
Passion Batch 2019
Microbiology Notes
Lecture Title: Specific and Non-Specific Host Defense
Lecture Number: #25
Done BY:
- Ahmad Daas
- Noor Hussein
Passion
Batch-YU

Phagocytosis

- Engulf (phagocytosis)
- Professional phagocytes (M & N)
- Phagocytic granulocytes (N & E; 1st >> 2nd)
- Monocytes → Macrophages
  - Wandering macrophages
  - Fixed macrophages: Histiocytes in C.T.,
    Liver: Kupffer cells, Brain: microglia
- **Phagocytosis steps**:

Chemotaxis, Attachment, Ingestion, Digestion

Monocytes (macrophages)

neutrophiles

Main phagocytes of human being

Neutrophiles are much more efficient thane eosinophiles

Connective tissue

Monocytes present in the blood
Macrophages present in tissues

Eosinophiles are main phagocytes in allergy and parasitic infections

Table 15-1 Four Steps in Phagocytosis

Step	Brief Description
1. Chemotaxis	Phagocytes are attracted by chemotactic agents to the site where they are needed
2. Attachment	A phagocyte attaches to an object
3. Ingestion	Pseudopodia surround the object, and it is taken into the cell
4. Digestion	The object is broken down and dissolved by digestive enzymes and other mechanisms

Opsonization will help in attachment through anti bodies or complemts (as C3B) or attachment could be direct

[g]Various types of cells within the human body, including cells of the immune system, communicate with each other. They do so by means of chemical messages—proteins known as cytokines. If the cytokines are chemotactic agents, attracting leukocytes to areas where they are needed, they are referred to as chemokines.

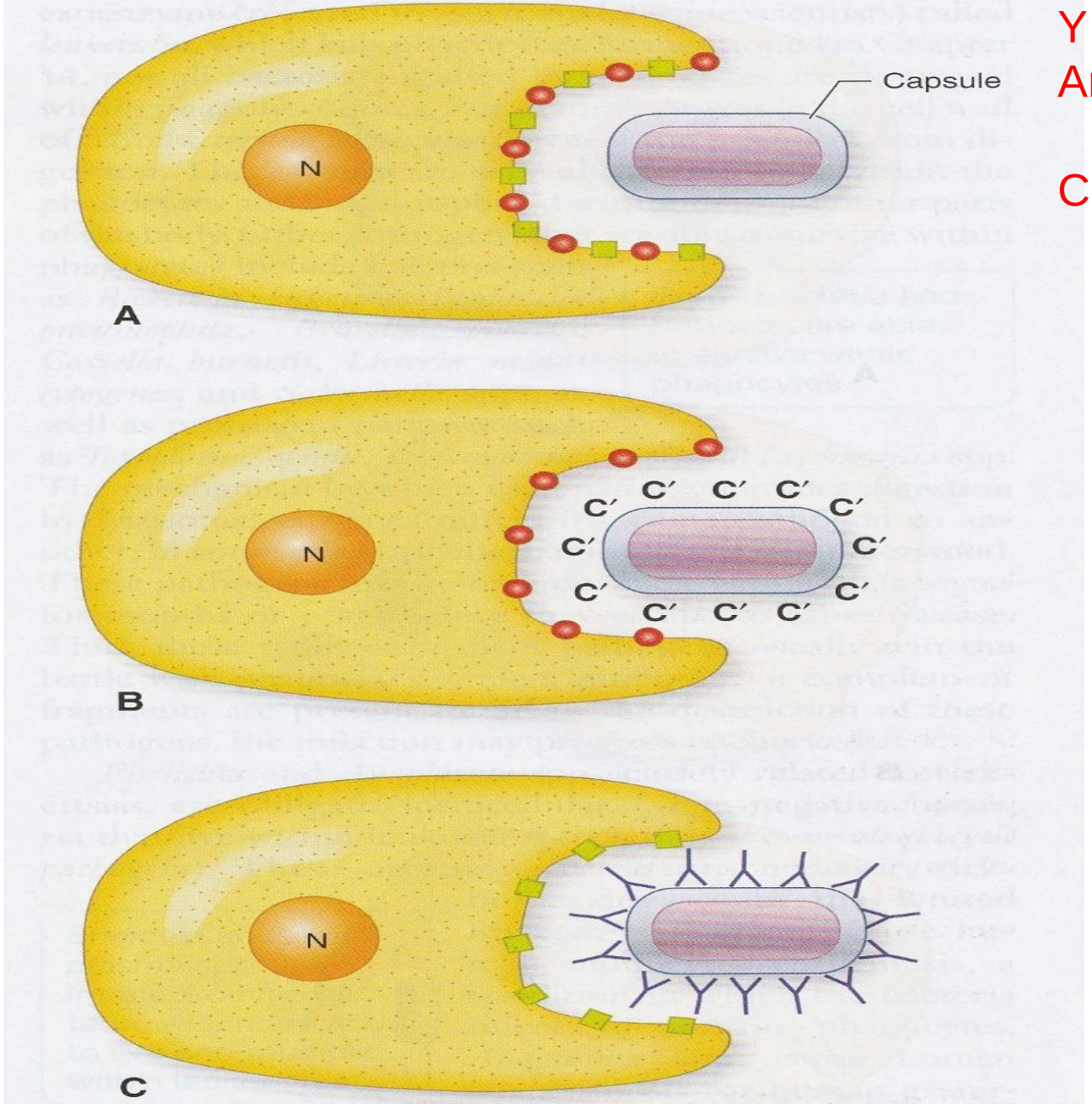
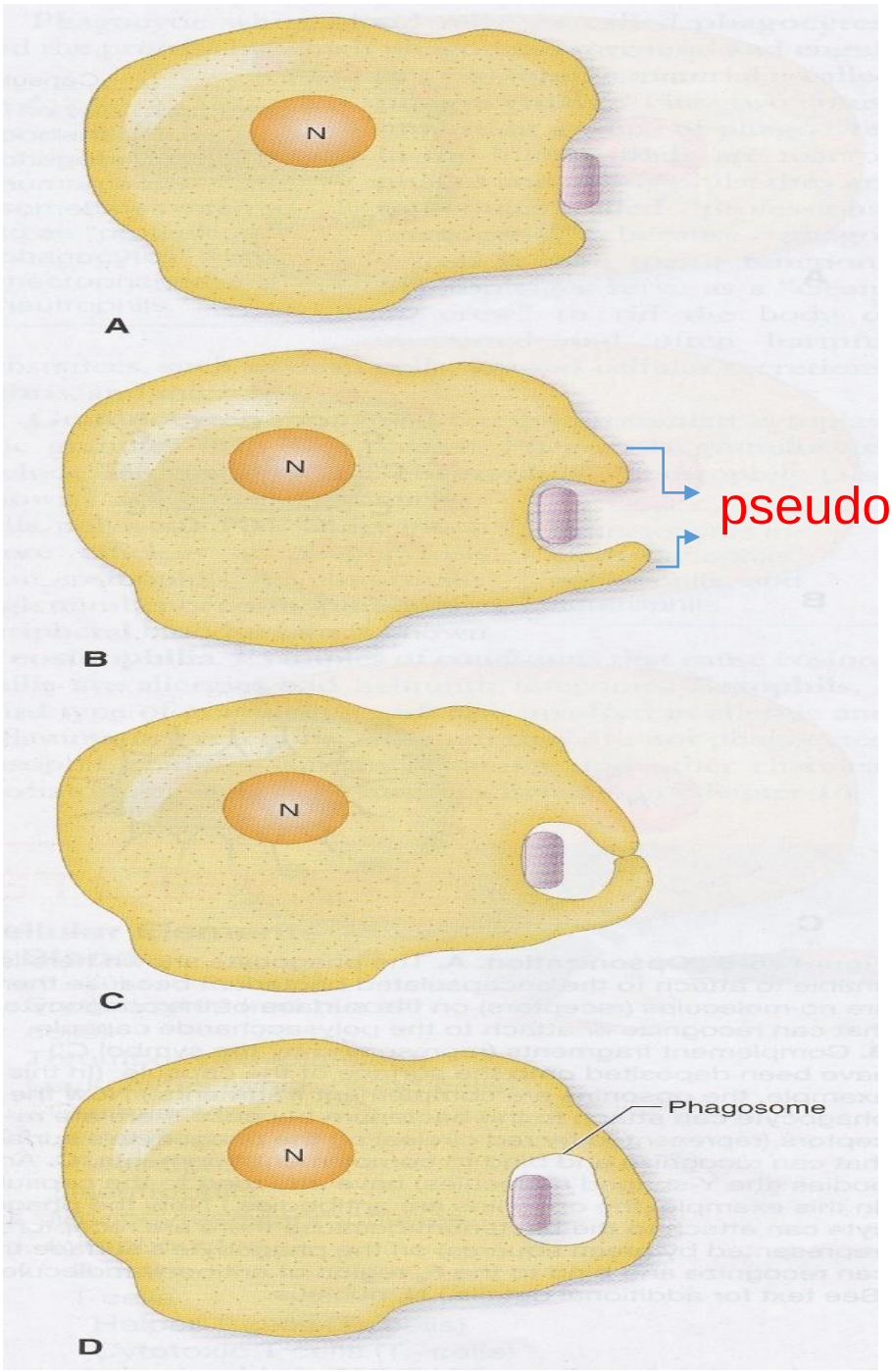
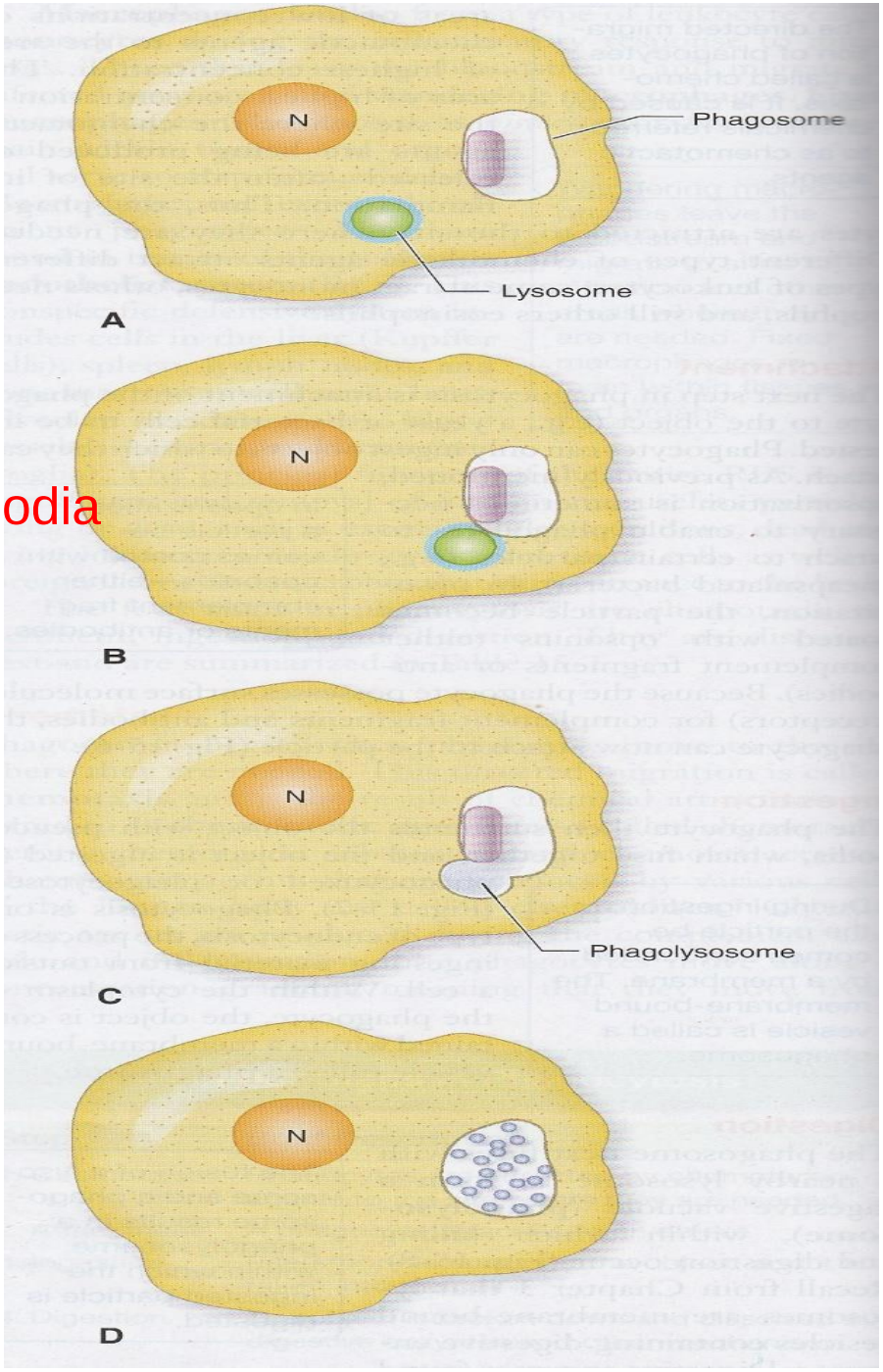


Figure 15-6. **Opsonization. A.** The phagocyte shown here is

Y shaped figure means Anti body

C’ means complement c


N
A
N
B
pseudopodia
N
C
N
Phagosome
D


N
Phagosome
Lysosome
A
N
B
N
Phagolysosome
C
N
D

Pathogens escape destruction

- Capsule: Anti-Phagocytic effect

- One of reason why opsonization help in phagocytosis

- Leukocidin by m.o.: Kills phagocytes

- Such as Micro organism enzymes

- Wax protects: *Mycobacterium tuberculosis*

Has anti phagocytic effect (resist phagocytosis)

- Survival inside phagocytes: Transported

e.g. *Salmonella* spp., *Brucella abortus*,

Toxoplasma gondii, *Leishmania* spp.

causes toxoplasmosis داء القطط

Table 15-2 Additional Factors That Can Impair Host Defense Mechanisms

Factor	Comments
Nutritional status	Malnutrition is accompanied by decreased resistance to infections
Increased iron levels	High concentrations of iron make it easier for bacteria to satisfy their iron requirements; high concentrations of iron reduce the chemotactic and phagocytic activities of phagocytes; increased iron levels may result from a variety of conditions or habits
Stress	People living under stressful conditions are more susceptible to infections than people living under less stressful conditions
Age	Newborn infants lack a fully developed immune system; the efficiency of the immune system and other host defenses declines after age 50
Cancer and cancer chemotherapy	Cancer chemotherapeutic agents kill healthy cells and malignant ones
AIDS	Destruction of the AIDS patient's T_H cells decreases the patient's ability to produce antibodies to certain pathogens (discussed in Chapter 16)
Drugs	Steroids and alcohol, for example
Various genetic defects	B-cell and T-cell deficiencies, for example

Specific Host Defenses
&
Vaccination

(Two Lectures)

BY

Prof. DR. Zainalabideen A. Al-Abdulla,
DTM&H., MRCPI, Ph.D., FRCPath. (U.K.)

Learning Objectives/First Lecture

- Define the following terms: immunology, immunity, antigenic determinant, immunoglobulins, primary response, secondary response, agammaglobulinemia, hypogammaglobulinemia, T cell, B cell, plasma cell, and immunosuppression
- Differentiate between humoral immunity and cell-mediated immunity
- Distinguish between active acquired immunity and passive acquired immunity
- Differentiate between natural active acquired immunity and artificial active acquired immunity and cite an example of each
- Distinguish between natural passive acquired immunity and artificial passive acquired immunity and cite an example of each

Learning Objectives/Second Lecture

- Outline the steps involved in the processing of T-independent antigens and T-dependent antigens
- Identify the two primary functions of the immune system
- Construct a diagram of a monomeric antibody molecule
- Identify and describe the five immunoglobulin classes (isotypes)
- List the types of cells that are killed by natural killer (NK) cells
- Name the four types of hypersensitivity reactions
- Outline the steps involved in allergic reactions, starting with the initial sensitization to an allergen and ending with the typical symptoms of an allergic reaction
- Cite six examples of allergens
- List five possible explanations for a positive tuberculosis (TB) skin test

Immunology

Is the scientific study of the immune system and immune response.

- Immune system: Third line of defense/*Specific*

- Immune response (IR): Complex interactions between different items of immune system

(Details given below)

Antigens (Ag)

Are molecules that stimulates the immune system to produce antibodies. They are commonly proteins (most **potent** antigens).

Could be carbohydrate or combination (proteins are more potent)

Antibodies (Ab)

Are protein (only proteins) molecules that are produced by the immune system in response to antigens. Each antibody is specific for antigene (lock and key)

Functions of the immune system

1. Differentiate between "self" and "non-self" (foreign) antigens (main function)
2. Destroy the non-self antigens

Arms of the immune system

1. Humoral immunity
2. Cell-mediated immunity (CMI)

Immune responce

N.B: "Danger-Model" is a new theory to explain IR on the basis of damaged tissues (1994)?!

Damaged tissue will be attacked by immune system

Intact tissue won't be attacked

Humoral immunity (Antibody-Mediated Immunity "AMI")

- Antibodies (Ab): Play a major role
- Ab: Present in blood/plasma/serum, lymph, body secretions/extracellular fluid, and on surface of some lymphocytes (B-cells) (not all of Them)

Cell-Mediated Immunity (CMI)

- Involve various types of cells
- Antibodies play only a **minor** role (Table)

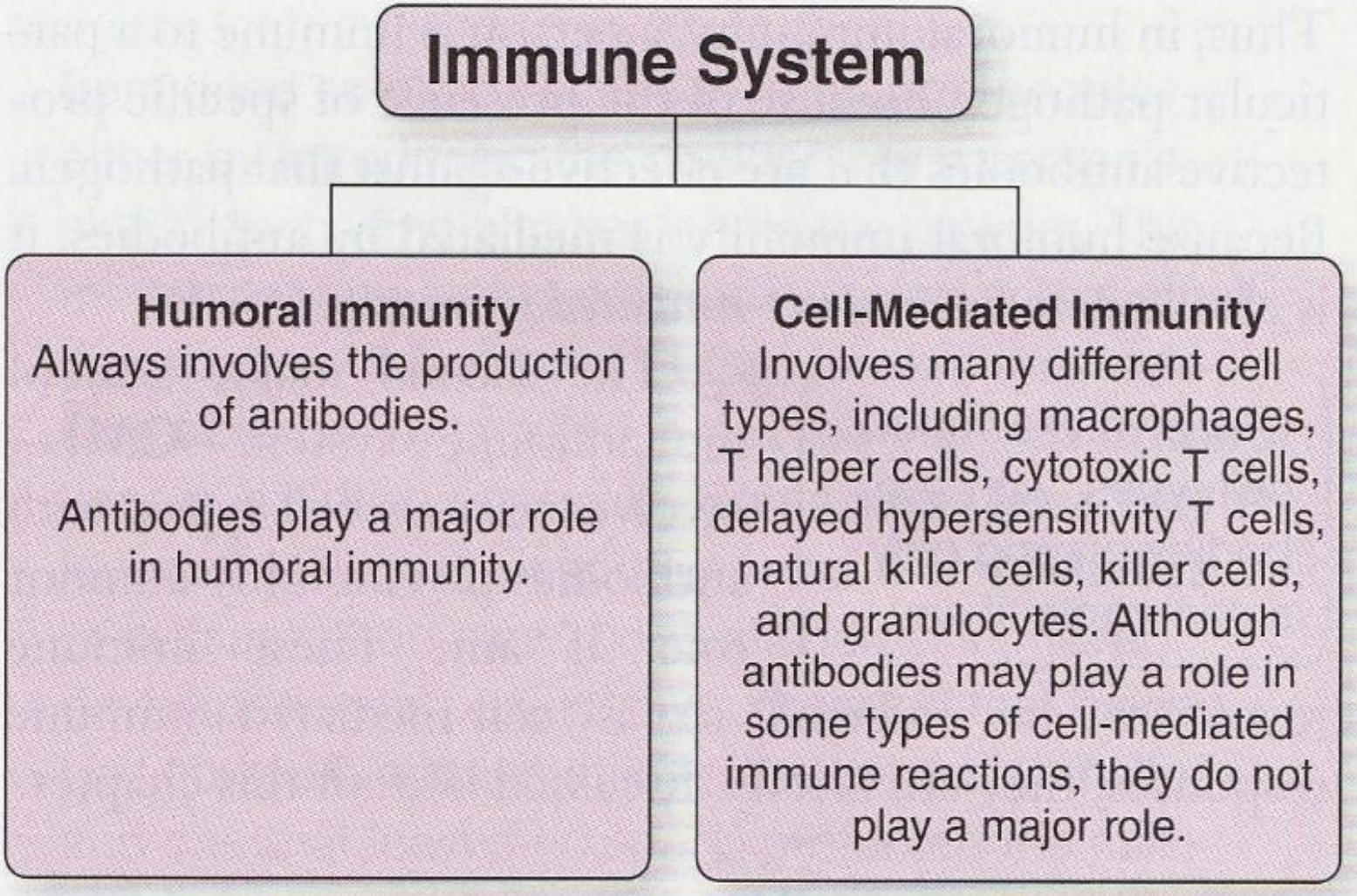


Figure 16-1. The two major arms of the immune system.

Types of acquired immunity (AI)

1. **Active**: Ab produced by the body, long-acting:

   A. Natural: Infections; protective Ab → Anti Body not Anti Biotic ☺

Like some diseases which give the patient immunity against it self

   B. Artificial: Vaccination → which produces Anti Bodeis and memory cells

Edward Jenner, Cowpox

Vacca = Cow

Edward used cow's disease (cowpox) to immunize against human's disease (smallpox)

2. **Passive**: Ab "*received*"; short-lasting: (From outside of the body)

   A. Natural: Mother to fetus (IgG, IgA; 6 m) — IgG during Birth, IgA through breastfeeding

   B. Artificial: Preformed AB to patients,

(Synthetic) eg. after HBV exposure

hepatitis B Virus

Natural Passive Acquired Immunity

- **IgG** is the only Ab can cross the placenta
- Colostrum (Milk few days before/after delivery

causes milk to be yellow

is very rich in secretory **IgA**)

Artificial Passive Acquired Immunity

- Temporary protection (for short time)
- Gamma globulin (pooled immune serum globulin "ISG") e.g. Measles, Mumps, Polio

تم جمعه من أشخاص عاديين

- Hyperimmune serum (high level) e.g. HBIG, (Hepatitis B), tetanus, rabies, botulism

Table 16-1 Types of Acquired Immunity

Active acquired immunity	
Natural active acquired immunity	Immunity that is acquired in response to the entry of a live pathogen into the body (i.e., in response to an actual infection)
Artificial active acquired immunity	Immunity that is acquired in response to vaccines
Passive acquired immunity	
Natural passive acquired immunity	Immunity that is acquired by a fetus when it receives maternal antibodies in utero or by an infant when it receives maternal antibodies contained in colostrum
Artificial passive acquired immunity	Immunity that is acquired when a person receives antibodies contained in antisera or gamma globulin

Vaccine

Material that can artificially induce immunity to infectious disease; injected or ingested (there are other routes).

- Produce Ab and memory cell

Vaccine is "infectous-agent like" with no toxic effect

- Ideal Vaccine:

  - Enough antigenic determinants

(*Ag-surface sites recognized by immune system*)

  - Against all causative strains

  - It does not cause a disease (must be safe in order to use)

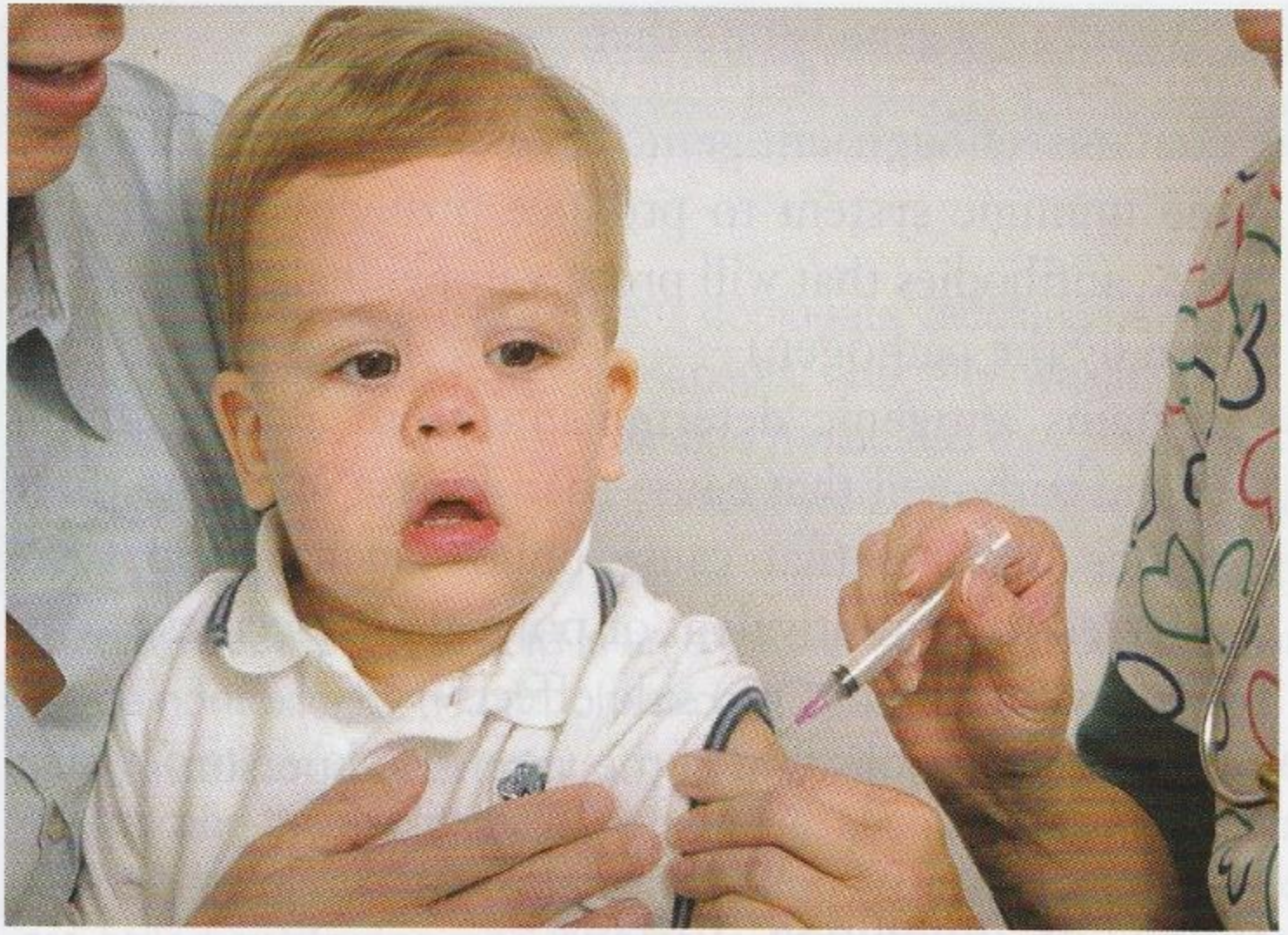


Figure 16-2. Child receiving a vaccine. (Courtesy of Judy Schmidt, James Gathany, and the CDC.)

Types of vaccines

1. Living organisms (harmless or attenuated)
   - Attenuated = Modified/ Weakened
   - Most effective
   - Some given at birth (Hepatitis A & B, Rota, Hib, Polio, MMR, Chicken-pox, Influenza, Pneumococcal, Meningococcal
   - Others: On need, e.g. cholera
   - Antigenic variation: e.g. Influenza virus

We don't kill bacteria because killing it will destroy antigenic determinants

MMR : Measles,mumps,rubella

2. Inactivated (Killed): Weaker/shorter protection

   e.g. Hepatitis A, Rabies, Polio

cont./…

Inactivated (Killed) vaccine is weaker than Living organisms vaccine because some AG's are lost during killing

cont./… types of vaccines

3. Subunit vaccines (acellular) Like Bacteria Capsules
   - Part of a microbe , e.g. Pertussis, *N.gonorrhea*.
   - Genetically produced part, e.g. Hepatitis B surface Ag (*produced in yeasts by genetic engineering*)
4. Conjugate vaccine, e.g. Hib, Pneumococcal (MIXING)
5. Toxoid (detoxified) e.g. Diphtheria, Tetanus

Toxin:Toxic
Toxoid:Untoxic

6. DNA vaccines (e.g. Zika virus, 2016):

DNA or DNA/capsid (Ag) ➡ Human ➡ wide IR

7. Autogenous vaccines- From the same patient:

Isolated m.o. ➡ Killed ➡ Injected ➡ >>Ab against the same bacteria

How vaccines work

1. Antibodies:
    - Anti-Toxin, e.g. anti-tetanus toxin
    - Anti-surface Ag/Pili; Prevent attachment

      e.g. *Neisseria gonorrhoeae*
    - Opsonization (aids in phagocytosis)
    - C activation → Lysis & other effects

complement activation

2. Memory cells (lymphocytes) T or B

    - Very important outcome of vaccination

Cells of the immune system

1. T lymphocytes (T cells)
2. B lymphocytes (B cells)
3. Natural Killer (NK) cells (is also a type of lymphocytes)
4. Macrophages

B.M. ➡ Lymphoid Stem Cells ➡ Lymphocytes (T, B, & NK)

T- cells

Cluster of differentiation

1. T helper (TH) = CD4

IL-2 / IL-12 / IF- γ

Cell mediated immunity

- TH1: Help CMI; produce type 1 cytokines
- TH2: Help B cells (Ab-production), produce type 2 cytokines

-Comes from parents
-Differs between people

- Restricted action with MHC (HLA) class-II

Human leukocyte antigene

Major Histocompatibility Complex

2. T cytotoxic (Tc)- CD8

- Killer: Virally infected cells, foreign cells, tumor cells
- Restricted action with MHC (HLA) class-I

Location of immune response

- Ag in the blood → Spleen
- Ag in tissues → Local L.N. lymph nodes
- Ag via mm (mucous membrane) → Mucosal-associated lymphoid tissues

Examples:

- Intranasal/inhaled Ag → Tonsils/Adenoids
- Ingested Ag → Microfold (M) cells → Peyer's patches of the intestine (part of intestine's villi)

Humoral Immunity :

Antigens

- Antibody-generating surface substances are called antigenic or immunogenic determinants .

Dalton (unit of measurement)

- Proteins (> 10,000 Da) are immunogenic (stimulates immune system, Polysaccharides (> 60,000 Da), or larger DNA or RNA and combinations: glycoproteins, lipoproteins, nucleoproteins

- Best antigen: Proteins (more immunogenic)

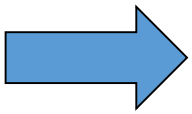
Antigenic determinants (AD) "Epitope"

Are the surface molecules that stimulate the antibody production (> AD // > Immunogenicity) >more stimulation to immune system

Haptens → Small antigens but not immunogenic

Are antigens that can bind antibodies, but can **not** stimulate their production unless coupled to a larger carrier molecule such as protein.

Example:

Penicillin (hapten) **+** Serum albumin (carrier) 

Allergy (**Type-I Hypersensitivity**) in some individuals