Lecture 7

Immune response

Is the body's response originating from immune system activation by antigens. Immune response can be innate (natural or nonspecific) or adaptive (acquired or specific).

Immune response also can be defined as : Defense against microbes is mediated by the effector mechanisms of innate and adaptive immunity.

The survival and pathogenicity of microbes in a host are critically influenced by the ability of the microbes to evade or resist the effector mechanisms of immunity.

1- Bacterial immunity :-

The principal mechanisms of innate immunity to extracellular bacteria are **complement activation**, **phagocytosis**, and **the inflammatory response**.

There are basic mechanisms by which the adaptive immune responses combat bacterial infections:

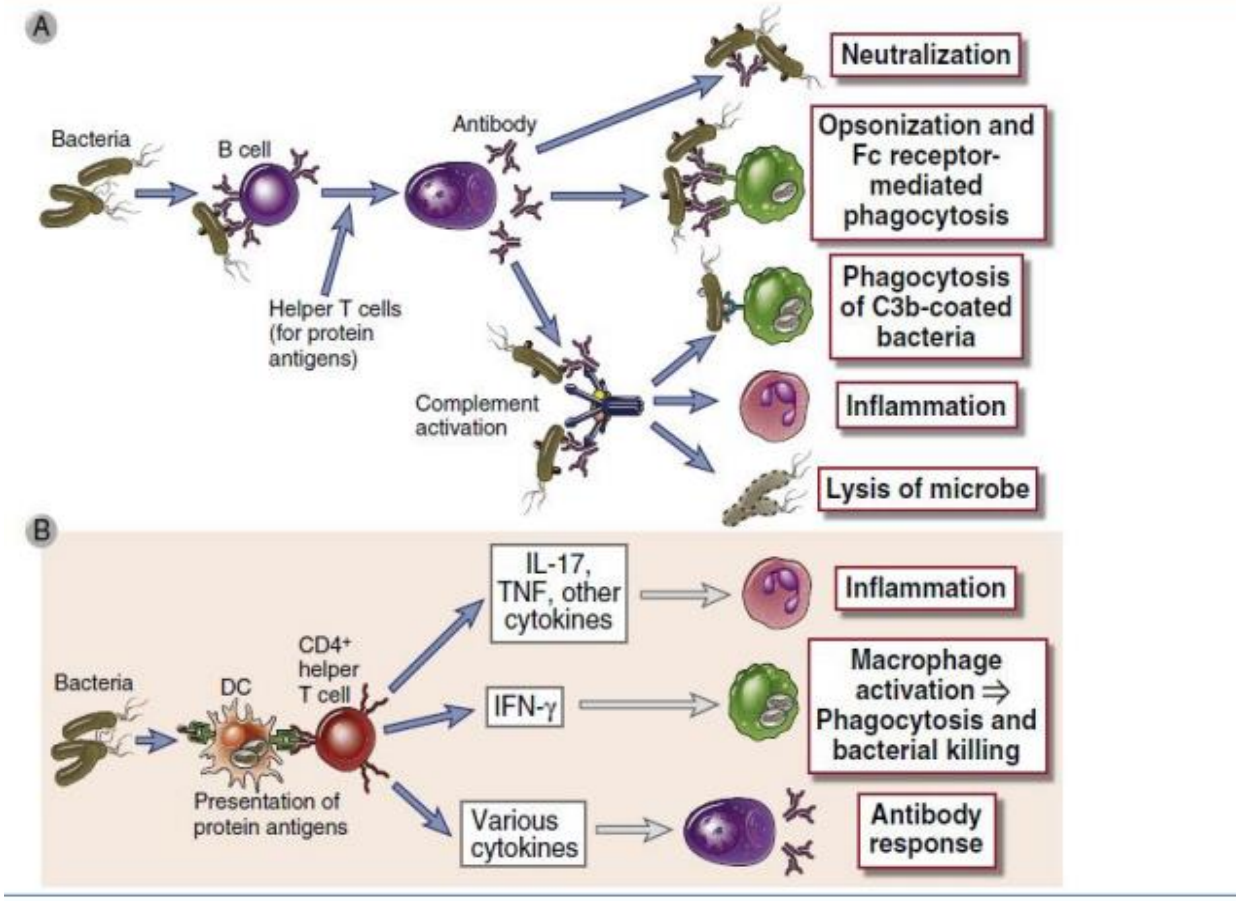
(1) neutralization of toxins or enzymes by antibody.

(2) killing of bacteria by the classical complement pathway.

(3) opsonization of bacteria by antibodies and complement, resulting in their Phagocytosis and destruction.

(4) destruction of intracellular bacteria by activated macrophages.

(5) direct killing of bacteria by cytotoxic T cells and NK cells.



Bacteria evade Immune System by :

1- Presence of capsule.

2-Multiplication of bacteria inside the macrophages, like salmonella, Brucella, Listeria, and Mycoplasma.

3- Changing of surface antigens: some bacteria like Campylobacter fetus.

4- Suppression of T lymphocytes: some bacteria have the ability to inhibit T cells, like Mycoplasma mycoides

5- Production of alpha toxins: This toxin inhibits immune responses.

6- Release of cAMP (cyclic adenine monophosphate): This prevents fusion of lysosomes with phagosomes.

2- immunity to viruses :-

A-Innate immunity to virus occurs by **interferon**.

B- Adaptive immunity against viral infections is mediated by **antibodies**, which block virus binding and entry into host cells (neutralizing them), and **Cell-mediated** responses are primarily responsible for antiviral immunity.

The major mechanism involved is the killing of virus infected cells by cytotoxic T cells. Because viruses are obligate intracellular parasites, they employ a wide variety of methods of evading the immune response .

Viruses evade Immune system by :

1. Changing of viral surface antigens: like influenza viruses.

2. Changing of cellular surface antigens: like measles viruses.

3. Integration of viral N.A. (Nucleic acid) with cellular N.A.: like HIV virus in AIDS.

4. Immuno-suppression due to lymphatic tissue infection.

5. Stress factors and Steroids.

3-Parasite immunity:-

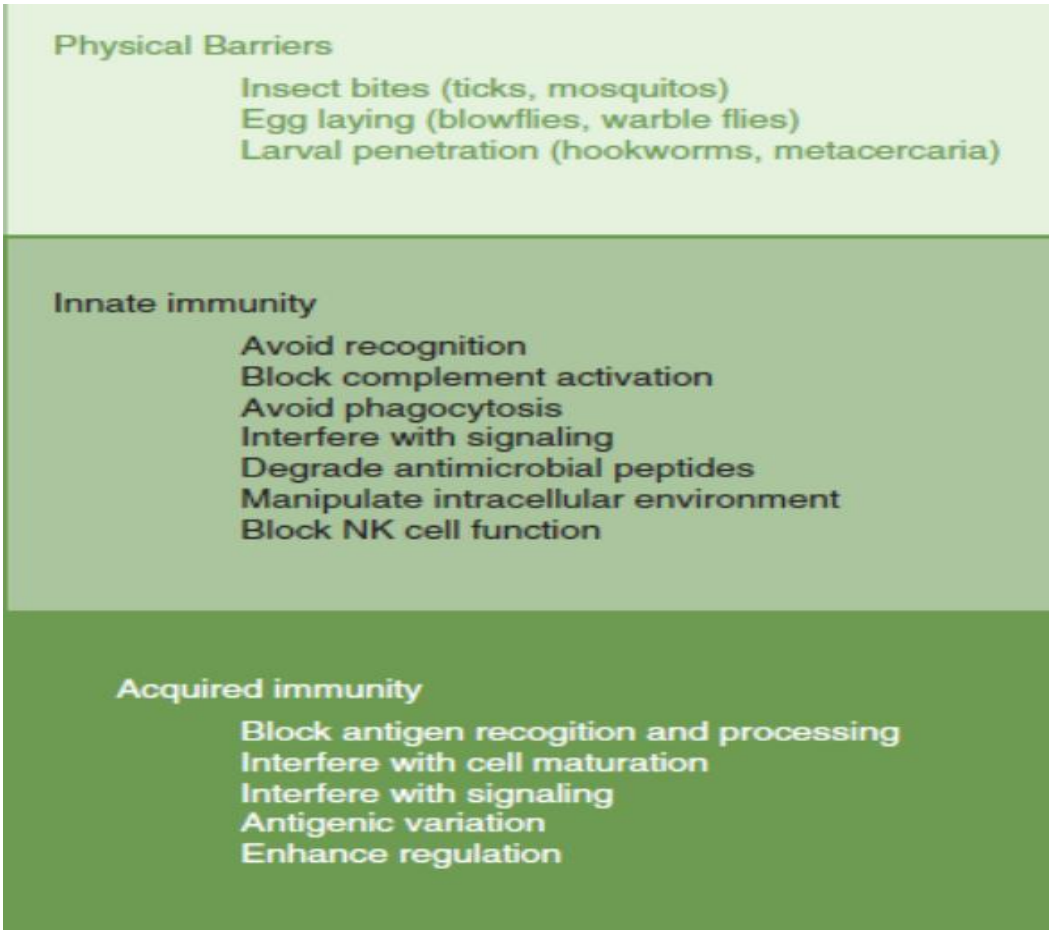
Parasites, by definition, are able to evade their host's immune response for at least sufficient time for the parasite to reproduce.

In general antibody-mediated immune responses protect against extracellular protozoa, whereas cell-mediated responses control intracellular protozoa..

Helminth parasites have a unique ability to trigger T responses and immunoglobulin E (IgE) production. IgE may have evolved as an antiparasite antibody.

Parasitic worms have a thick cuticle that protects them against damage caused by most protective cells. However, Eosinophil appear to be uniquely able to damage and kill helminthes.

Parasite Evade immune system by :



Lecture 8

Antigens

Antigens: is any structure that binds to the components of the immune system, including antibodies, B cells receptors, and T cells receptors.

Immunogen is a substance that induces a specific immune response. All immunogens are antigens but not all the antigens are immunogens.

Antigen and **immunogen** are two types of molecules that bind to the components of the immune system. Antigens can be either proteins, polysaccharides, lipids or nucleic acids while immunogens are normally proteins and large polysaccharides. However, lipids and nucleic acids can also be immunogenic after binding to proteins or large polysaccharides.

Furthermore, there are four main types of antigens that occur in the body. They are:

1- Exogenous antigens – Antigens on the surface of pathogens found in the extracellular space.
2- Endogenous antigens – Antigens generated inside the cell as a result of the cell metabolism.
3- Autoantigens – Endogenous antigens wrongly recognized as non-self-antigens by the immune system (This results in the destruction of self-tissues, causing autoimmune diseases).
4- Neoantigens – Antigens expressed on the surface of the infected cells by oncogenic viruses.

Immunogenicity is the ability to induce a humoral and/or cell-mediated immune response.

Another difference between antigen and immunogen is that antigens can be either immunogenic or non-immunogenic while immunogens are immunogenic.

Factors that influence immunogenicity

A. Contribution of the immunogen

1. **Foreignness:** When an antigen is introduced into an organism, the **degree of its immunogenicity depends on the degree of its foreignness**.

2. **Molecular size:** There is a correlation between the size of a molecule and its immunogenicity. However, in general, the larger the molecule the more immunogenic it is likely to be.

3. **Chemical composition**: All four levels of protein organization contribute to the structural complexity of a protein and affect its immunogenicity. In general, the more complex the substance is chemically the more immunogenic it will be.

- **Chemical nature of immunogenes**

a. **Proteins: The** vast majority of immunogens are proteins.
b. **Polysaccharides**
c. **Nucleic Acids**
d. **Lipids**

4. **Physical form**: particulate antigens are more immunogenic than soluble antigens.

B. Contribution of the biological system

1. **Genetic Factors:**

2. **Age**: Age can also influence immunogenicity.

C. Method of Administration

1. **Dose**: The dose of administration of an immunogen can influence its immunogenicity. An insufficient dose will not stimulate an immune response. A single dose of most experimental immunogens will not induce a strong response.

2. **Route of administration:**

3. **Adjuvants:** Adjuvants are often used to boost the immune response when an antigen has low immunogenicity or when only small amounts of an antigen are available.

Haptens: are small organic molecules that are antigenic but not immunogenic.

- Haptens are incapable by themselves of inducing a specific immune response.
- Many biologically important substances, including drugs, peptide hormones, and steroid hormones, can function as haptens.

Superantigens: superantigens activate a large fraction of the T cells (up to 25%). The massive activations results in overproduction of T helper cell cytokines leading to systemic toxicity, figure (1).

- Superantigens are viral or bacterial proteins
- Both exogenous and endogenous superantigens have been identified.

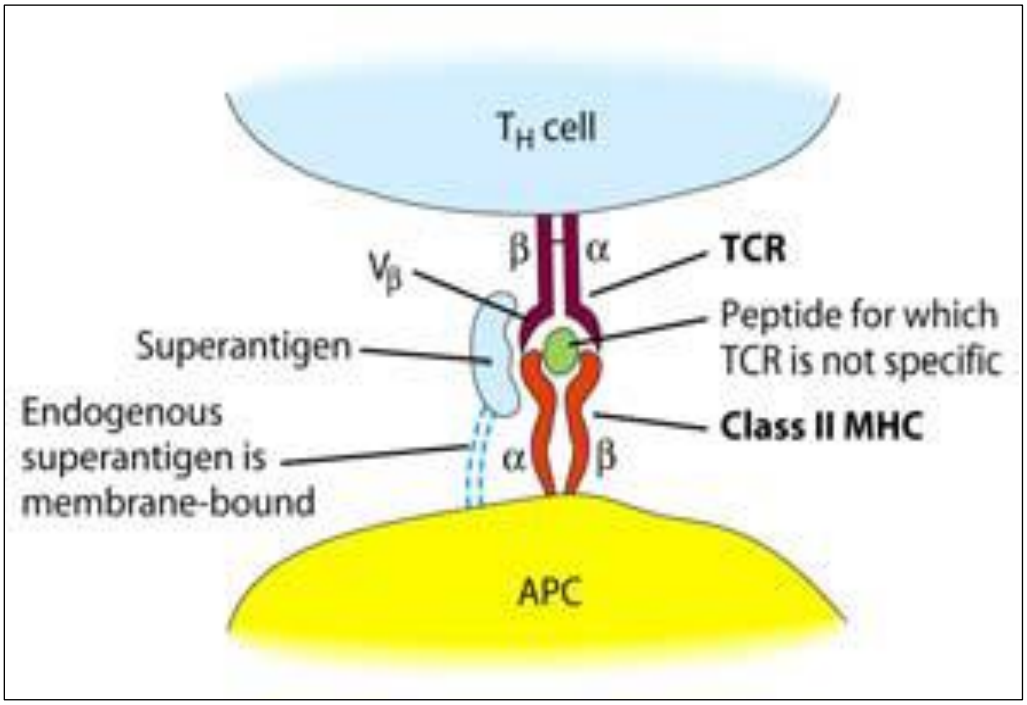


Figure (1): Superantigens

Lecture 9

Antibodies

An antibody is a protein component of the immune system that circulates in the blood, recognizes foreign substances like bacteria and viruses, and neutralizes them. After exposure to a **foreign substance, called an antigen**, antibodies continue to circulate in the blood, providing protection against future exposures to that antigen.

Antibody is a part of the host cell's defense. **It's made by a certain type of white blood cell that's called a B cell**.

The structure of the antibody consists of: two light chains and two heavy chains, and at the very tip of the antibody is a hypervariable region, and this hypervariable region allows the antibody to make different types of antibodies that will respond to all of the antigens that will attack the body.

An antigen is anything that is foreign to the human body. It can be a virus, it can be bacteria, and in some cases your own body will appear as foreign. And so you can have in certain instances where your own body will make antibodies against parts that are part of your body, figure (2).

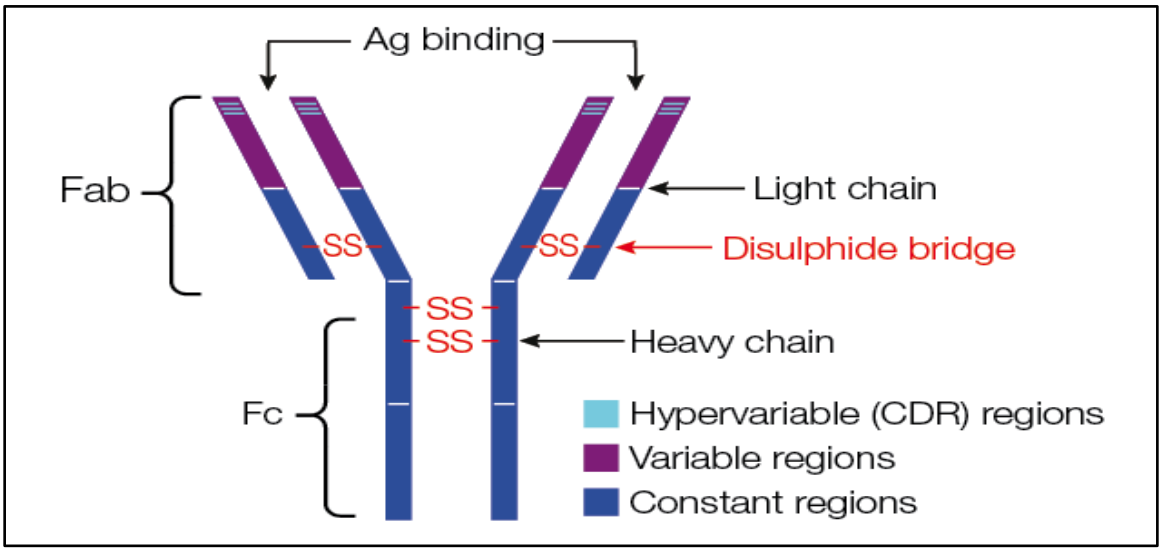


Figure (2): The structure of the antibody

Immunoglobulin (Igs) group of complex protein related with Ab function present in blood or secretion produce in lymphoid organs such a (liver, bone marrow) as a result of activated by specific Ag Igs can be sub divided according to different antigenic properties to five classes (IgG ,IgM ,IgA ,Igd,Ige) Igs they include different chemicals structure binding with different Ags, figure (3).

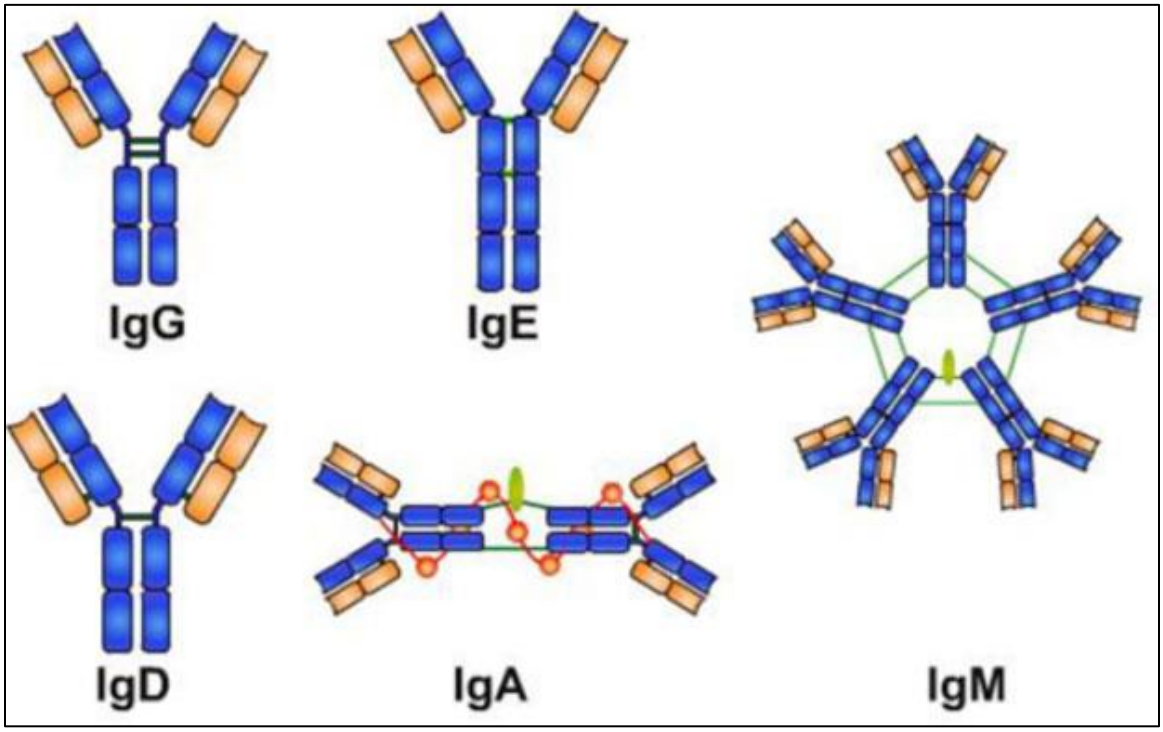


Figure (3): The types of Abs

1- **IgG**

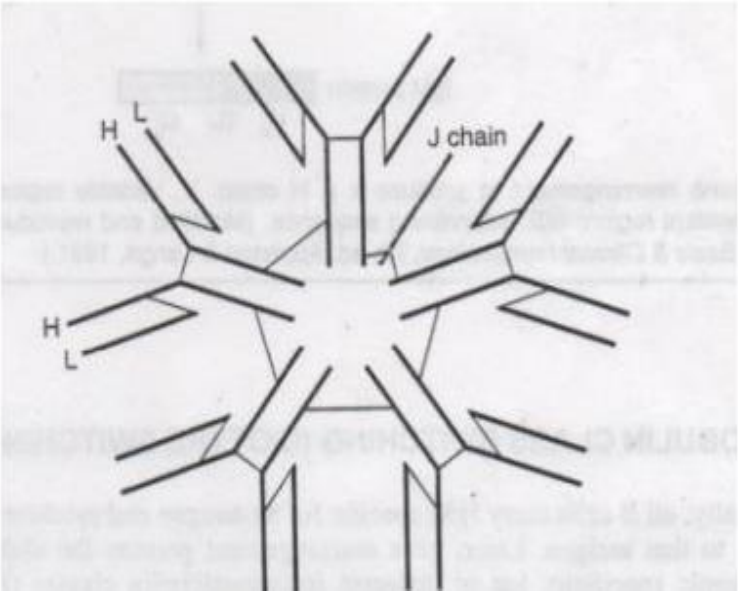
Is the most **abundant Ab in blood & tissue fluid** surrounding cells. Basic structure of Immunoglobulin.

Only Ab that normally transmitted cross the placenta from mothers blood to the fetal circulation IgG called maternal Ab (give some resistance to pathogen) . The different between the domine constant region of H chain response for sub divided IgG to 4 sub class (IgG1, IgG2, IgG3, IgG4) , and variable arrangement of the disulphide bonds .

2- IgM

Also known (Macroglobulin) consist of 5 units each unite similar to IgG & another polypeptide called (J) chain .

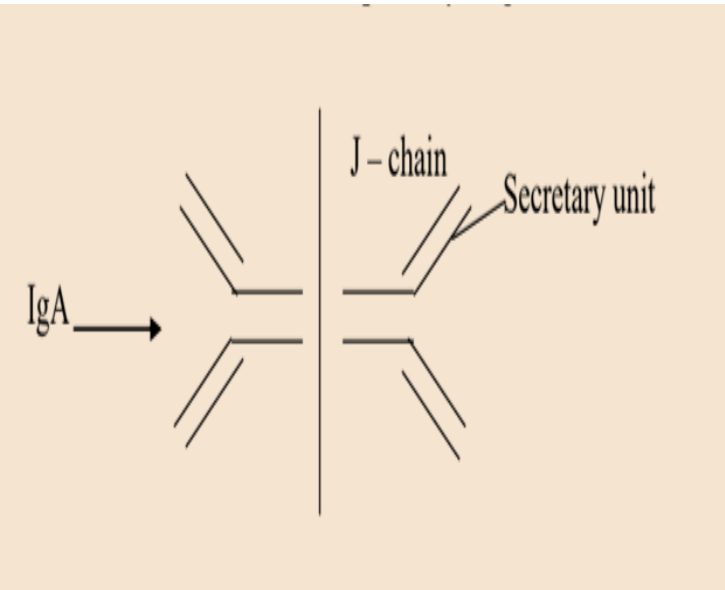
IgM :- Ab are **first Ab molecules that synthesis by the Initial stimulation**. IgG & IgM together responsible for most of activation associated with Ab-Ag function.



3- IgA

present in blood Mucous & other secretions .There are two sub class IgA1 & IgA2 . Some IgA is dimer units bind together by polypeptide called (J) chain with second polypeptide called secretor protein that attached IgA which transported by (Epthelial cells) to tears , saliva. Mucous of respiratory & gastrointestinal tract .

Attachment of the IgA with secretary segment and lead to resisted to proteinase enzyme and give the dimmer form in the mucous surface. **IgA inhibit the attachment of M.o. to the surface of mucosal cell and preventing to entry in to the body.**



‘S form is found in secretions (example: Saliva, milk, and tears) and fluids of the respiratory and genital tracts. IgM opsonizes indirectly by activating complement. This produces C3b, with is an opsonin.

Lecture 10

Autoimmunity

Autoimmunity is the system of immune responses of an organism against its own healthy cells, tissues and other body normal constituents. Any disease resulting from this type of immune response is termed an "**autoimmune disease**". There are more 80 type of autoimmune disease .

Examples:

1- Diabetes mellitus type 1 (DM Type 1)
2- Rheumatoid arthritis (RA)
3- Scleroderma (Hard skin): Excessive production of collagen in skin and tissues of body.

The Factors Caused Self reaction:-

1) Genetic factors: most increase in family with history of Autoimmune disease .

2) Environmental factors: such as mutation, radiation, chemotherapy.

3) Chemical factors: which bind to the self & stimulate immune-reaction to self (self to non self) such as autoimmune hemolytic anemia & sensitive to penicillin .

4) Age factors: increased with increase age due to the disappear of

immune control .

The Mechanism of occurrence of Autoimmune diseases :

1- Ag role :-

a) Role of endo-Ag :

Such Ags disappear like thyroid gland, Brain protein, the immune system not recognized during labeling of lymphocytes & appearance led to know & occur autoimmune reaction such as thyroids disease .

b) Role of exo-Ag :

Such Ag of strep. pyogens similar to Ag present in hart & cause rheumatic fever.

2) the role of (T&B) lymphocytes :

Auto reaction limit under T cell & any problem in T cell start to infect the self. B- lymphocyte produce auto Abs and T-lymphocyte infect the self .

3) The role of MHC type :

Such as Hashimoto's disease is an autoimmune disorder affecting the thyroid gland it is. In Hashimoto's disease, immune-system cells lead to the death of the thyroid's hormone-producing cells. The disease usually results in a decline in hormone production (hypothyroidism). The primary treatment is thyroid hormone replacement.

MHC (mixed histocompatibility complex) cluster of three classes of Ags genes Long arm of [chromosome 6 in human] (chromosome 17 in mouse)

map of human MHC code for three classes of protein & gluco oxidase locus (Glo).

4) Such as invading viral such as EBV caused auto reaction

Symptoms:

Symptoms of autoimmune disease similar include fatigue, muscle ache and low fever.

The classic sign of an autoimmune disease is inflammation that causes redness, heat, pain and swelling.

Treatment:

The goals of treatment are:

1. Reduce inflammation and control the autoimmune process.
2. Reduce immune overactivity.

Medical intervention techniques:

a. Hormone replace therapy
b. Blood transfusions
c. Anti-inflammatory medication
d. Pain medication
e. Immunosuppressive medication
f. Physical therapy

Lecture 11

Transplantation :- transfer of many tissues or organs between different parts of the body or between different individuals.

Autograft:- graft moved to a different part of an animal's own body, such transplants do not trigger an immunresponse. Examples of autografting include the use of skin to cover a burn in plastic surgery and the use of a segment of vein to bypass blocked cardiac arteries.

Isografts:- are grafts transplanted between two genetically identical individuals. Thus a graft between identical twins is an isograft. Similarly, Since the animals are identical, the immune system of the recipient does not differentiate between the graft and normal body cells.

Allografts:- are transplanted between genetically different members of the same species. Most grafts performed on animals or humans for therapeutic reasons are of this type because tissues are obtained from a donor who is usually unrelated to the graft recipient. Because the major Histocompatibility complex (MHC) and blood group molecules on the allograft are different from those of their host, allografts induce a strong immune response that causes graft rejection.

Xenografts:- are organ grafts transplanted between animals of different species. Thus, the transplant of a baboon heart into a human infant is a xenograft. Xenografted tissues differ from their host both biochemically and immunologically. As a result, they can provoke a rapid, intense rejection response that is very difficult to suppress.

Mechanisms of tissue rejection :- Allografted organs represent a major source of these foreign molecules. They include antigens such as the foreign blood group and MHC molecules expressed on the grafted cells The response to MHC antigens on another individual's cells is one of the strongest immune responses known. The acute response to donor histocompatibility antigens causes acute rejection and is mainly mediated by cytotoxic T cells attacking graft vascular endothelium. Chronic rejection and rejection directed against donor blood groups is mainly antibody mediated. The mechanisms of allograft rejection are basically depended on synergism action between antibodies and T cells.

Lecture 12

Hypersensitivity:- (Allergy)

it is acquired state develops as a result of exposure to some environmental against that cause harmful effect to the normal immune system. Excessive stimulation of the effectors leads to tissue damage.

There are five main types of hypersensitivity:

1-Type 1 hypersensitivity reaction

Type 1 hypersensitivity causes an immediate response and occurs after a person has exposure to an antigen. With this type of reaction, the body responds to an antigen by producing a specific type of antibody called IgE.

There are different components that can trigger type 1 hypersensitivity responses, including antigens that come from:

- food products, such as nuts, shellfish, and soy
- animal sources, such as cats, rats, or bee stings
- environmental sources, such as mold, latex, and dust
- allergic conditions, such as allergic rhinitis, allergic asthma, and conjunctivitis

Some physical symptoms of type 1 hypersensitivity can include: rash, flushing, hives, itching, edema, wheezing, rhinitis, stomach cramps.

Responses can also cause: nausea and vomiting, shortness of breath, cardiac symptoms

Type 2 hypersensitivity reaction

Similar to type 1, type 2 hypersensitivity reactions also involve antibodies. In fact, type 2 and type 3 hypersensitivity both result from the same class of antibody, called IgG. The difference between them lies in the form of antigens that generate a response. Additionally, type 2 can also involve IgM antibodies.

Type 2 hypersensitivity causes cytotoxic reactions, meaning that healthy cells die as they respond to the antigens. This can cause long-term damage to cells and tissues, resulting in conditions such as:

- the blood disorder immune thrombocytopenia if there are not enough platelets
- autoimmune hemolytic anemia if the red blood cells burst
- autoimmune neutropenia if the body destroys neutrophils
- autoimmune conditions such as Graves' disease

Type 3 hypersensitivity reaction

In type 3 hypersensitivity, antigens and antibodies form complexes in the skin, blood vessels, joints, and kidney tissues. These complexes cause a series of reactions that lead to tissue damage.

Causes of a type 3 hypersensitivity reaction can include:

- drugs that contain proteins from different organisms, such as antivenins
- animal sources, such as insect stings or tick bites

Type 3 hypersensitivity reactions can lead to: serum sickness, rheumatoid arthritis.

Type 4 hypersensitivity reaction

Unlike the other types, type 4 hypersensitivity reactions are cell-mediated.

Instead of antibodies, white blood cells called T cells control type 4 hypersensitivity reactions. This type also differs from the other three in that it causes a delayed reaction.

The three subsets of type 4 hypersensitivity are as follows:

- contact dermatitis
- tuberculin-type hypersensitivity
- granulomatous-type hypersensitivity

Some common causes of type 4 hypersensitivity reactions include exposure to poison ivy, certain metals, and drugs such as antibiotics or anticonvulsants.

AIDS (Acquired immuno deficiency syndrome)

The detection of Ab to human immunodeficiency virus (anti-HIV-test)

AIDS :- It is an acquired failure of the immune system, transmission of the disease through infection with blood of serum.

Signs :-

1- repeated infection with microorganism.

2-Patient with aids have repeated infection with Candida Spp (fungus).

3-Dicrease in No. of the T. helper .