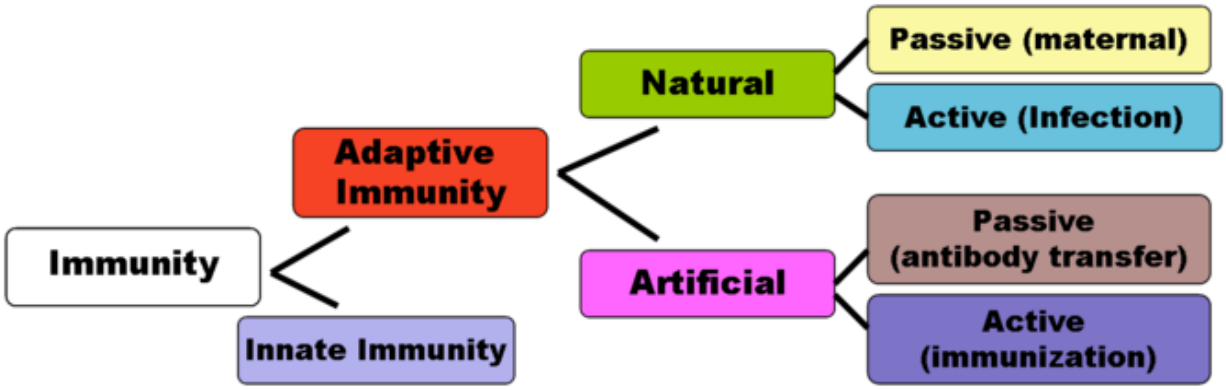
Immunity:

Immunity is the state of protection against infectious disease conferred either through an immune response generated by immunization or by previous infection or other non-immunological factors.



Types of immunity:

Broadly there are two types of immunity.

1. Innate or natural immunity
2. Acquired immunity

Innate or Natural immunity:

- Immunity with which an individual is born is called innate or natural immunity.
- Innate immunity is provided by various components such as Skin, mucus membrane, Phagocytic cells etc
- Innate immunity acts as first line of defense to particular microorganisms.

Mechanism of innate immunity:

Anatomical barriers provide immunity by following ways.

- At first skin and mucus membrane prevent entry of microorganism into host body by mechanical separation. For example, Skin surrounds the host body from external and mucus membrane surrounds the body tracts.
- They also have mechanism to kill the pathogen before entry to body. For example; lysozyme, acidic pH, sebum, high salt concentration in sweat are antimicrobial agents found in skin and mucus membrane.
- Skin and mucus membrane provides first line of defense against microorganism as they are first component to encounter with microorganism.

Physicochemical barrier includes physiological barrier and chemical barrier.

- **Physiological** conditions of body such as normal body temperature, normal body pH etc provides immunity.
- Some species are resistant to certain disease simply because of their higher body temperature. For example, mammals are susceptible to anthrax but birds are resistant to anthrax. It is because *Bacillus anthracis* are killed by higher body temperature of birds (39°C).
- Similarly, body pH also provides immunity. For example acidity of stomach kills most of the ingested bacteria and provides immunity. In infants stomach is less acidic. This is the reason why infants suffer more from gastrointestinal disturbance than adults.
- **Chemical barriers** include various antimicrobial chemicals found in body fluids. For examples, Lysozyme found in tear and mucus kills many Gram +ve bacteria.
- Interferon found in blood and lymph kills viruses. Other antimicrobial chemicals found in body fluids include complement protein, collectins, etc.

Phagocytosis is an important defense mechanism of host to provide immunity. Most of the bacteria that enter into host are killed by phagocytic cells such as Neutrophils, monocytes and macrophages.

Inflammation is an important defense mechanism of host to prevent infection. It is induced in response to tissue damage caused by microorganism, toxins or by mechanical means.

- The inflammation may be acute; for eg. in response to tissue damage or chromic; for eg. Arthritis, cancer etc.
- Main aim of inflammation is to prevent spread of injected microorganism or toxin from site of injection and kill them on spot by phagocytosis.

Types of innate immunity:

1. Species immunity
2. Racial immunity
3. Individual immunity

1. Species immunity:

- If one species is resistant to certain infection and the other species is susceptible to the same infection then it is called as species immunity.
- Anatomic, physiological and metabolic differences between species determine species immunity. For example, Birds are resistant to anthrax but Human are susceptible. It is simply because higher body temperature of birds kills *Bacillus anthracis*.
- Anatomic differences between species also determine species immunity. For example, Human are more susceptible to skin infection whereas Cattles are more resistant to the same skin infection. It is because of tough and hairy skin (hides) of Cattles.

2. Racial immunity:

- If one race is susceptible while other race is resistant to same infection, then it is called Racial immunity.
- For examples; certain African race are more resistant to malaria and yellow fever where are Asian or Americans are susceptible to same infection. Similarly Orientals (East Asia) are relatively resistant to syphilis.
- Racial immunity is determined by difference in Socio-economic status, habitat, culture feeding habits, environments, genetic, etc.

3. Individual immunity:

- If one individual of certain race or cast is resistant while other individuals of same race or cast are susceptible to certain infection, then it is called as individual immunity
- Individual immunity is determined by various factors such as health status, nutritional status, previous illness, personal hygiene, genetic differences etc.
- For examples; Individual with genetic deficiency of glucose-6 phosphate dehydrogenase are resistant to Malaria.

Acquired or Developed immunity:

- Immunity which is developed later in life after microbial infection in host is called as Acquired or developed immunity. For example, If an individual is infected with chicken pox virus, he/she become resistant to same virus in later life.
- Acquired immunity is provided by Antibodies and certain T-lymphocytes.
- Components of acquired immunity such as Antibodies and T- cells are specific to particular microorganism. Therefore acquired immunity is also known as Specific immunity.

Characteristics of Acquired immunity:

- Specificity
- Self/non-self recognition
- Immunological memory
- Diversity

Types of acquired immunity:

1. Active immunity
2. Passive immunity

1. Active immunity:

- If host itself produces antibodies, it is called active immunity.
- Active Immunity results when exposure to a disease organism triggers the immune system to produce antibodies to that disease. Active immunity can be acquired through natural immunity or vaccine-induced immunity.
- It is of two types; artificial active immunity and natural active immunity.
- **Artificial active immunity:** Immunity provided by vaccination. It is acquired through the introduction of a killed or weakened form of the disease organism through vaccination.

- **Natural active immunity:** immunity provided by natural infection. It is acquired from exposure to the disease organism through infection with the actual disease.

2. Passive immunity:

- If host does not produce antibodies itself but antibodies produced in other host provides immunity, than it is known as Passive immunity. It is provided when a person is given antibodies to a disease rather than producing them through his or her own immune system.
- newborn baby acquires passive immunity from its mother through the placenta.

- People can also get passive immunity through antibody-containing blood products such as immune globulin, which may be given when immediate protection from a specific disease is needed.

The major advantage to passive immunity is that protection is immediate, whereas active immunity takes time (usually several weeks) to develop. However, passive immunity lasts only for a few weeks or months. Only active immunity is long-lasting.

- It is of two types; natural passive immunity and Artificial passive immunity
- **Natural passive immunity:** IgG antibody produced in mother cross placenta and protects fetus up to 6 month old age.
- **Artificial passive immunity:** if preformed antibody are injected into host for immunity. Eg. Anti-venom, Rabies vaccine (* it is not a vaccine, it is preformed anti rabies antibody)

Hypersensitivity:

- When immune system works properly, it helps in elimination or removal of antigens from host body by means of effector molecules. The effectors molecules generally induce local inflammatory response and removes antigen without extensively damaging host tissues. However in certain conditions such as when immune system does not work properly or over activated, it causes deleterious effects resulting in significant tissue damage, serious disease and even death. Such unwanted, inappropriate and damaging immune response is termed as **hypersensitivity.**

Immediate hypersensitivity reaction:

- Immediate hypersensitivity reaction is mediated by humoral antibody and manifests within minutes to few hours.
- The anaphylactic reaction initiated by antibody or Ag-Ab complex are referred as immediate hypersensitivity because it occurs within minutes or few hours after a sensitized host encounter with antigen
- Type-I, II and III hypersensitivity reaction are immediate

Delayed hypersensitivity reaction:

- Delayed hypersensitivity reaction is mediated by sensitized CD4 T cells and manifests slowly usually after 24 hours or more.
- It is called delayed because symptoms appear days after exposure to antigen.
- In delayed hypersensitivity reaction, the effector molecules are various cytokines secreted by activated CD4 T cells themselves.

- Type-V hypersensitivity depends upon activation of T cells and occurs within cell mediated branch of immune response and termed as delayed type hypersensitivity reaction (**DTH**).
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Gell and Coomb's Classification of Hypersensitivity reaction

- Hypersensitivity reactions are classified as Immediate or delayed type on the basis of time required by sensitized host to response to shocking dose of antigen.
- Hypersensitivity reactions can be distinguished by immune response and difference in effectors molecules generated in course of reactions.
- G.H Gell and R.R.A Coomb classified hypersensitivity reactions into four types.

1. **Type-I hypersensitivity reaction (Allergic hypersensitivity) :**
   IgE antibody mediated.
   Allergen-specific IgE antibodies bind to mast cells via their Fc receptor. When the specific allergen binds to the IgE, cross-linking of IgE induces degranulation of mast cells.
   Principle: Antibody-mediated degranulation of granulocytes leads to the destruction of cells.
   Primary Mediator: IgE
   Other components as mediators: Mast cells, Basophils, histamine & other pharmacological agents
   Reaction time: Immediate or within a few hours.
   Eg:Atopy, Anaphylaxis, Asthma, Churg–Strauss Syndrome

2. **Type-II hypersensitivity reaction(Cytotoxic hypersensitivity)**:
   Antibodies mediated.
   IgG or IgM antibody binds to a cellular antigen, leading to complement activation and cell lysis. IgG can also mediate ADCC with cytotoxic T cells, natural killer cells, macrophages, and neutrophils.
   Principle: Antibody-mediated destruction of healthy cells.
   Primary Mediator: IgG/IgM
   Other components as mediators: Complement, Neutrophils
   Reaction time: 5-8 hours
   Eg: Autoimmune hemolytic anemia, Rheumatic heart disease, Thrombocytopenia, Erythroblastosis fetalis, Goodpasture's syndrome, Graves' disease, Myasthenia gravis, Pemphigus vulgaris

3. **Type-III hypersensitivity reaction(Immune complex hypersensitivity):**
   Antigen-antibody complex mediated.
   Antigen-antibody complexes are deposited in tissues. Complement activation provides inflammatory mediators and recruits neutrophils. Enzymes released from neutrophils damage tissue.
   Principle: Antigen-antibody complex-mediated destruction of cells.
   Primary Mediator: IgG/IgM
   Other components as mediators: Complement, phagocytes and K cells
   Reaction time: 2-8 hours

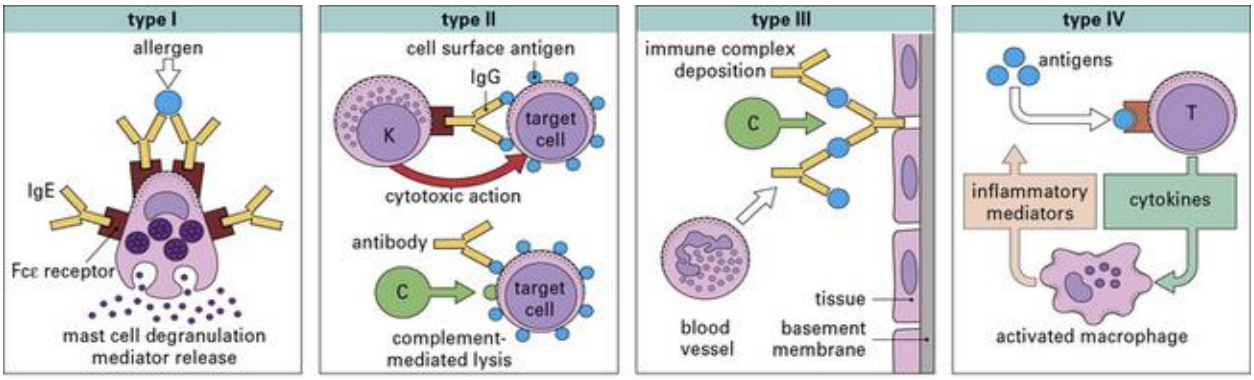
Eg: Serum sickness, Rheumatoid arthritis, Reactive arthritis, Lupus nephritis, Systemic lupus erythematosus

4. **Type-IV hypersensitivity reaction (Cell-mediated hypersensitivity/ Delayed type of hypersensitivity):**
   Activated T-cell and cytokines mediated.
   Th2 cells secrete cytokines, which activate macrophages and cytotoxic T cells.
   Principle: T lymphocytes mediated the destruction of cells.
   Primary Mediator: Specific subsets of CD4+ helper T cells or CD8+ cytotoxic T cells.
   Other components as mediators: Dendritic cells, macrophages, and cytokines
   Reaction time: After 24 hours only, mostly 48-72 hours after contact
   Eg: Multiple sclerosis, Coeliac disease, Hashimoto's thyroiditis, Granuloma annulare

Two additional types, Type-V and Type-VI hypersensitivity reaction are also proposed.

5. Type-V hypersensitivity reaction: Antibody mediated

6. Type-VI hypersensitivity reaction: Both antibody and cell mediated



Causes of Hypersensitivity

Immune responses that are the cause of hypersensitivity diseases may be specific for antigens from different
sources:

- Autoimmunity: reactions against self antigens.
- Reactions against microbes.
- Reactions against non-microbial environmental antigens.

Treatment

Immediate hypersensitivity reactions

The treatment of immediate hypersensitivity reactions includes the management of anaphylaxis with intramuscular adrenaline (epinephrine), oxygen, intravenous (IV) antihistamine, support blood pressure with IV fluids, avoid latex gloves and equipment in patients who are allergic, and surgical procedures such as tracheotomy if there is severe laryngeal edema.

1. Allergic bronchial asthma can be treated with any of the following: inhaled short- and long-acting bronchodilators (anticholinergics) along with inhaled corticosteroids, leukotriene antagonists, use of disodium cromoglycate, and environmental control. Experimentally, a low dose of methotrexate or cyclosporin and omalizumab (a monoclonal anti-IgE antibody) has been used.
2. Treatment of autoimmune disorders (e.g., SLE) include one or a combination of NSAIDs and hydroxychloroquine, azathioprine, methotrexate, mycophenolate, cyclophosphamide, low dose IL-2, intravenous immunoglobulins, and belimumab.
3. Omalizumab is a monoclonal antibody that interacts with the binding site of the high-affinity IgE receptor on mast cells. It is an engineered, humanized recombinant immunoglobulin. Moderate to severe allergic bronchial asthma can improve with omalizumab

Delayed hypersensitivity reactions

Treatment of type 4 HR involves the treatment of the eliciting cause.

1. The most common drugs to treat tuberculosis include isoniazid, rifampin, ethambutol, and pyrazinamide. For drug-resistant TB, a combination of antibiotics such as amikacin, kanamycin, or capreomycin should be used.
2. The most common drugs to treat leprosy include rifampicin and clofazimine in combination with dapsone for multibacillary leprosy. A single dose of antimicrobial combination to cure single lesion paucibacillary leprosy comprises ofloxacin, rifampicin, and minocycline.
3. Praziquantel can be useful for treating infections caused by all *Schistosoma* species.
4. Hydroxychloroquine and chloroquine can use in the therapy of sarcoidosis involving the skin, lungs, and the nervous system.
5. The use of anti-TNF monoclonal antibodies such as adalimumab and certolizumab have been approved for Crohn disease.