

2<sup>nd</sup> Year Pharm D  
Pharmaceutical Microbiology

# Immunology

**Dr. S. Sudha**, M.Pharm., PhD.

Professor, Department of Pharmaceutical Biotechnology,  
Devaki Amma Memorial College of Pharmacy,  
Chelembra, Malappuram, Kerala.

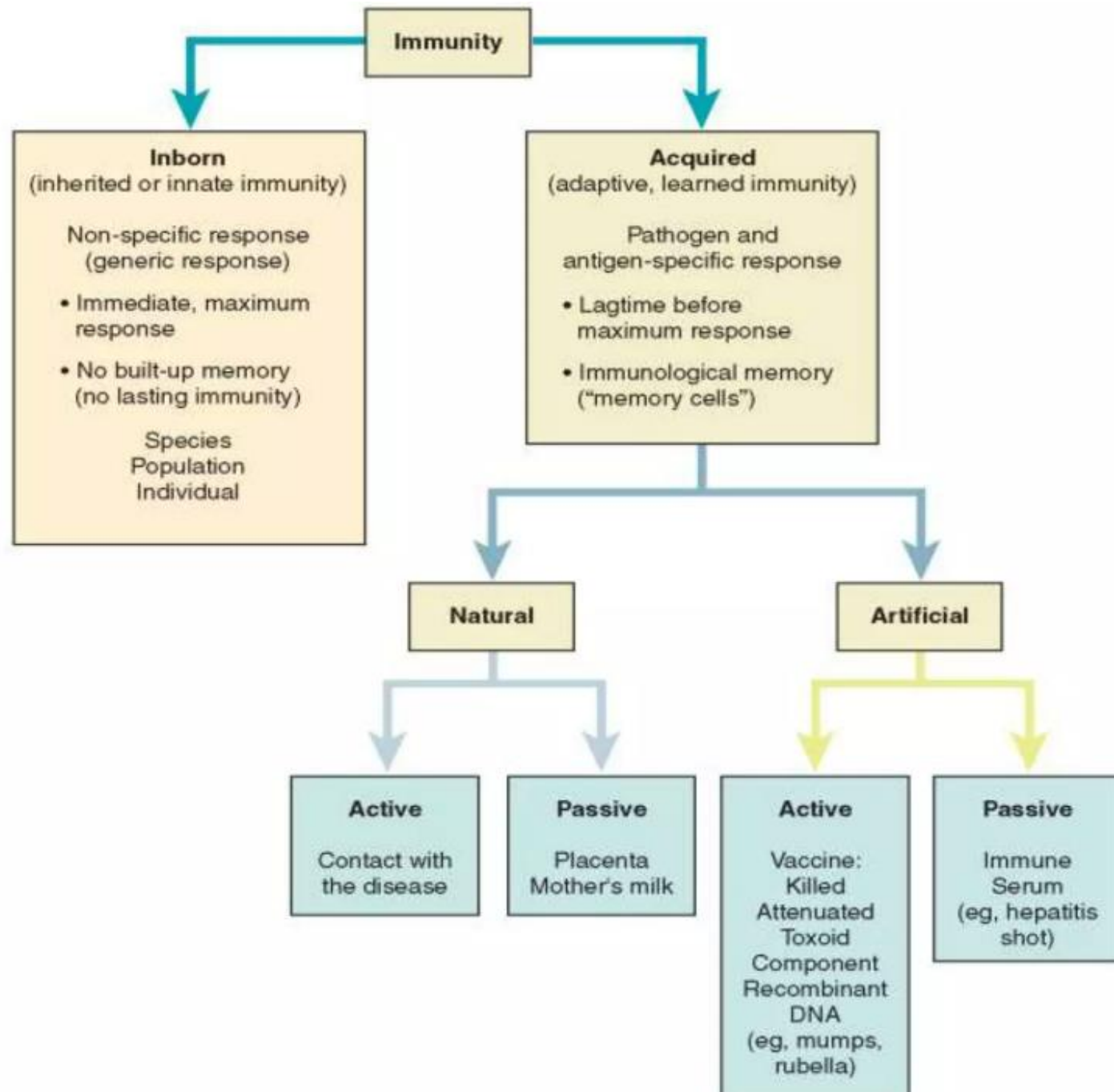


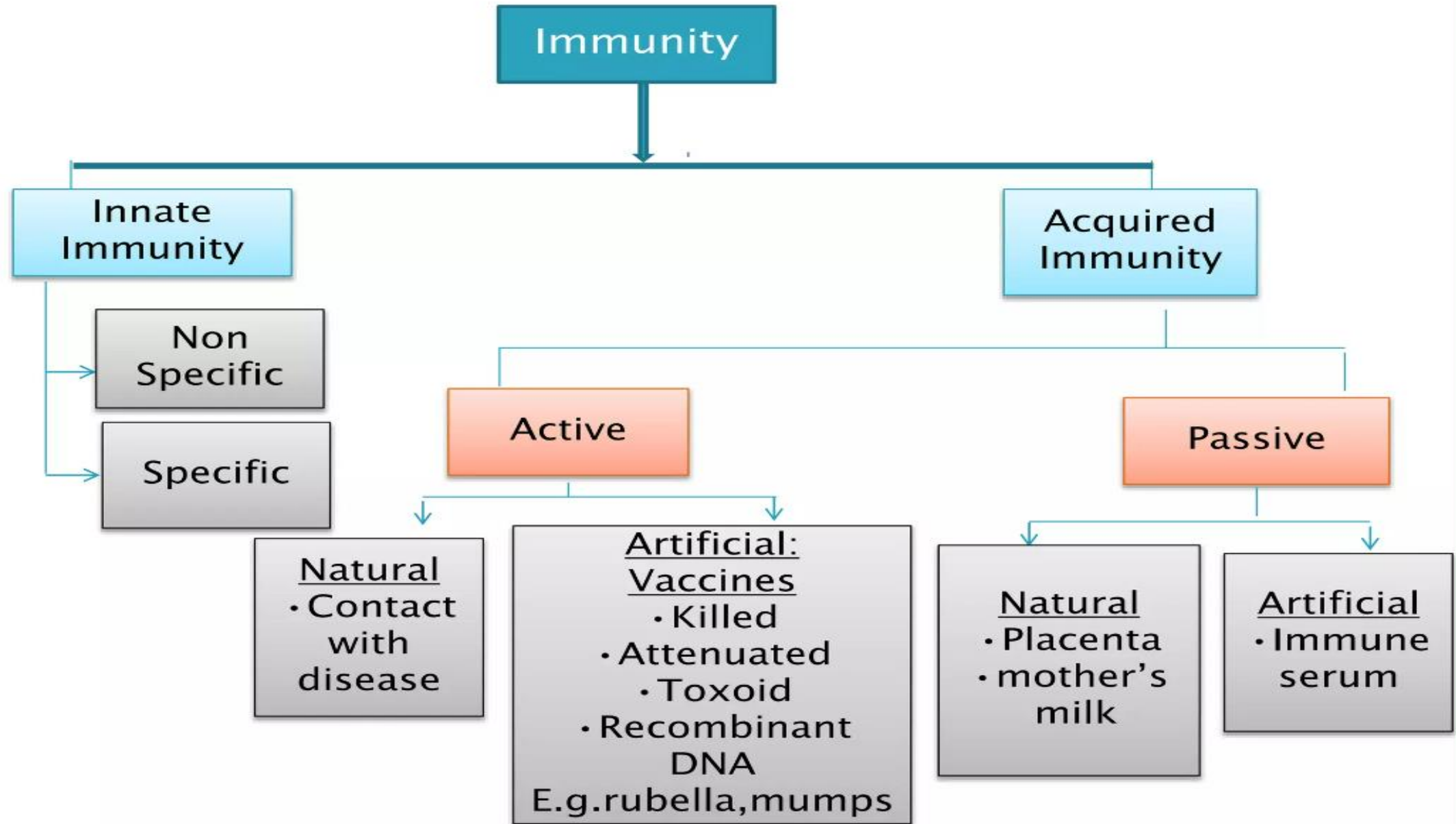
# Immunity:

- ▶ State or quality of being immune.
- ▶ Resistance exhibited by the host against any foreign antigen and towards injury caused by microorganisms and their products.

# Types:

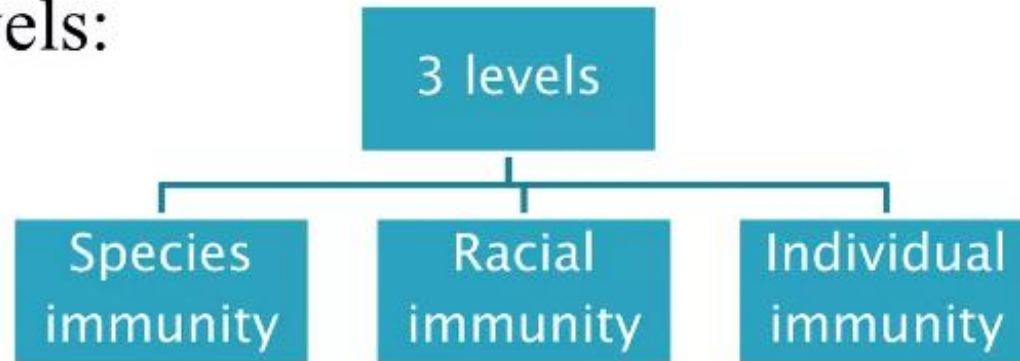
- ▶ 2 types
- ▶ Innate or Native Immunity
- ▶ Acquired or Adaptive Immunity





# A. Innate or Native Immunity:

- ▶ Resistance possessed by an individual by birth i.e. inherited.
- ▶ Provides first line of defense against infections.
- ▶ 3 levels:



## Factors affecting innate immunity:

- ▶ Age
- ▶ Hormones
- ▶ Nutrition



# Contd....

- **AGE:**

- Foetus or new born and old persons (2 extremes of life) carry higher susceptibility to various infections.



- In foetus, immune system is immature where as in old age there is gradual waning of immune responses.



- In some diseases, clinical illness is more severe in adults than in young children due to more active immune response which causes greater tissue damage.e.g: chicken pox and poliomyelitis.



## Cont.....

- **HORMONES:**

- Certain hormonal disorders enhance susceptibility to infections.e.g:- diabetes mellitus,adrenal dysfunctions and hypothyroidism
- Staphylococcal sepsis is more common in diabetes ,which may be caused by increased level of carbohydrates in tissues
- Corticosteroids depress host resistance by its antiinflammatory,antiphagocytic effects and by inhibiting antibody formation.



## cont.....

### ▶ Nutrition:

- Both humoral and cell mediated immunity are reduced in malnutrition
- In Kwashiorkor (severe protein deficiency), cell mediated immune response reduces.



# Mechanisms of innate immunity:

- ▶ Epithelial surfaces
- ▶ Antibacterial substances
- ▶ Cellular factors
- ▶ Inflammation
- ▶ Fever
- ▶ Acute phase proteins



## cont.....

### 1. Epithelial surfaces:

#### Skin:

- provides mechanical barrier to microorganisms
- provides bactericidal secretions
- the resident bacterial flora of skin and mucous surfaces **prevent colonization by pathogen**
- alteration of normal flora may lead to invasion by extraneous microbes and cause serious diseases.e.g,clostridial enterocolitis following oral antibiotics.

## Cont.....

### ▶ Respiratory tract:

- respiratory tract is lined by moist musous surfaces which **act as trapping mechanism**.
- inhaled particles are arrested in nasal passage on moist mucous membrane surfaces.
- the hair like cilia propels the particles towards pharynx and are swallowed or coughed out.
- some **particles which manage to reach alveoli are ingested by phagocytes**



## cont.....

### Intestinal tract:

- saliva present in mouth inhibits many microorganisms.
- acidic ph of gastric juices destroys the swallowed bacteria if any.
- normal flora of intestine prevent colonization of pathogens.

### Conjunctiva:

- Tears flush away bacteria and other dust particles
- lysozyme present in tears has bactericidal action.

### Genitourinary tract:

Urine eliminate bacteria from urethra by its flushing action.

Acidic ph of vaginal secretion of female due to fermentation of glycogen by lactobacillus makes vagina free from microorganisms.

In males, semen is believed to have some antibacterial substance.





## Contd.....

### 2. Antibacterial substances in blood and tissues:

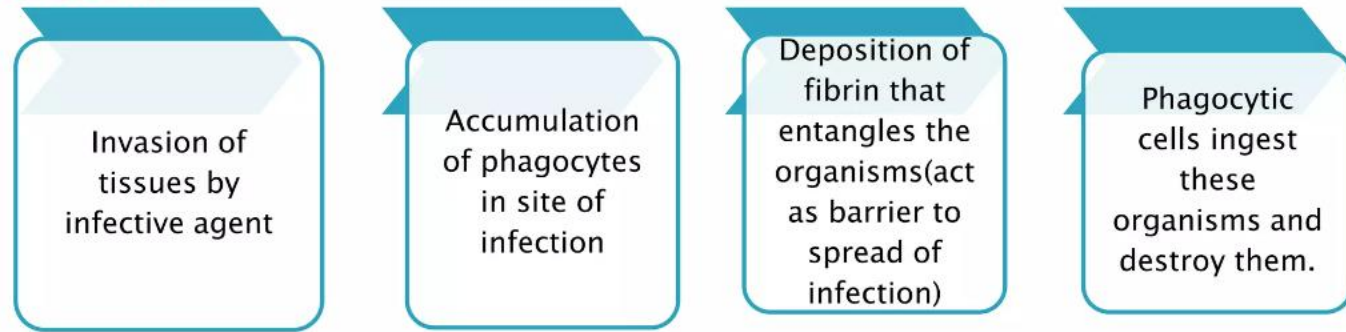
There are no. of antibacterial substances present in blood and tissues

- **Beta lysin**: relatively thermostable substance active against anthrax and related bacilli.
- **Basic Polypeptide**: e.g., leukins and plakins
- **Acidic substances**: lactic acid present in tissue and infected area
- **Interferon** : protects against certain acute and viral infections.



### 3. Cellular factors:

- ▶ Once the infective agent cross the epithelial barriers, **tissue factors come into play for defense.**
- ▶ **Process:**



Presentation last saved: Just now

Phagocytic cells are classified as:

- i) Microphages e.g. polymorphonuclear leucocytes (neutrophils)
- ii) Macrophages e.g. mononuclear phagocytic cells





## Phagocytic action are divided into 4 stages:

### i) Chemotaxis:

Phagocytes reach the site of infection attracted by chemotactic substances

### ii) Attachment:

Infective agent gets attached to phagocytic membrane

### iii) Ingestion:

Phagocytes engulf the infective material into vacuole

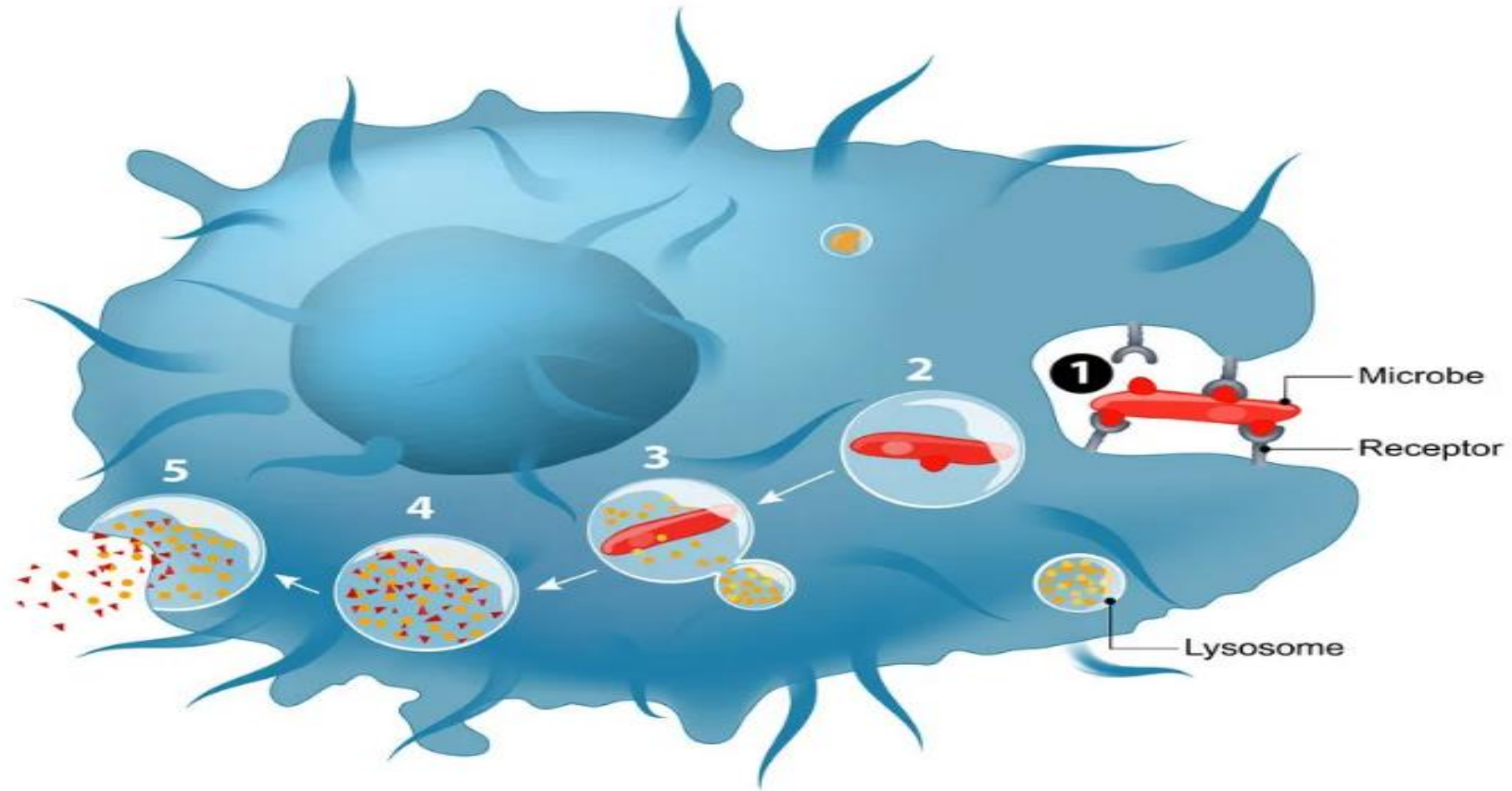
Membrane of phagosome fuses with lysosomes to form a phagolysosome.

### iv) Intracellular killing:

Most bacteria are destroyed by phagolysosomes by hydrolytic enzymes of lysosomes

Natural killer cells play an important role in non specific defence against viral infections and tumour.

# PHAGOCYTOSIS



1. Binding and absorption

2. Phagosome formation

3. Phagosome and lysosome to form a phagolysosome

4. Digestion

5. Release of microbial products

## 4. Inflammation:

- ▶ An important non-specific defense mechanism
- ▶ Occurs as a result of tissue injury, initiated by entry of pathogens.
- ▶ Leads to vasodilation, increased vascular permeability and cellular infiltration
- ▶ Due to increased vascular permeability, plasma pours out and dilutes the toxic products present.
- ▶ Fibrin barrier is laid to wall off the site of infection



## 5.Fever:

- ▶ Rise in temperature following infection is natural defense mechanism.
- ▶ Destroys the infecting organism
- ▶ Stimulates the production of interferon, which help in recovery from viral infections



6. Acute phase proteins: after injury ,there is sudden increase or decrease in plasma concentration of certain proteins, collectively called Acute phase proteins

- ▶ E.g. C reactive protein (CRP),Mannose binding proteins etc.
- ▶ They activate the alternative pathway of complement
- ▶ Prevent tissue injury and promote repair of inflammatory lesions





## B. Acquired or Adaptive immunity:

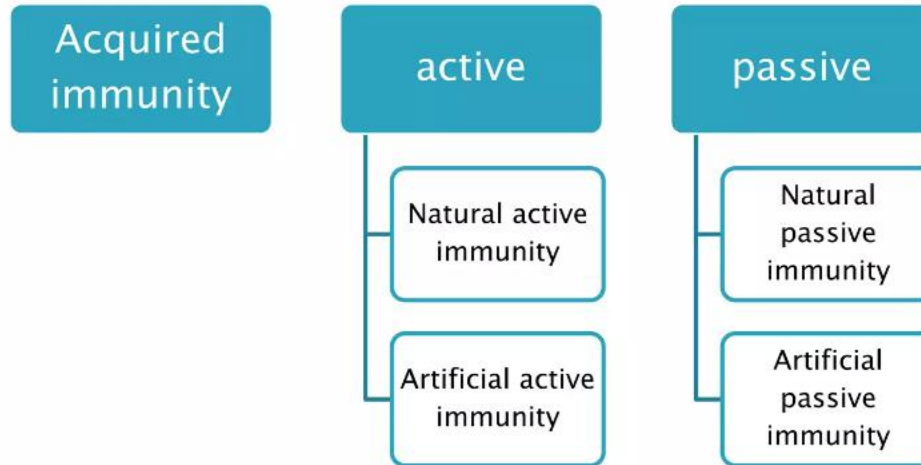
- The resistance acquired by an individual during life by recognizing and selectively eliminating specific foreign molecules.
- Provides second line of defense against infection.

## Characteristics:

- ▶ **Antigen specificity:** immune system or antibodies can distinguish among antigens, even between two proteins that differ in only one amino acid.
- ▶ **Diversity:** immune system is capable of generating large antibody diversity in its recognition molecules.
- ▶ **Immunologic memory:** immune system exhibits memory on second encounter of same antigen by generating a secondary response which is more specific and quick.
- ▶ **Self/non-self recognition:** does not react with body's own molecule but effectively eliminates foreign antigens.

# Types

- ▶ Active acquired immunity
- ▶ Passive acquired immunity



- ▶ **Active immunity:**
- ▶ also known as adaptive immunity
- ▶ Resistance developed by an individual as a result of an antigenic stimulus
- ▶ Used for prophylaxis to increase body resistance
- ▶ 2 types: • natural active immunity
  - artificial active immunity



▶ **Passive immunity:**

- ▶ Resistance transmitted passively to a recipient in a readymade form.(recipient's immune system plays no active role)
- ▶ Used for treatment of acute infection
- ▶ 2 types: :
  - natural passive immunity
  - artificial passive immunity



Active Immunity	Passive Immunity
Produced actively by host's immune system	Received passively, no active participation of host's immune system
Induced by infection or by immunogens	Conferred by administration of readymade antibodies
Long-lasting & effective protection	Short-term & less effective protection
Immunity effective only after lag period (time required for generation of antibodies.)	Immediate immunity
Immunological memory present	No memory
Booster effect on subsequent dose	Subsequent dose less effective
Negative phase may occur	No negative phase
Not applicable in immunodeficient,	Applicable in immunodeficient





# Types of active immunity

- ▶ **Natural active immunity:**

- ▶ Results from either a clinical or an inapparent infection by a microbe.
- ▶ Usually long lasting
- ▶ E.g., person recovering from chicken pox and measles develop natural active immunity.

- \* **premuniton:** “special type of immunity seen in syphilis”.

- immunity to the re-infection lasts only as long as the original infection remains active.(once the disease is cured the patient becomes susceptible to the spirochetes again)



## cont....



- ▶ Artificial active Immunity:
- ▶ Resistance induced by vaccination.
- ▶ **Vaccines:** preparations of live or killed microorganisms and their products (antigens or toxoids)
  - ▶ bacterial vaccines: live or attenuated- **BCG for tuberculosis**  
killed- **Cholera vaccine**  
Subunit- **Typhoid Vi antigen**  
Bacterial products- **Tetanus toxoids**
  - ▶ Viral Vaccines: live or attenuated-oral polio vaccine-Sabin  
killed-injectable polio vaccine-Salk  
Subunit-**Hepatitis B Vaccine**



# Types of passive Immunity:

## ▶ Natural passive Immunity:

Resistance passively transferred from mother to foetus or infant, through placenta(transplacentally) and through milk(colostrum).



Artificial passive immunity:

resistance passively transferred to a recipient by administration of antibodies.

- Agents used:
- hyperimmune sera of animal
  - convalescent sera
  - pooled human gamma globulin

“These are used for prophylaxis and therapy”.



- ▶ **Combined immunization:**
- ▶ combination of active and passive method of immunization
- ▶ Whenever passive immunization is employed for immediate protection, combined immunization is preferred
- ▶ E.g. protection of non-immune individual with a tetanus prone wound i.e., injection of TIG in one arm and first dose of tetanus toxoid in other arm followed by full course of phased tetanus toxoid injections.
- ▶ **“TIG provided the protection necessary till active immunity is able to take effect”**



# Local immunity

- ▶ Natural infection or live vaccine administered orally or intranasally provides local immunity at site of entry such as :gut mucosa,nasal mucosa
- ▶ IgA plays important role in local immunity.





# Herd Immunity

- ▶ Overall level of immunity in a community
- ▶ Is relevant in control of epidemic diseases
- ▶ “Eradication of communicable diseases depends on the development of high level of herd immunity rather than on development of high level of immunity in individuals”

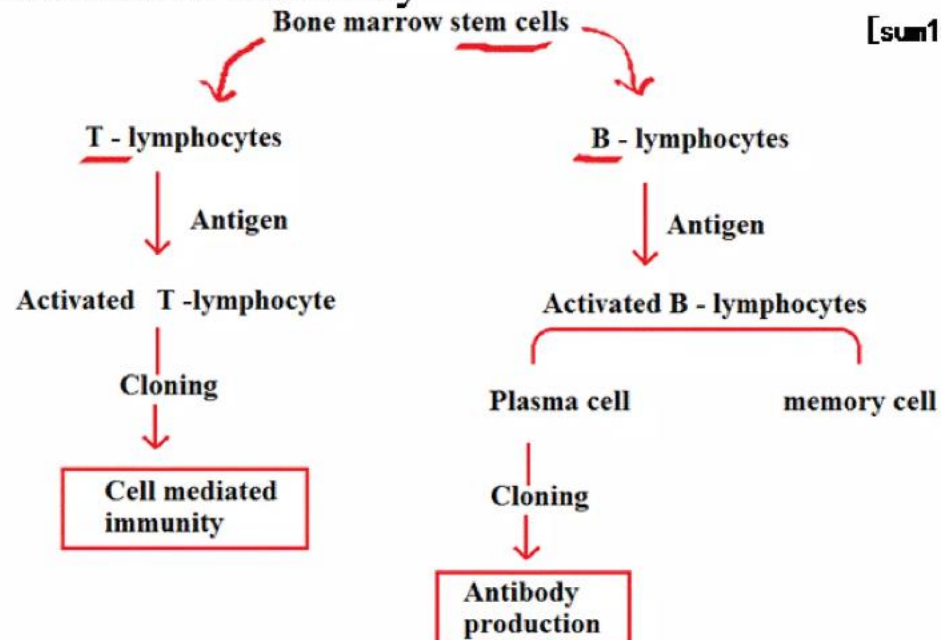


# IMMUNITY

## Classification

- 2<sup>nd</sup> type of classification

Cellular and humoral immunity



[sum15, sum12] [win13]



# IMMUNITY

## Classification

- 2<sup>nd</sup> type of classification

Cellular and humoral immunity

### A. Cellular immunity

- Cell mediated immunity
- Involves the activation of macrophages, NK cells and cytokines
- CD4 cells and helper T cell are participate in defense mechanism
  
- Activity depends on T lymphocyte
- Cells produce immunity are ----

# IMMUNITY

## Classification

- Cells produce immunity are ----

Cell	Functions
Helper T cell	Activates B cell
Suppressor T cell	Immune response regulation
Cytotoxic T-Cell	Destroy target cell
Killer cell	Attack antibody-coated target cell
NK cells	Attack and kill antibody-coated target cell

# IMMUNITY

## Classification

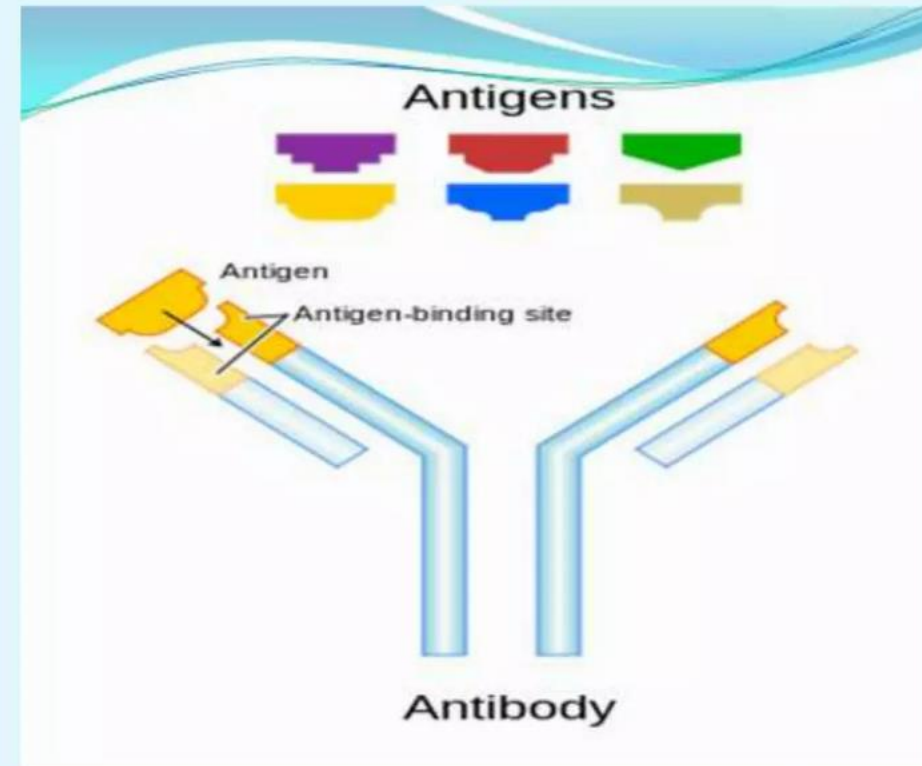
### A. Humoral immunity

- Antibody mediated immunity is called humoral immunity
- Generated by B cells, B cells are responsible for the production of Ab
- This immunity is effective against extracellular pathogens because Ab readily binds with extracellular Ag.



## ANTIGEN

An antigen is a molecule that induces an immune response in the body.



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# IMMUNOGLOBULINES

## IMMUNOGLUBULINES

[sun13] [win13, win12]

**Synonym:** Antibody

**Definition:**

‘specialized serum proteins those are formed in response to an antigen or one very closely related to it’

{ very closely related to it = vaccine of dead antigen }

- Chemically Ig are globulins (glycoproteins)



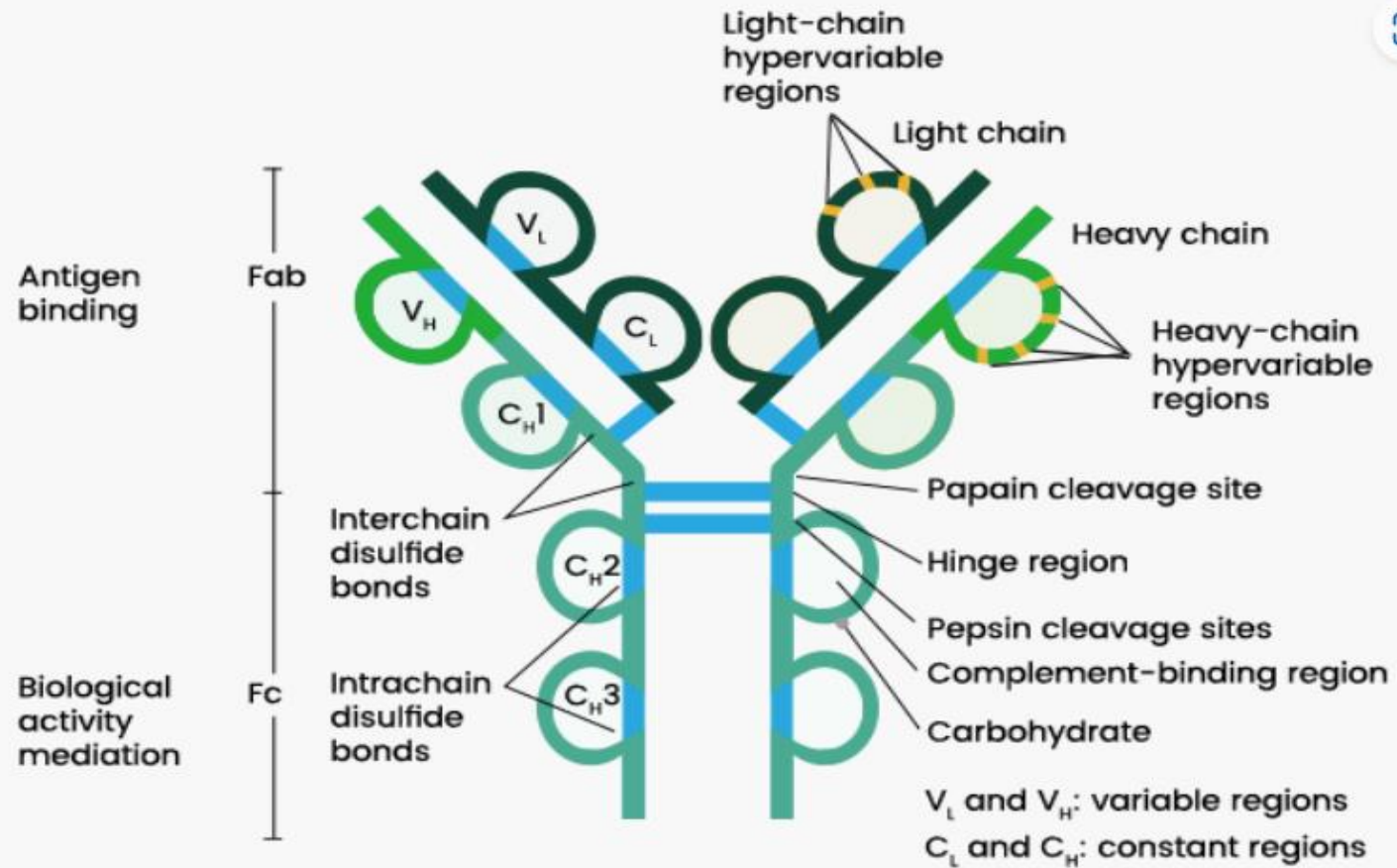


Fig 1. Antibody structure diagram



## IMMUNOGLOBULINES

### Structure:

- Basically it is Y- shape four polypeptide molecule
- Composed of two **Light** polypeptide chain and two **heavy** polypeptides joined by disulfide bond.
- Each light and heavy chain contain variable (**V**) region and constant (**C**) region.
  
- Antibody divides in to 3 fragments on enzymatic fragmentation
  - a. Two Fab fragments, each with a single antigen binding site.
    - called as '*antigen binding site*'
- They locate at aminoterinus region
- Heavy chain of this portion is called Fd piece

## IMMUNOGLOBULINES

### Structure:

- b.** Third fragment do not binds with antigen.  
called as '*crystallizable fragment (Fc)*'
- It contains carboxyterminus region of antibody
- Important for the fixation at tissue, skin, stationary surface

### Heavy chain

- The area or heavy chain CH1 and CH2 is the **Hinge region**
- Hinge region gives flexibility in structure, antibody can convert to T- shape in the absence of antigen binding.

### Disulfide bonds

- May create a folded region in structure called as 'domains'
- Light chain have 2 domains, one V and other on C region
- Heavy chain have 4 domains, one at V and other 3 at C region.



# IMMUNOGLOBULINES

## Classification:

- Five classes IgG, IgM, IgA, IgD and IgE

### (1) IgG

- major immunoglobulin in human serum, about 80% of total Ig.
- only immunoglobulin molecule able to cross the placenta and provide natural immunity to foetus

## Subclassification

IgG<sub>1</sub>, IgG<sub>2</sub>, IgG<sub>3</sub> and IgG<sub>4</sub>

- About 65% of the total serum IgG is IgG<sub>1</sub>, and 23% is IgG<sub>2</sub>.

## Functions

- Provide passive immunity to foetus
- IgG<sub>2</sub> antibodies protects against toxins



## IMMUNOGLOBULINES

### Classification:

- IgG1 and IgG3, upon recognition of their specific antigens, bind to receptors expressed on monocytes and macrophages and make them better phagocytes.
- The IgG4 antibodies function as skin sensitizing immunoglobulins

### (2) IgA

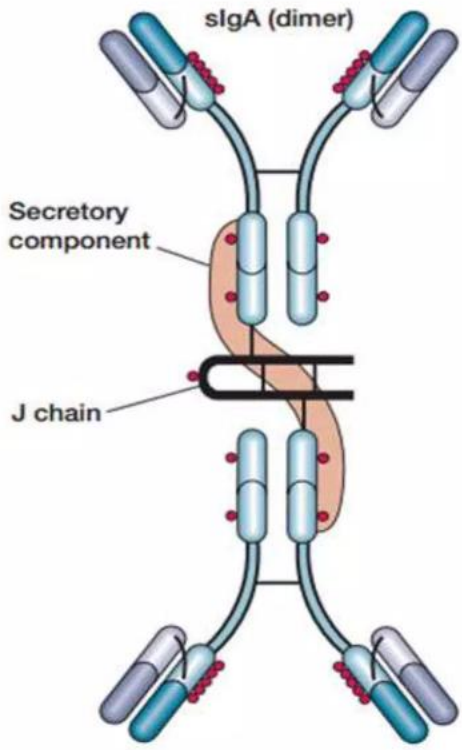
- Second major Ig in human serum, about 15% of total Ig.
- IgA is present in the serum as a **monomer**, Most IgA occurs in mucous secretions as a polymerized **dimer** held together by a J chain (shown in figure)

### Location

- Tears, saliva, urine, breast milk , other imp fluid parts

# IMMUNOGLOBULINES

## Classification:



- Secretory IgA (sIA) is a dimeric form
- Contains glycine rich secretory component



# IMMUNOGLOBULINES

Classification:

Subclassification

IgA1 and IgA2

Functions

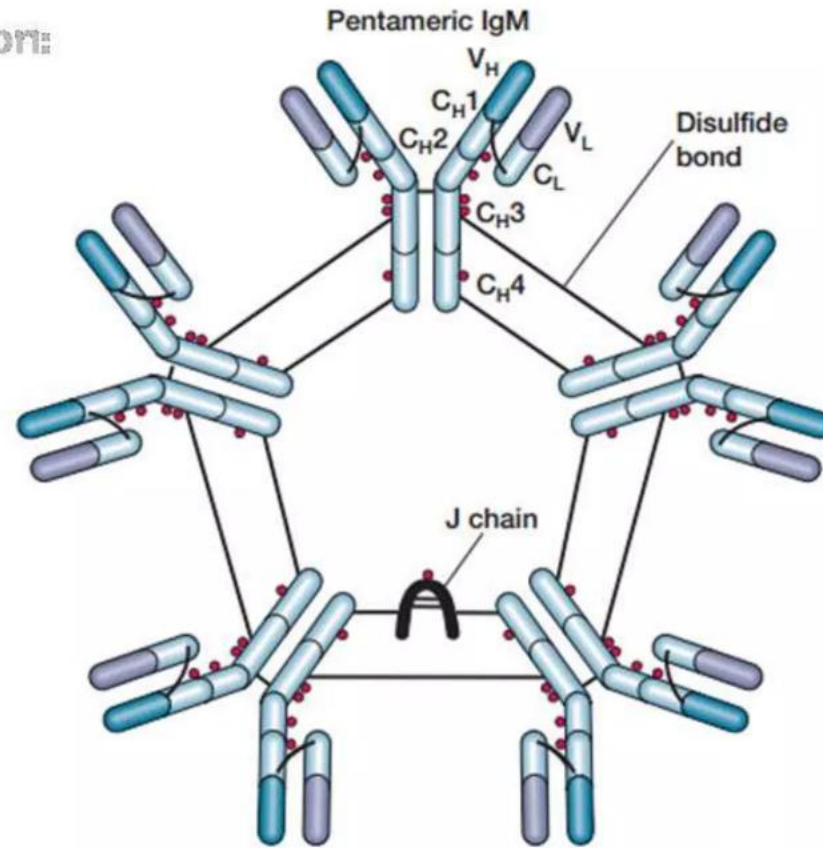
- Protect against infectious microorganisms
- In the intestine, sIgA attaches to viruses, bacteria, and protozoan parasites such as *Entamoeba histolytica*.
- In breast milk sIgA helps protect nursing newborns.

(3) IgM

- about 5- 10% of total Ig
- Largest pentameric Ig, 5 monomeric units held together by disulfide bonds and J chain

# IMMUNOGLOBULINES

Classification:



# IMMUNOGLOBULINES

Classification:

Functions

- IgM is the first Ig made during B-cell maturation.
- Have shorter half life
- IgM agglutinates bacteria, activates complementary system by the classical pathway, and enhances the ingestion of pathogens by phagocytic cells.

## IMMUNOGLOBULINES

### Classification:

#### (4) IgD

- About 1% of total Ig
- IgD antibodies do not fix complement and cannot cross the placenta, but they are abundant in combination with IgM on the surface of B cells and bind antigens, thus signaling the B cell to start antibody production.

#### (5) IgE

- Very small% of total Ig

#### Location

- Respiratory and intestinal tracts

#### Functions

- IgE is responsible for hypersensitive and anaphylactic reactions

