Phagocytosis and Antigens

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Phagocytosis :-

- It means the engulfment of the particles by cells. Phagocytes actually endocytose both particulate and liquid substances .
- The process of phagocytosis is mediated :-

1-Poly morph nuclear leukocyte (microphage) :-

It occur mainly by neutrophils. The ability of these cells to inactivate depends upon many lysosomal enzymes, most of which produce lethal oxygen molecules and many of these enzymes involved in metabolic activities responsible for intracellular bacterial killing utilize essential nutrients and energy for optimal function. while eosinophils and basophils have only a minor phagocytic role.

2 - Mono morph nuclear leukocyte (macrophage) :-

This cells distributed throughout the body both circulating in blood (monocytes) and fixed in the tissue like macrophage of connective tissues ,kupffer cells of the liver ,alveolar macrophages of the lung .

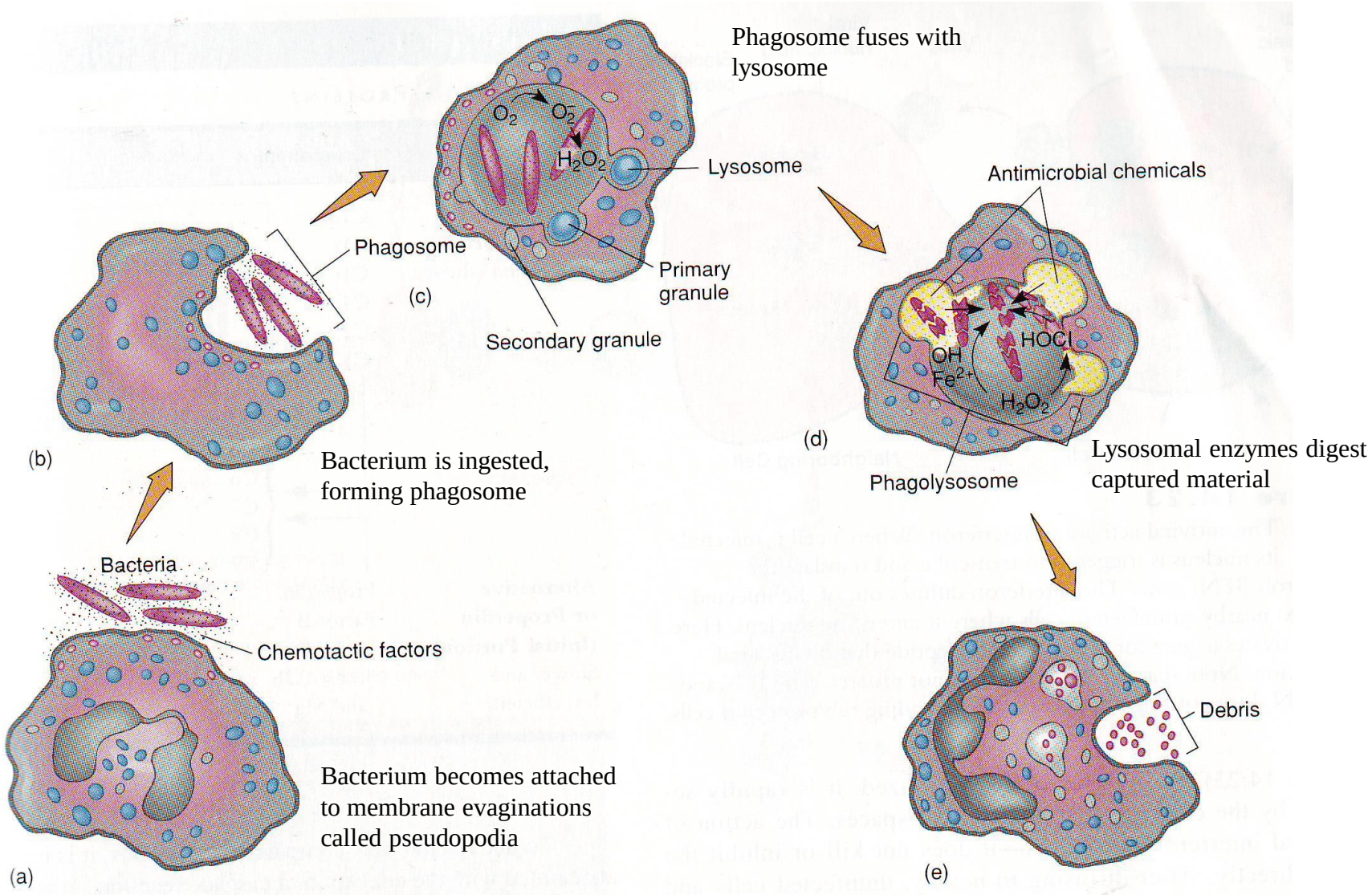
Stage of phagocytosis:-

1-Opsonization and chemo taxis:- is a process that coats the surface of microorganisms with antibodies or complement ,thereby facilitating recognition and engulfment.

2-**Ingestion:-** Once the phagocyte has made contact with antigen ,it extend pseudo pods that enclose the particles in pocket and internalize them in a vacuole called a phagosome.

3-Phagolysosome formation and killing :-Lysosome migrate to the phagosome and fuse with it to form phagolysosome and other granules are release their contact to the phagolysosome ,all of these will be lead to ingestion of the material.

4- **Release of the debris :-** The small bits of indigestible debris are exocytose and released .


Bacteria
Chemotactic factors
(a)
Bacterium becomes attached to membrane evaginations called pseudopodia
(b)
Phagosome
Bacterium is ingested, forming phagosome
(c)
O_2
O_2^-
H_2O_2
Lysosome
Primary granule
Secondary granule
Phagosome fuses with lysosome
(d)
Antimicrobial chemicals
OH
Fe^{2+}
HOCl
H_2O_2
Phagolysosome
Lysosomal enzymes digest captured material
(e)
Debris
Digestion products are released from cell

Mechanisms For Killing Bacteria

- There are many ways in which these cells are able to kill bacteria and other foreign bodies but basically they belong to two categories.

Oxygen dependent
or
Oxygen independent

Oxygen dependent mechanisms

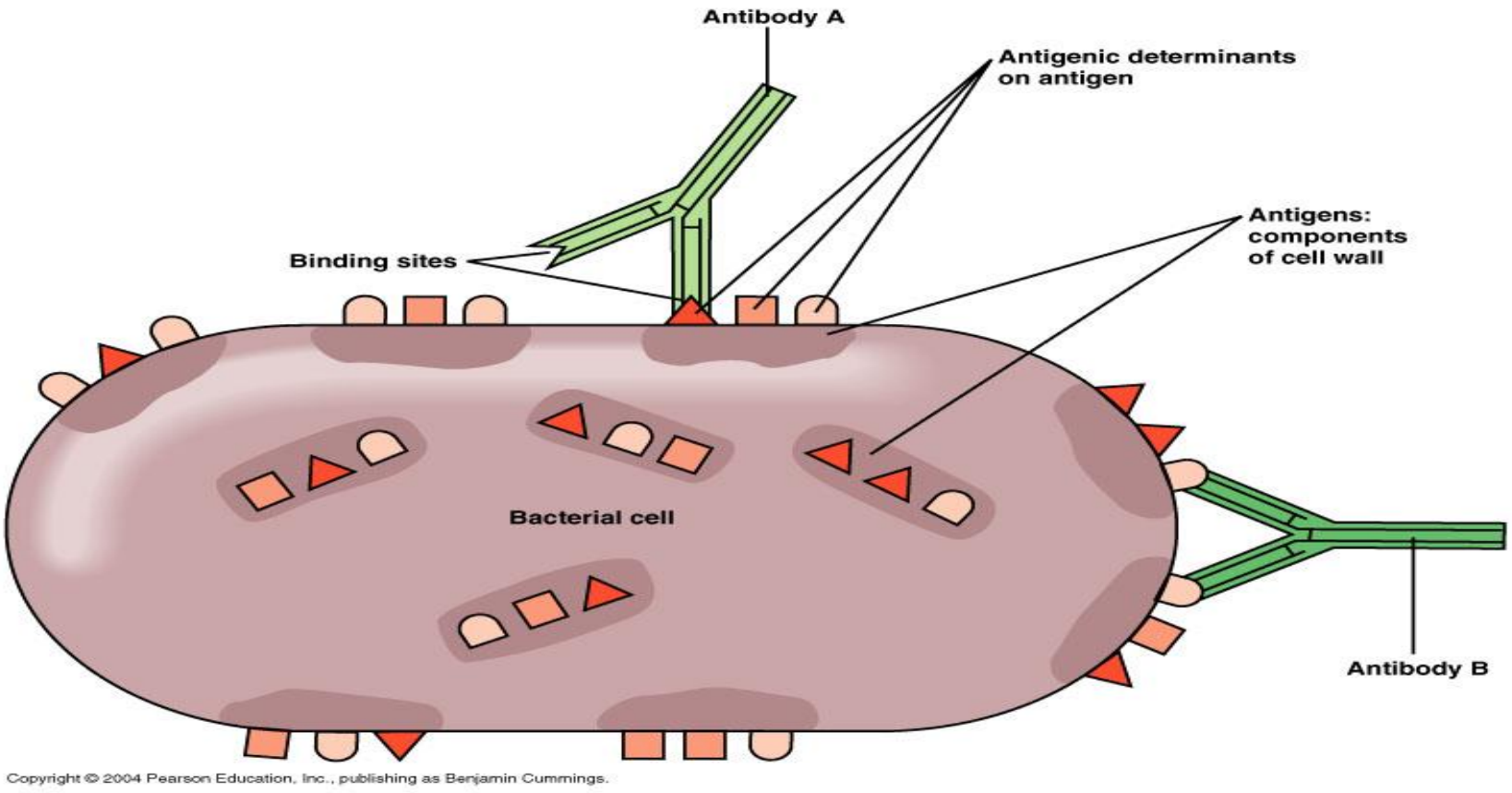
- Oxygen dependent mechanisms basically result from the respiratory burst associated with the act of phagocytosis. This results in the release of two chemicals H2O2 (hydrogen peroxide) and HOCl (hydrochlorous acid)
- These are two very powerful chemicals that are able to break down the protective wall of bacteria and other micro-organisms.

Oxygen independent mechanisms

- **Lysozyme** : an enzyme that attacks cell wall of some bacteria (especially Gram + ve).
- **Lactoferrin** : a chemical which binds onto iron thus inhibiting cell growth especially in bacteria
- **Major Basic Protein (MBP)** : a cationic protein found in eosinophils principally active against parasitic infections such as roundworms, liver flukes etc.
- **Bactericidal Permeability Increasing Protein :** as it's name suggests this substance increases permeability of cell membrane of many micro-organisms making them more vulnerable to attack from other agents of the immune system.
- In addition to this white blood cells produce a lower pH (more acidic) environment which adds to the anti-bacterial properties.

Antigen:-

Any foreign substance when introduced in to a host induces formation of immune response (specific antibodies or T lymphocytes) that react with this antigen. The word originated from **anti-, antibody** and **gen** to **gen**erate



Antigenic determinants (epitopes) :-are small chemical groups called antigenic sites whose chemical and physical nature give specific characteristic of the antigen molecules and against which the immune system form antibody or sensitize lymphocyte .

Immunogenicity & antigenicity:-

Immunogenicity is the ability of a substance (the antigen) *to induce* humoral antibodies or cell mediated (activated T cells).The inducing substance is called an **immunogen**

While **antigenicity** is the ability of a substance *to react* with specific antibodies or activated T cell and the substance is called **antigen**.

All immunogen are antigen , but not all antigen are immunogen. Why???

Characteristics of antigens/ Factors Influencing Immunogenicity

Immunogenicity is determined by:

1. Foreignness

An antigen must be a foreign substances to elicit an immune response.

2. Molecular Size

The most active immunogens tend to have a molecular mass of 14,000 to 6,00,000 Da.
Examples: tetanus toxoid, egg albumin, thyroglobulin are highly antigenic.
Insulin (5700) are either non-antigenic or weakly antigenic.

3. Chemical Nature and Composition

In general, the more complex chemical substance is more immunogenic. Proteins are more immunogenic than polysaccharides.

4. Physical Form

In general particulate antigens are more immunogenic than soluble ones.
Denatured antigens are more immunogenic than the native form.

5. Degradability

Antigens that are easily phagocytosed are generally more immunogenic. This is because for most antigens (T- dependant antigens) the development of an immune response requires that the antigen be phagocytosed, processed and presented to helper T cells by an antigen presenting cell (APC).

6. Dose of the antigen

The dose of administration of an immunogen can influence its immunogenicity. There is a dose of antigen above or below which the immune response will not be optimal.

7. Route of Administration

Generally the subcutaneous route is better than the intravenous or intragastric routes. The route of antigen administration can also alter the nature of the response. Antigen administered intravenously is carried first to the spleen, whereas antigen administered subcutaneously moves first to local lymph nodes.

CHEMICAL NATURE OF IMMUNOGENS

A. Proteins

The majority of immunogens are proteins. These may be pure proteins or they may be glycoproteins or lipoproteins. In general, proteins are usually very good immunogens.

B. Polysaccharides

Pure polysaccharides and lipopolysaccharides are good immunogens.

C. Nucleic Acids

Nucleic acids are usually poorly immunogenic. However, they may become immunogenic when single stranded or when complex with proteins.

D. Lipids

In general lipids are non-immunogenic, they may be haptens.

Types of Antigen

On the basis of immune response

1. Complete Antigen or Immunogen

Posses antigenic properties i.e. they are able to generate an immune response by themselves. Have a high molecular weight (more than 10,000) (may be proteins or polysaccharides)

2. Incomplete Ag

These are the foreign substance, usually non-protein substances. They are unable to induce an immune response by itself, they require carrier molecule to act as a complete antigen.

The carrier molecule is a non-antigenic component and helps in provoking the immune response. Example: Serum Protein such as Albumin or Globulin.

Ex:- Haptens

Haptens can react specifically with its corresponding antibody.

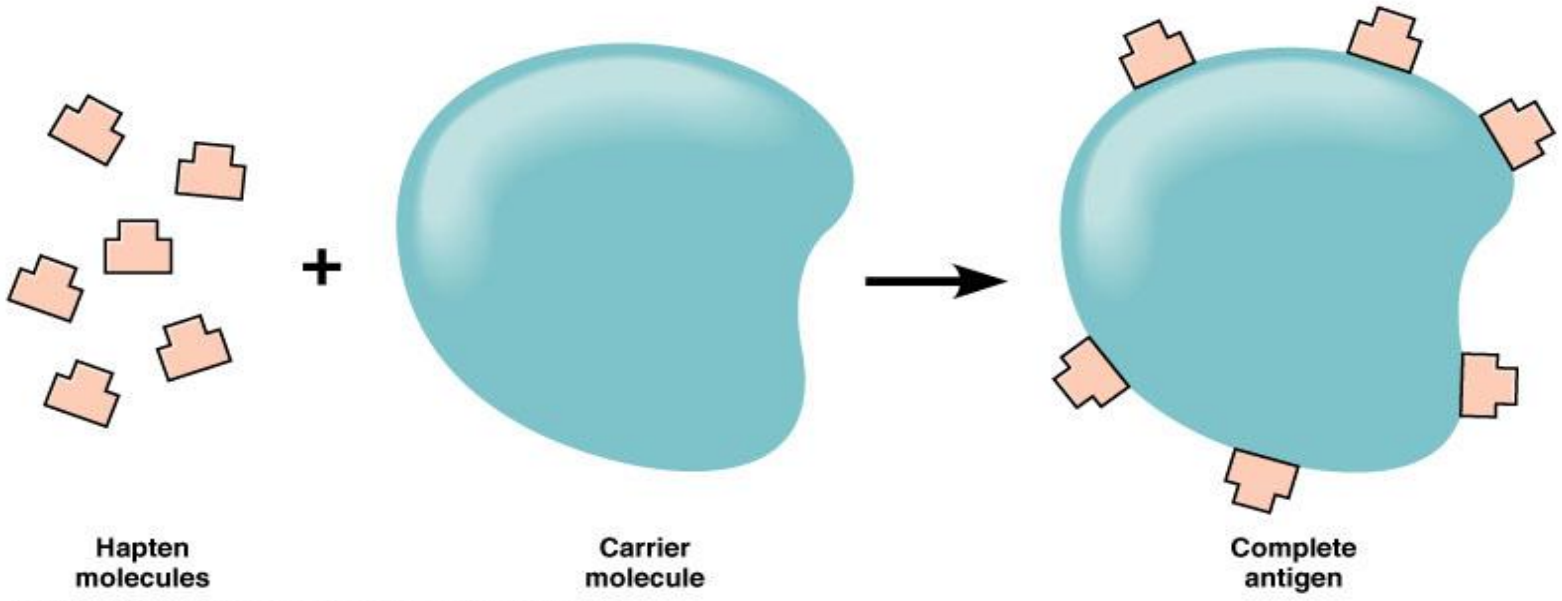
Examples: Capsular polysaccharide of pneumococcus, polysaccharide “C” of beta haemolytic streptococci, cardiolipin antigens, etc.

Hapten :- molecules that can combine with antibody , but cannot induce an immune response unless they are bound to larger carrier molecules(**usually proteins)** .So that the hapten is antigenic but not immunogenic

Hapten is classified according to how many determinants have:

Simple hapten have one antigenic determinant

Complex hapten have two or more of antigenic determinant



3- Tolergen:-

It is antigenic substance that induce tolerance rather than immune responsiveness .ex. low and high dose of antigen

4-Allergen :-

A substance capable of causing an allergic reaction. The reaction may result after exposure via ingestion, inhalation, injection, or contact with skin.

5- Superantigen:-

A class of antigens that cause non-specific activation of T-cells (resulting in polyclonal T cell activation) and massive cytokine release. Examples of superantigens include: Staphylococcal enterotoxins (food poisoning) and Staphylococcal toxic shock toxin (toxic shock syndrome).