodies.

2- If the substrate remains colorless means that the serum has no anti Hiv antibodies.




## 4) Immunofluorescence

This technique depends on the usage of a radioactive antibody that emits light when it is subjected to ultraviolet rays.

# Chapter 10 : Disorders of the immune system

## Document 1 :

### 1- Congenital immunodeficiencies

It is due to a recessive gene that leads to:

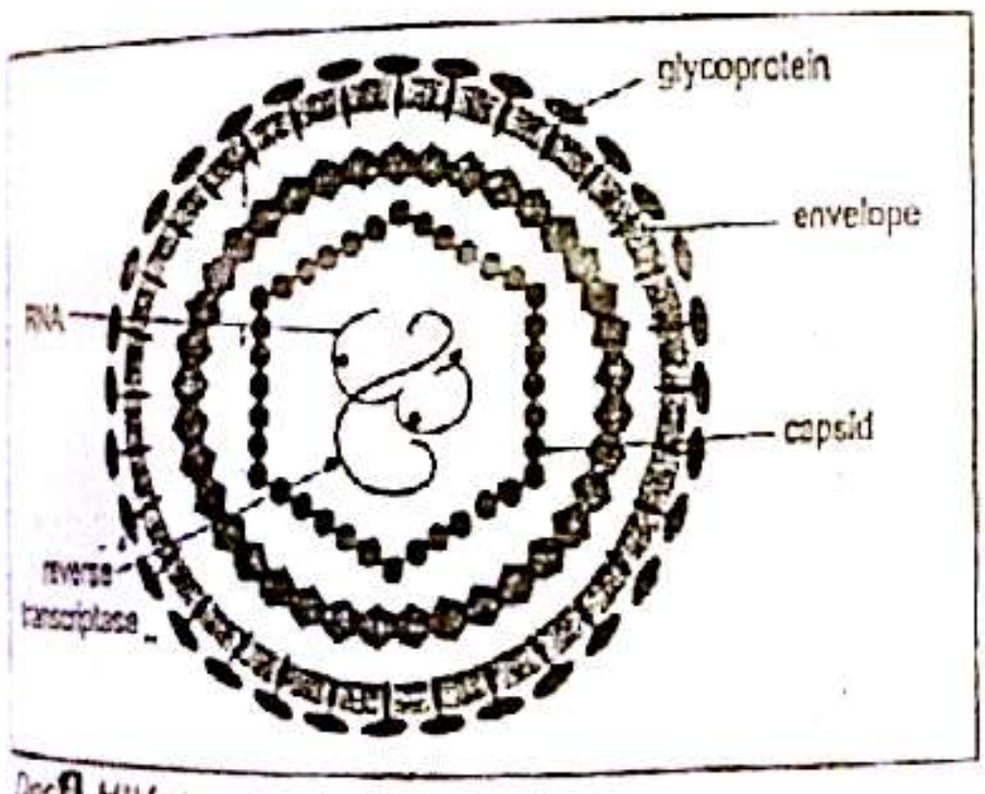
1. An abnormality in the complement, phagocytes and B cell development.
2. A T cell abnormality which is much more serious.

### 2- Acquired immunodeficiencies: Structure and replication of HIV (life cycle)

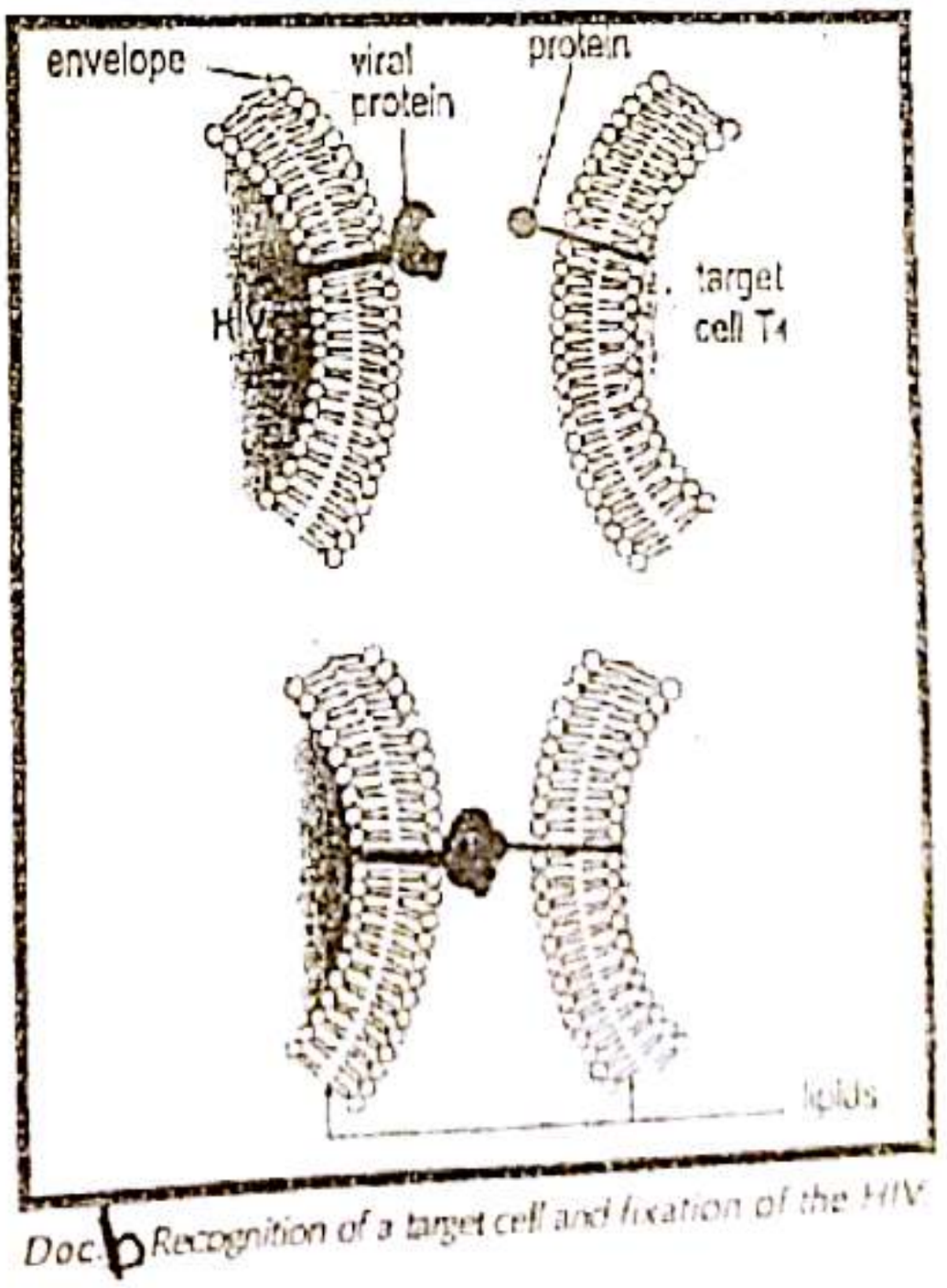
HIV is made of an RNA genome packaged by a protective shell of protein called capsid surrounded by an envelope of glycoprotein spikes. It is a retrovirus that has the ability to transform from RNA to DNA under the action of reverse transcriptase enzyme to be inserted in the infected genome.

HIV may remain dormant in the cell or replicate when the cell is activated it then buds at the cell surface and infects other cells.

This virus attacks the cells carrying the $CD_4$ protein which is found on the macrophage and $T_4$.




Doc a HIV structure




Doc. b Recognition of a target cell and fixation of the HIV

### 3- Progression of HIV

This progression includes.

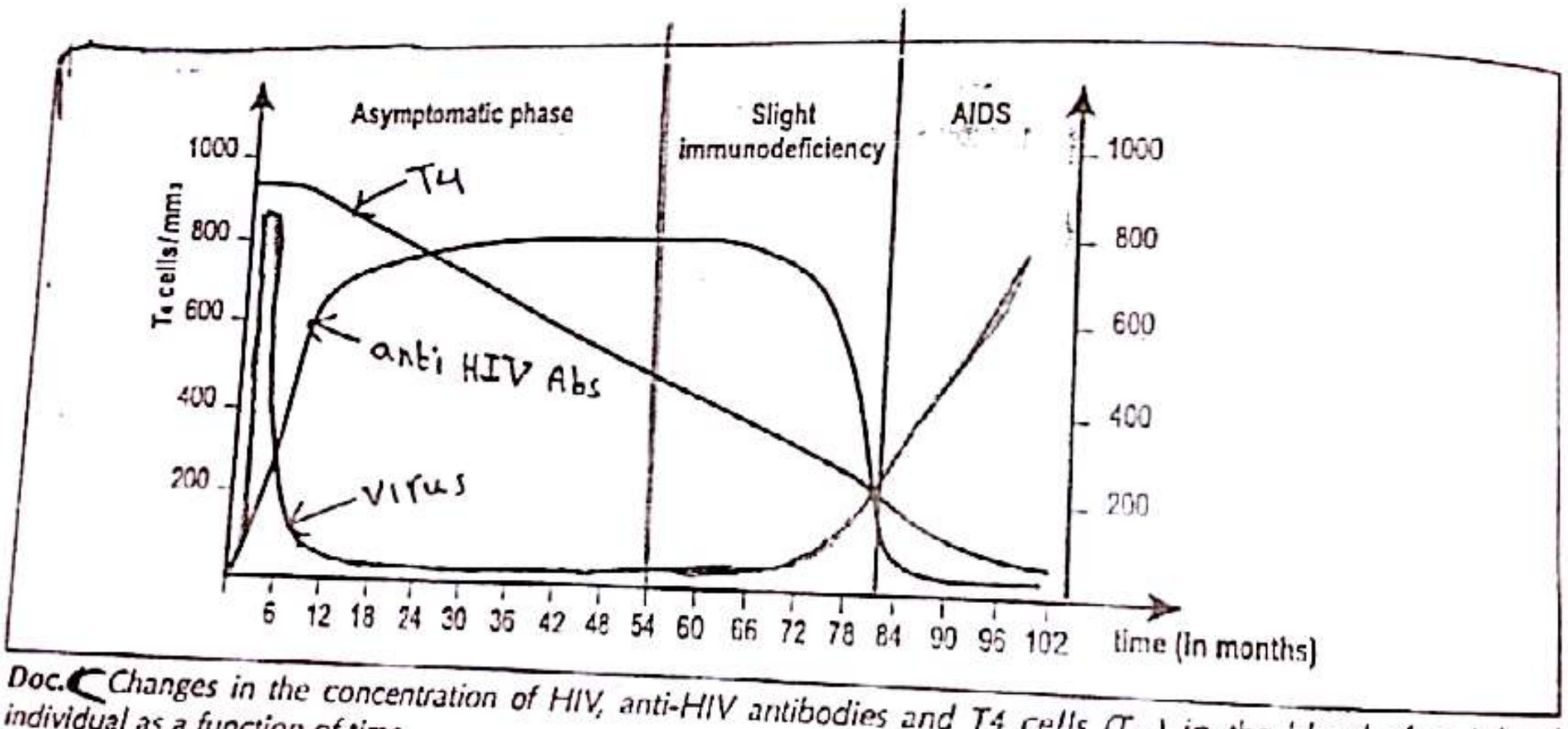
1) **Asymptomatic phase:** (about 4.5 years)

The infection is unnoticed for several years since the body resists the invasion of the virus. During this phase the concentration of $T_4$ starts to decrease.

2) **Slight immunodeficienvy** (about 2.5 years)

There is an increase in the number of opportunistic infections. During this phase the amount of $T_4$ continues its decreasing and the amount of antibodies _starts its decreasing while the concentration of the virus starts to increase.

3) **AIDS:** In this phase, there is no $T_4$, no antibodies and as a result, the concentration of the virus increases rapidly until the death of the patient.




**Doc.** *Changes in the concentration of HIV, anti-HIV antibodies and T4 cells ($T_H$) in the blood of an infected individual as a function of time.*

## Document 3 : Auto-immune diseases

### Auto immunity

Our immune system, and during maturation, eliminates all the lymphocytes that recognize our self antigens whether free or within HLA, but in the case of auto immune disease, there is malfunction in this maturation.

The immune reaction can't eliminate or destroy totally our self antigen but causes a chronic inflammation that destroys the tissues and may be fatal.

The auto immune diseases may be specific for some organs like malfunction in the thyroid, pancreas, ... etc or not specific in the organs, like diseases that affect the skin and the joints.

### Examples :

1) Rheumatoid arthiritis : It is due to the deposition of immune complex in the small joints like in the fingers leading to inflammatory reactions edema, pain and distortion of fingers.

2) Insulin Dependent diabetes Mellitus (IDDM) . It is due to the destruction of B cells of the pancreas.

3) Multiple sclerosis: It is due to the destruction of the myelin sheath that cover some nerve fibers and leads to neurological deficiencies.