DEFENCE MECHANISM OF THE BODY

UNIT-3

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What is antimicrobial resistance?

- Antimicrobial resistance (AMR) is resistance of a microorganism to an antimicrobial medicine to which it was originally sensitive. Resistant organisms (they include bacteria, fungi, viruses and some parasites) are able to withstand attack by antimicrobial medicines, such as antibiotics, antifungals, antivirals, and antimalarials, so that standard treatments become ineffective and infections persist increasing risk of spread to others. The evolution of resistant strains is a natural phenomenon. The misuse of antimicrobial medicines accelerates this natural phenomenon. Poor infection control practices encourages the spread of AMR.

Resistance increase if?

- Anti microbial drug is used in sub therapeutic dose
- Improper indication
- Duration of therapy is less than the standard therapy

Sensitivity /Susceptibility

- **Antibiotic sensitivity** is the susceptibility of bacteria to antibiotics
- 'The "susceptible" category implies that isolates are inhibited by the usually achievable concentrations of antimicrobial agent when the recommended dosage is used for the site of infection.

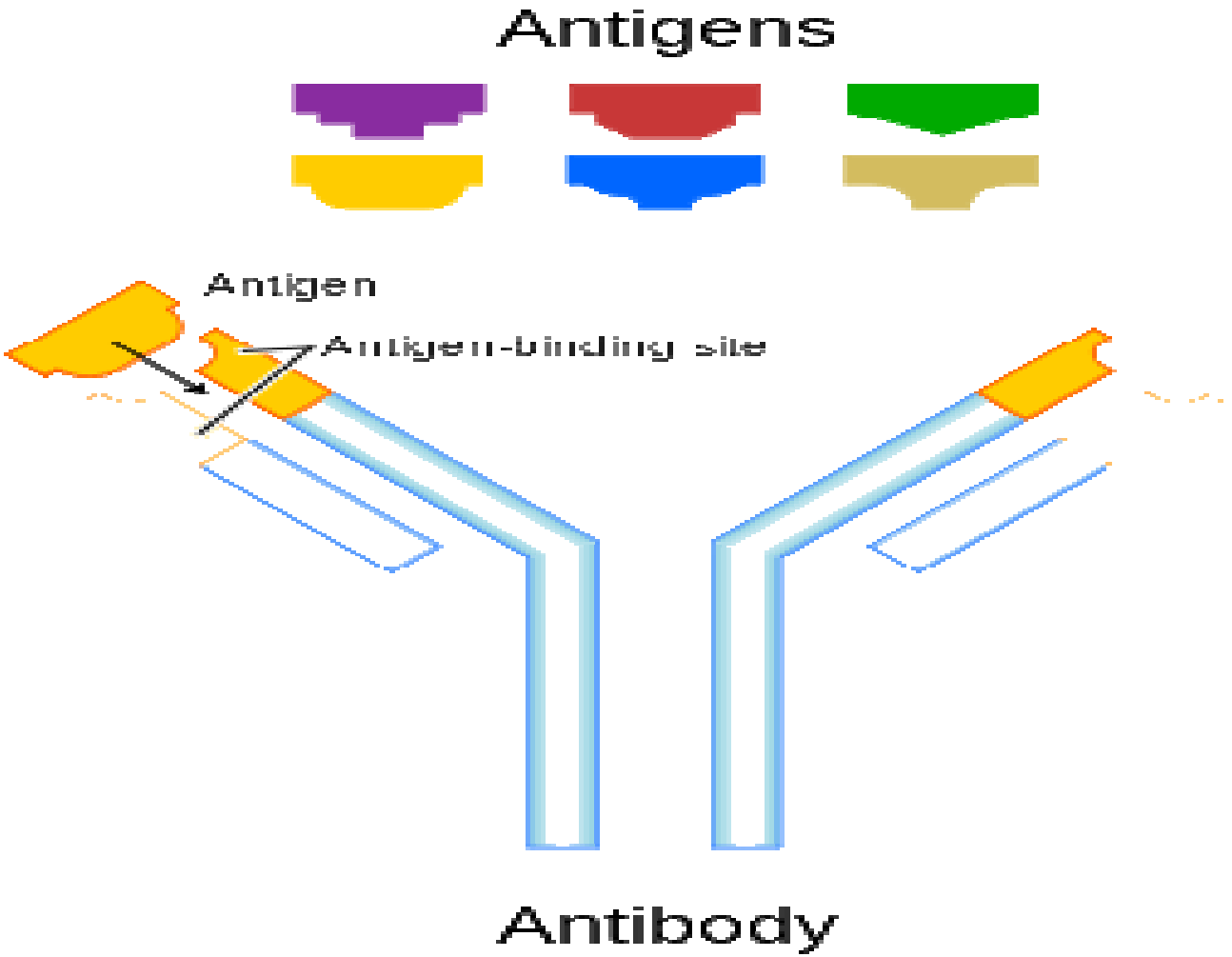
Phagocytosis

- **Phagocytosis** (from Greek phagein) , means "to eat up (cyto) , means "cell", and *-osis*, means "process") is the process by which a cell engulfs a solid particle to form an internal vesicle known as a phagosome.
- Phagocytosis is a specific form of endocytosis involving the vesicular internalization of solids such as bacteria, and is therefore distinct from other forms of endocytosis such as the vesicular internalization of various liquids (pinocytosis).
- In the immune system, phagocytosis is a major mechanism used to remove pathogens and cell debris. For example, when a macrophage ingests a pathogenic microorganism, the pathogen becomes trapped in a phagosome which then fuses with a lysosome to form a phagolysosome. Within the phagolysosome, enzymes and toxic peroxides digest the pathogen.

Antibody

- ***Antibody*** (Ab), also known as an **immunoglobulin** (Ig), is a large Y-shape protein produced by plasma cells that is used by the immune system to identify and neutralize foreign objects such as bacteria and viruses. The antibody recognizes a unique part of the foreign target, called an antigen.Each tip of the "Y" of an antibody contains a paratope **(**also called an antigen-binding site, is a part of an antibody which recognizes and binds to an antigen) that is specific for one particular epitope (the part of an antigen molecule to which an antibody attaches itself) on an antigen, allowing these two structures to bind together with precision. Using this binding mechanism, an antibody can *tag* a microbe or an infected cell for attack by other parts of the immune system, or can neutralize its target directly (for example, by blocking a part of a microbe that is essential for its invasion and survival). The production of antibodies is the main function of the humoral immune system.

Antigen & Antibody



ANTIBODIES

- Antibodies are proteins made up of two light chains and two heavy chains. The heavy chain determines the type of antibody class and is bound to the light chain by sulfhydryl linkages.
- Antibodies are composed of a light chain protein and a heavy chain protein that come together and form a Y-shaped structure. The base of the Y is a conserved region that all antibodies have in common, while the tips of the forks of the Y are unique to each antibody. The tips react with the antigen, while the conserved base interacts with the immune system.
- Five types of antibodies are formed in the body: IgG, IgM, IgA, IgD and IgE

ANTIBODIES

- Antibodies have the interesting challenge of needing to respond to a wide array of antigens, yet still be recognizable to the immune system. They therefore, need to interact with two different types of macromolecules, antigens and parts of the immune system.
- The upper variable region react with antigen and the lower constant region interact with the immune system.
- Plasma cells synthesize a number of different types of antibodies and these serve different functions for the cell..

Classes Of Antibodies

- The general structure of antibodies falls into just five classes and this is based upon the type of heavy chain present in the antibody.
- Each antibody binds to a specific antigen; an interaction similar to a lock and key.

Immunoglobulin G

- ***IgG*** is the most abundant circulating antibody, making up 80% of the total antibodies and 75% of that found in serum. It contains a single antibody protein complex, with two heavy chains and two light chains. IgG is the second type of antibody synthesized in response to an infection and is the only antibody that can pass through the wall of small blood vessels to access antigens present in the extracellular spaces. It is also the only antibody capable of crossing the placenta in humans, where it confers the mother's immunity onto the fetus and newborn. This immunity protects a baby for the first 6-12 months of its life and allows it time for its own immune system to mature. IgG is particularly effective at attacking extracellular viruses and protein toxins. It helps to prevent the systemic spread of infection and facilitates recovery from many infections. Finally, IgG is the antibody that serves as an efficient handle for phagocytes, allowing phagocytes to bind to a pathogen and rapidly phagocytize a pathogen.

Immunoglobulin M

- ***IgM*** is the largest antibody, with five Y structures being joined by their Fc regions in a circular configuration. A J chain (another polypeptide) links the five antibodies together. IgM is present in serum, making up about 10 % of antibodies in the blood. The presence of its ten antigen reactive sites helps agglutinate or clump antigens .making it easier for the immune system to eliminate them. IgM is more efficient than IgG at activating the complement pathway. IgM is synthesized by plasma cells early in a primary infection and is very important in slowing or stopping the spread of a pathogen during the initial stages of an illness. IgM is also found on mature B cells in a monovalent form, where it serves as a receptor.

Immunoglobulin A

- ***IgA*** is present in serum, mucus, saliva, tears, sweat and milk. Two subclasses with different heavy chains are made, IgA1 and IgA2. IgA1 is synthesized in the bone marrow and makes up most of the serum IgA. IgA2 is synthesized by B cells. The antibodies are synthesized as dimers that are joined by a short J chain polypeptide. As the secreted IgA2 passes through the intestinal epithelium, a second secretory protein attaches. Dimerization and binding of the J and secretory proteins make IgA more resistant to proteases present in the environments that it protects. IgA in breast milk interferes with the colonization of the GI tract by harmful microorganisms in the first few months of life. The mother's IgA in the GI tract of newborns keeps these pathogens at low populations, preventing them from causing serious disease, but still allowing the stimulation of the infant's own immune system. The newborn thus develops its own immunity while being partially protected by the mother. IgA molecules do not activate the classical complement pathway, but may activate the alternative complement pathway.

Immunoglobulin E/D

- ***IgE*** is a monomeric antibody that accounts for only 0.002 % of the total serum antibodies. Almost all IgE is bound to tissue cells, especially mast cells and eosinophils in various parts of the body. Contact of IgE with antigen leads to release of a set of signal molecules from the mast cells, which effectively recruits various agents of the immune response to fight the infection. IgE and MALT serve to detect penetrating pathogens and amplify the immune response in an area leading to the repulsion of the invader. Antigen reactions with IgE are also responsible for atopic allergic reactions (e.g., hives, asthma, hay fever etc.)
- ***IgD*** is found on the surface of B-lymphocytes and together with monomeric IgM, serves as antigen receptor for the activation of B cell as described previously. IgD is monovalent.

Difference between innate immunity, and acquired immunity

- Innate immunity-Non-specific
- Inborn
- Acquired from mother

- Acquired immunity-Specific
- Which is acquired after a specific antigen exposure
- Eg..exposure to small pox, chiken pox etc

Specific resistance

- Also known as (Acquired Immunity).
- It is a type of immunity which is very much specific.
- Its against a specific type of antigen (foreign object).
- AB(antibody) mediated.

Antigen(Ag)

- A substance the body recognizes as FOREIGN and to which it mounts IMMUNE response
  -Non-self
  -Immunogenic: Stimulates an immune response(immunogen)
  -Reactive: reacts w/ immune response
  -Large complex molecules

Nonspecific resistance(Innate Immunity)

- -Physical barriers
- -Chemical barriers
- -Cellular defenses-phagocytes & phagocytosis
- -Inflammation
- -Fever

Antibodies

- (Ab) are
- -Proteins that circulate in the bloodstream
- -Immunoglobins
- -Synthesized and secreted by plasma cells
- -B lymphocytes that circulate in the bloodstream and synthesize & secrete Ab
- -Each Ab is specific for a particular antigen
- -React w/ Ag ; Ex: toxins, viruse

Primary Ab response

- -Occurs first time an Ag is encountered
- -Ab begins to appear in ~5days
- -First Ab is IgM, then it decreases
- -Next Ab is IgG, appears in greater amount

Secondary Ab response

- -Occurs at second/subsequent Ag exposure
- -Results from B memory cells
- -Occurs more quickly than primary response
- -Produces more Ab then primary response
- -Last longer then primary response

How do antibodies work?

- (Opsonize)
- enhance phagocytosis
  -Ab is an opsonin, a handle for phagocytosis
- make (cells) more susceptible to the action of phagocytes
- (agglutinate)
- Clump particles together, making them easier to phagocytose
- united as if by glue
- (precipitate)
- Clump soluble molecules together, making them easier to phagocytose.
- Separate it just like a solid substance in suspension or after settling or filtering
- (Activate complement)
- Forms MAC(memory attack complex) resulting in Lysis, killing of pathogens

Types of acquired immunity

- Passive-Immune response provided to the host.
- Eg…breast feeding provides anti bodies

- Active-Immune response develops within the host.
- Eg…if some antigen comes inside the body, response is developed.

- Natural-Immune response develops naturally.
- Eg.. Against measles

- Artificial-Immune response develops after an intentional or purposeful action.
- Eg.. Vaccines

What is natural,active immunity?

- Exposure to infectious agent, or occurrence of infection
- Clinical or subclinical disease can trigger immune response.

- Eg (measles)

What is Artificial, active immunity

- Ex: immunization, vaccine in the form of live attenuated or killed agents.

What is natural, passive immunity

- Maternal Ab provided to fetus/newborn
- Ab crosses the placenta(protects for 3-6 months)
- Ab in colostrum & breast milk, protects G.I. tract

What is Artificial, passive Immunity

- Administration of preforms Ab to a host
- Antiserum, hyperimmune serum, immune globulin, or gamma-globulin
- E.g Tetanus immune globulin, Rabies immune globulin.

Hypersensitivity

- **Hypersensitivity** (also called **hypersensitivity reaction** or **intolerance**)
- It refers to undesirable reactions produced by the normal immune system, including allergies and autoimmunity.
- These reactions may be damaging, uncomfortable, or occasionally .
- An excessive or abnormal sensitivity to a substance.
- A person who is hypersensitive to a certain drug will often suffer a severe allergic reaction if given the drug.

Immediate (type I) hypersensitivity

- Immediate hypersensitivity is a rapid IgE- and mast cell-mediated vascular and smooth muscle response that occurs in genetically susceptible individuals upon exposure to certain environmental antigens to which they have been previously exposed.
- These reactions are also known as allergies, and the antigens that invistigate these reactions are commonly called allergens. The manifestations of these reactions can range in severity from mild hay fever or allergies to pet dander, to severe anaphylaxis brought on by ingestion of drugs such as penicillin or injection with insect venoms. Allergies are the most common disorders of the immune system and may affect up to 20% of the population.

Type 4 - Cell-mediated (Delayed-Type Hypersensitivity, DTH)

- Type 4 hypersensitivity reactions are often called delayed type as the reaction takes two to three days to develop. Unlike the other types, it is not antibody mediated but rather is a type of cell-mediated response.

- glycoprotein found on the surface of immune cells CD8+ cytotoxic T cells and CD4+ helper T cells recognise antigen in a complex with either type 1 or type 2 major **histocompatibility** (compatibility between the tissues of different individuals, so that one accepts a graft from the other without giving an immune reaction)complex. The antigen-presenting cells in this case are macrophages which secrete IL-1) is an **interleukin**, a type of cytokine signaling molecule in the immune system, which stimulates the proliferation of further CD4+ T cells

- CD4(**CD4** (cluster of differentiation 4) is a glycoprotein found on the surface of immune cells such as T helper cells, monocytes, macrophages, and dendritic cells)CD 4+ T cells secrete **IL-2 Interleukin-2** (**IL-2**) is an **interleukin**, a type of cytokine signaling molecule in the immune system. It is a 15,5 - 16 kDa protein that regulates the activities of white blood cells (leukocytes, often lymphocytes) that are responsible for immunity.) IL2 and interferon gamma, further inducing the release of other cytokines, thus mediating the immune response.

- MHC 1 **MHC** class I molecules are **one** of two primary classes of major histocompatibility complex (**MHC**) molecules (the other being**MHC** class II) and are found on the cell surface of all nucleated cells in the bodies of jawed vertebrates. They also occur on platelets, but not on red blood cells MHC 2+ANTIGEN> RECOGNITION BY CD4+ or CD8+ HELPER T CELLS> macrophages release IL-1 > proliferation of further CD4+ > release of IL-2 & interferon gamma > dealed immune response is produced

THE END

THANK YOU STUDENTS