Introduction to Basic Concepts of the Immune System-2

Inflammation: When a tissue is damaged either due to a wound or an invading pathogen, it induces a complex series of events called as inflammatory response. Its final manifestation on body can be called inflammation.
There are 5 signs of inflammation. Signs 1-4 were given by Celsus and 5 by Galen. These are :
1. Redness (rubor) 2. Swelling (tumor) 3. Heat (calor) 4. Pain (dolor) 5. Loss of function (functio laesa)
The series of events in an inflammatory response are described below.

1. Tissue damage initiates a release of vasoactive and chemotactic factors.
These factors trigger.
• **Vasodilation**: The diameter of blood capillaries supplying the affected area increases while diameter of vessels draining the affected area decreases. It causes a local increase in blood supply visible as tissue redness.
• **Increase in capillary permeability:** It facilitates movement of fluid and cells from blood vessel to damage site. This is manifested in fluid accumulation at damage site visible as swelling.
2. Influx of phagocytes: Due to increase in tissue permeability phagocytic cells from blood move to damage site.
This movement involves following steps:
(a) Margination: Phagocyte adheres to the endothelial wall of blood vessel.
(b) Diapedesis: Phagocytic cell crosses into tissue by emigrating between capillary-endothelial cells. It is also called extravasation.
(c) Chemotaxis: The phagocyte now migrates through the tissue to the site of damage.

The phagocytic cells once accumulated at damage site begin to kill pathogen by phagocytosis and releasing lytic enzymes. This clears the pathogen and leads to accumulation of dead cells, digested material and fluid. It is called pus.
There are many molecules involved in above described response. Two examples are:
• **Histamine:** It causes vasodilation and increased tissue permeability.
• **Kinins:** They are peptides. They cause vasodilation and increased tissue permeability. Some of them such as bradykinin stimulate pain receptors in skin.
Such molecules are called as mediators of inflammation.

During inflammatory response, components of blood-clotting system also reach the damaged area. They form a clot around the damaged area and separate it from rest of the body.
All the above described aspects of inflammation reveal it to be a protective response.

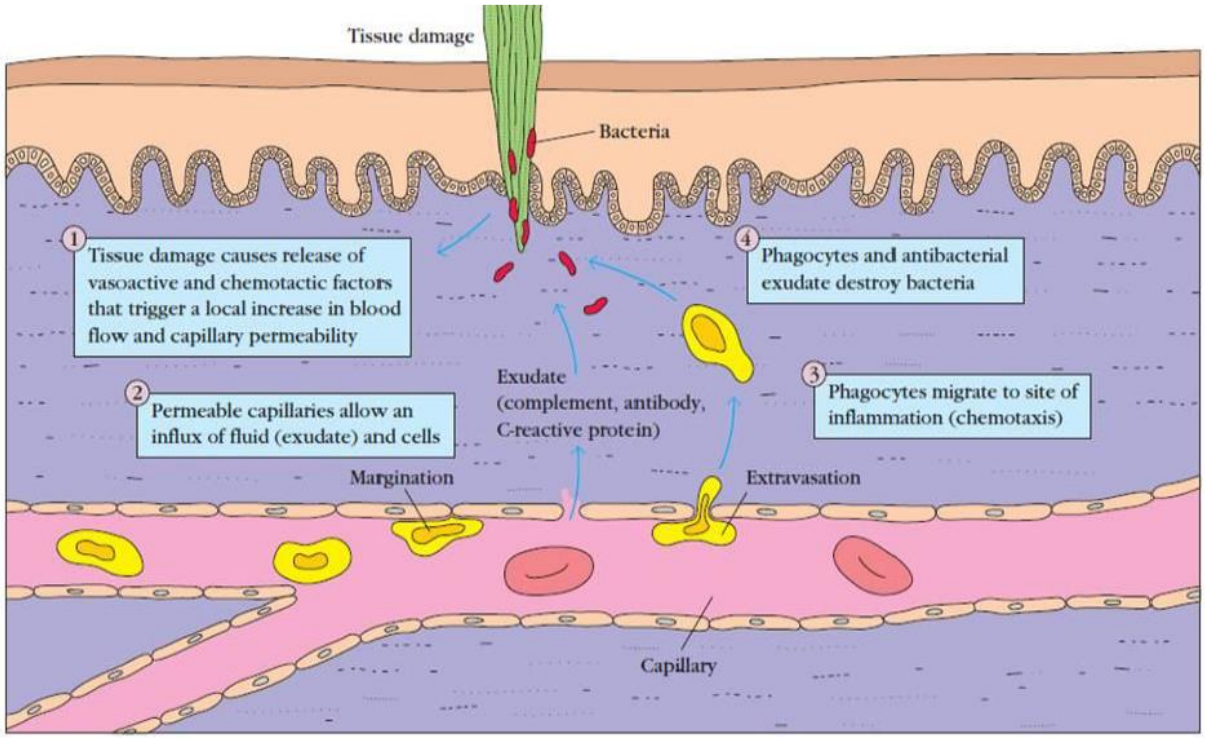


Figure for the inflammation.

Branches of immune system: There are two ways to define branches of immune system as compared below:

Humoral immunity	Cell mediated immunity
• It is called humoral because its effector factors were found in body fluids. These fluids are called as humor. Thus, immunity associated with them came to be called as humoral.	• It is called cellular because its effectors were such cells that comprise immune system.
• It is effected by antibodies. Thus, mediated by B-cells.	• It is effected by T-cells, APCs and target cells.
• It can be transferred without B-cells.	• It can not be transferred without T-cells.

	Innate immunity	Adaptive Immunity
Components	 1. Physical and chemical barriers 2. Phagocytic leukocytes 3. Dendritic cells 4. Natural Killer cells 5. Plasma proteins (complement)	 1. Humoral immunity (B cells, which mature into antibody secreting plasma cells) 2. Cell-mediated immunity (T cells, which mature into effector helper and cytotoxic T cells)
Activity	Always present	Normally silent
Response and potency	Immediate response, but has a limited and lower potency	Slower response (over 1-2 weeks, but is much more potent
Specificity	General: can recognize general classes of pathogens (i.e. bacteria, viruses, fungi, parasites) but cannot make fine distinctions	Recognizes highly specific antigens
Course	Attempts to immediately destroy the pathogen, and if it can't, it contains the infection until the more powerful adaptive immune system acts.	Slower to respond; effector cells are generally produced in 1 week and the entire response occurs over 1-2 weeks. However, this course can vary somewhat during different responses in an individual.
Memory?	No--reacts with equal potency upon repeated exposure to the same pathogen.	 Yes--memory cells "remember" specific pathogens; upon re-exposure to a pathogen, these cells mount a much faster and more potent second response

Two basic terms: These are two basic terms in immunology.

1. Antigen: Anything that can lead to generation of an immune response once inside the body, is called an antigen.

E.g. Antigen-A enters the body and causes immune reaction to happen. This reaction will be called Anti-A response.

2. Antibody: These are glycoprotein molecules that are among many molecules produced during an immune response. They are specific for an antigen and thus, named after the antigen they bind to.

E.g. Antibody against antigen -A is called Anti-A antibody.

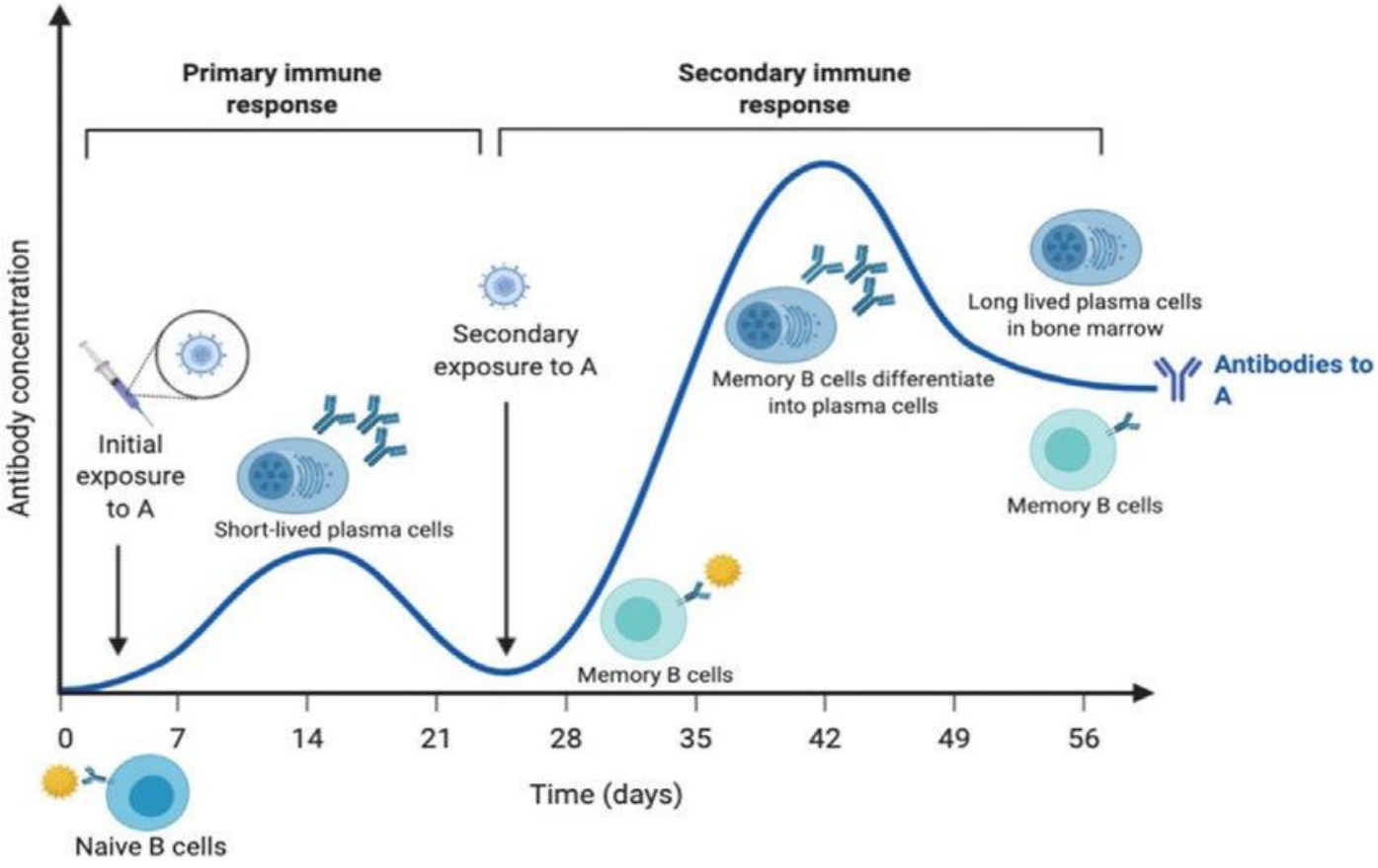
• Antigen is represented as Ag and antibody as Ab.

Few important concepts: These are few basic concepts central to understanding of immunology. These are explained below:

1. Primary vs secondary immune response: They are compared below and then explained for humoral immunity. The general principles outlined for humoral response are also applicable on the cell mediated immunity when we are dealing with primary vs secondary response.

IMMUNE RESPONSE	
Primary	**Secondary**
1. Immune response on *1st exposure* to an antigen is called primary immune response.	1. Immune response on *2nd exposure* to the *same* antigen is called as secondary response.
2. It is *slow* in onset. Peak response in 10-15 days.	2. It is *rapid* in onset. Peak response in 5-10 days.
3. It is *not applicable* to innate immune response.	3. It is *not applicable* to innate immune response.
4. It is *applicable* to adaptive immune response.	4. It is *applicable* to adaptive immune response.
5. It is *true* for humoral and cell mediated immunity.	5. It is *true* for humoral and cell mediated immunity.
6. It *does not* use immune memory.	6. It *uses* immune memory.

Primary vs secondary humoral response:



In above graph, when Ag-A is given for 1st time, the immune response by body is called primary anti-A response. It generates an immunologic memory of encounter with Ag-A.

When Ag-A is given for the second time, we get a large, rapid secondary anti-A response. It can be seen in reduced peak response time from 14 days to 8 days and large serum Ab level against Ag-A. This is because immune system recognized Ag-A due to memory formed during primary response.

Clonal Selection Theory: This was given by Dr Frank McFarlane Burnett in an attempt to explain the highly specific nature of the adaptive immune system.

Every functionally mature B and T-cells is specific for a particular antigen. These cell are called antigenically committed cells.

• These antigenically committed cells are called as naive cells till they have not interacted with their specific Ag.

• When these cells encounter their particular Ag, we say that cells have undergone clonal selection. Now, they undergo very fast expansion.

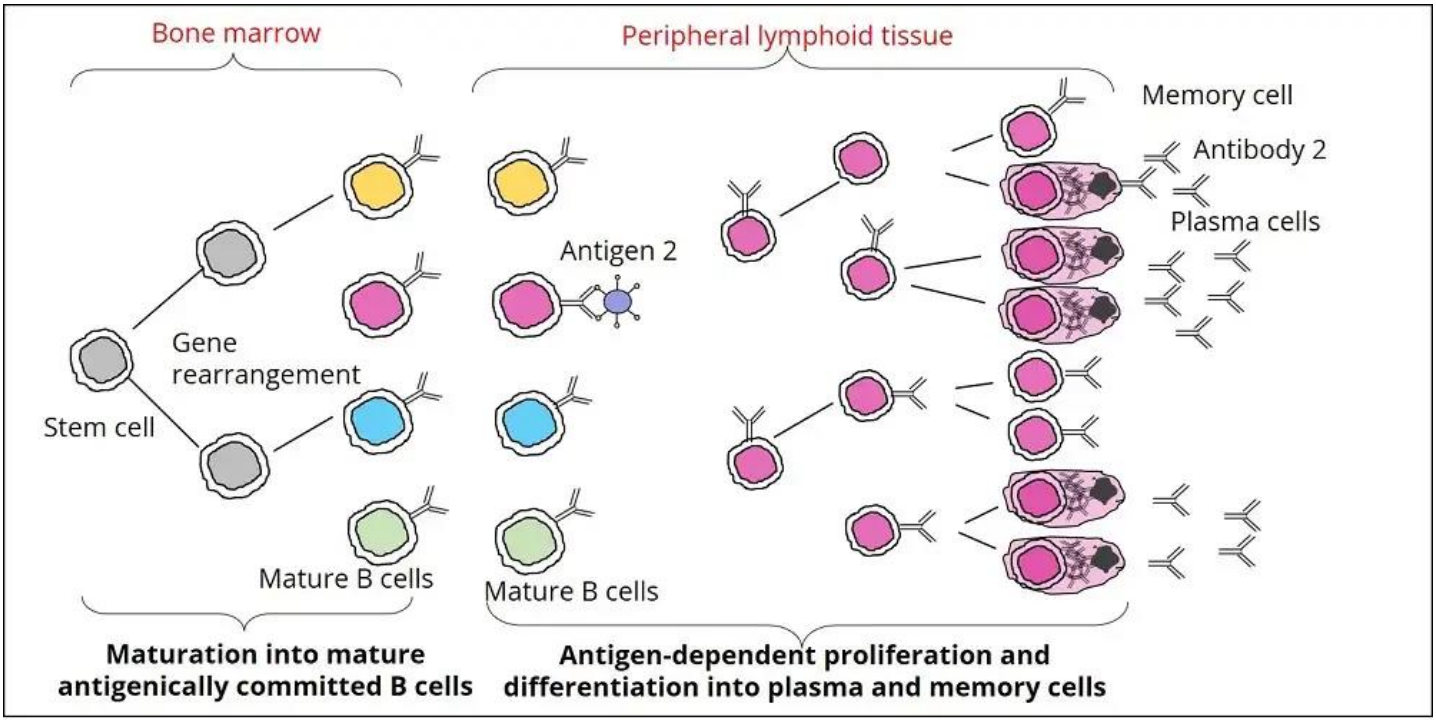
• This expansion happens by cell division. During this expansion, population of a cell specific to a particular Ag is expanded.

• This is called clonal expansion. Because, all the cells produced have exact antigenic specificity as per their parent cell.

• Clonal expansion is an important process in adaptive immune response, because, it is from this population of cells that different cells viz. effector and memory cells are derived.

• B-cells are matured in bone marrow while T-cells mature in thymus gland. But, clonal expansion occurs in peripheral lymphoid tissues.

This theory is explained in the figure below:



Immune dysfunction and its consequences: Immune system is the protector of body, it is natural that its dysfunction in any form will lead to diseased condition. Following are broad categories of immune dysfunction.

1. All forms of allergy. E.g. Asthma.

2. Graft rejection. E.g. Rejection of organ transplant.

3. Autoimmune diseases. E.g. systemic lupus erythematosus.

4. Immunodeficiency based diseases. E.g. SCID.