ANTIGENS

DEFINITIONS

A. **Immunogen** - A substance that induces a specific immune response.

B. **Antigen (Ag)** - A substance that reacts with the products of a specific immune response.

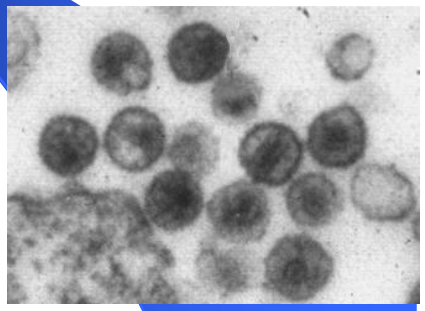
C. **Hapten** - A substance that is non-immunogenic but which can react with the products of a specific immune response. Haptens are small molecules which could never induce an immune response when administered by themselves but which can when coupled to a carrier molecule.

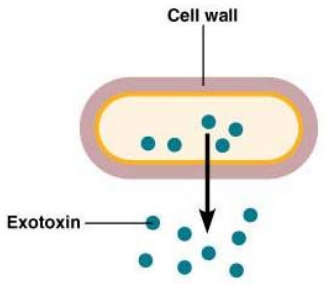
D. **Epitope or Antigenic Determinant** - That portion of an antigen that combines with the products of a specific immune response.

E. **Antibody (Ab)** - A specific protein which is produced in response to an immunogen and which reacts with an antigen.

What can be an Antigen?

- Ags can be:
  1. Foreign substances like micro organisms & its products, toxins etc.
  2. Body's own proteins, expressed in an inappropriate manner like tumor cells, autoantigens, transfused blood or the cells of transplanted organs





Properties of Antigen

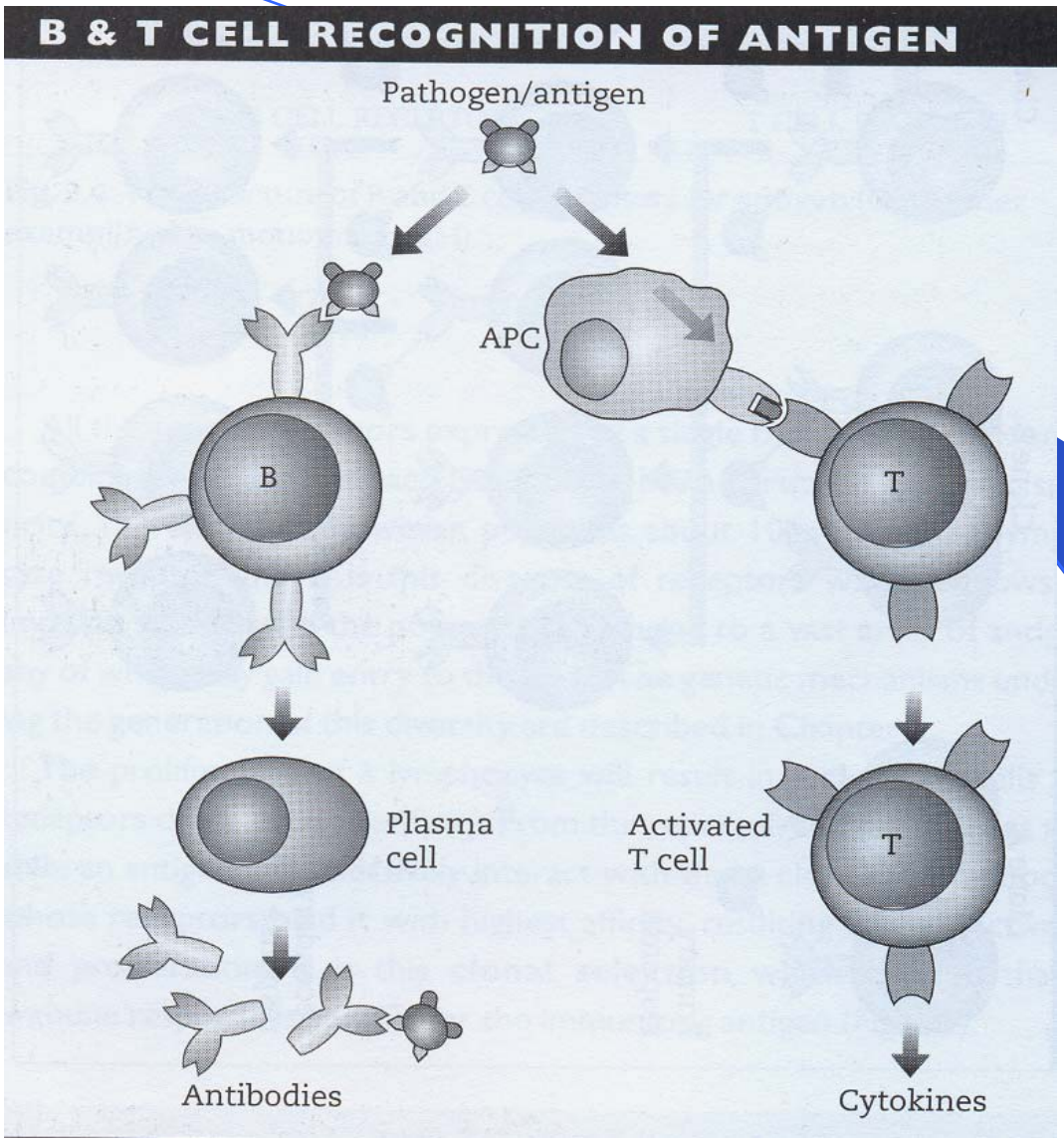
- 2 properties of antigen:

1. Immunogenicity – Induction of immune response
2. Immunological reactivity - Specific reaction with Abs or with T cells.

* Based on these 2 attributes, functional classification of Ags has been made.

Recognition of an Antigen

- Bacteria or viruses are not Ags by themselves but they contain Ags both on their surface and inside the cell.
- Ags are recognized by
  1. B cells and their surface Igs (sIgM) or
  2. the T cell receptor on T cells.
- Abs recognize the tertiary structure of a protein (i.e. the way it folds) whereas
- The T cells require the protein to be ingested, degraded and presented on the surface of a special cell called Antigen Presenting Cell (APC). The processed Ags are presented along with MHC/ HLA molecules by APCs


B & T CELL RECOGNITION OF ANTIGEN
Pathogen/antigen
APC
B
T
Plasma cell
Activated T cell
T
Antibodies
Cytokines

Classification of Antigens

- Based on
  1. Immunogenicity (functional classification)
  2. Origin of Ag
  3. Source of Ag
  4. Biological classification

1. Functional Classification

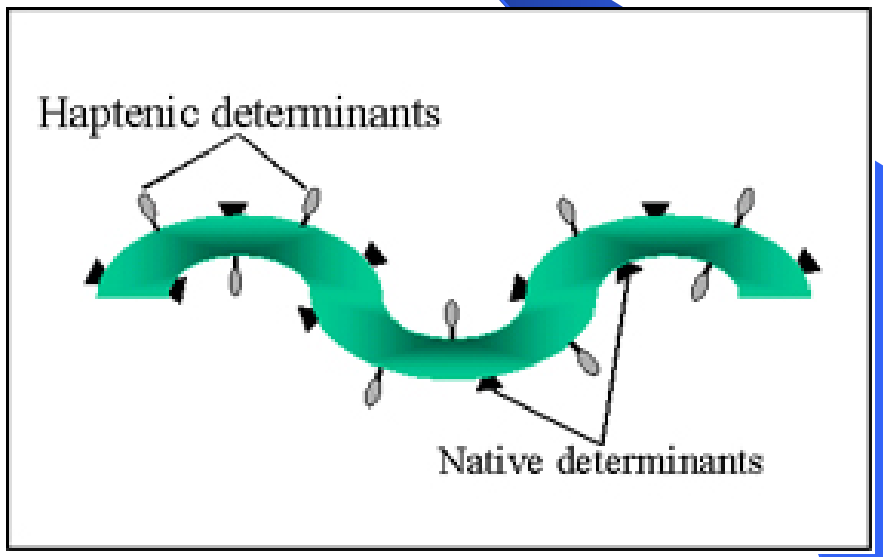
- Complete Ag - Able to induce Ab formation. Hence called as IMMUNOGENS.
  - Produce a specific & observable reaction with the Abs so produced.

- Haptens / Incomplete Ag - Substances which can not induce Ab formation by themselves but can react specifically with Abs.

Hapten + Carrier $\longrightarrow$ Complete antigen (Immunogen)

Hapten-carrier conjugates

- Definition
  - Ag only if bound to carrier protein
- Structure
  - Native determinants
  - Haptenic determinants



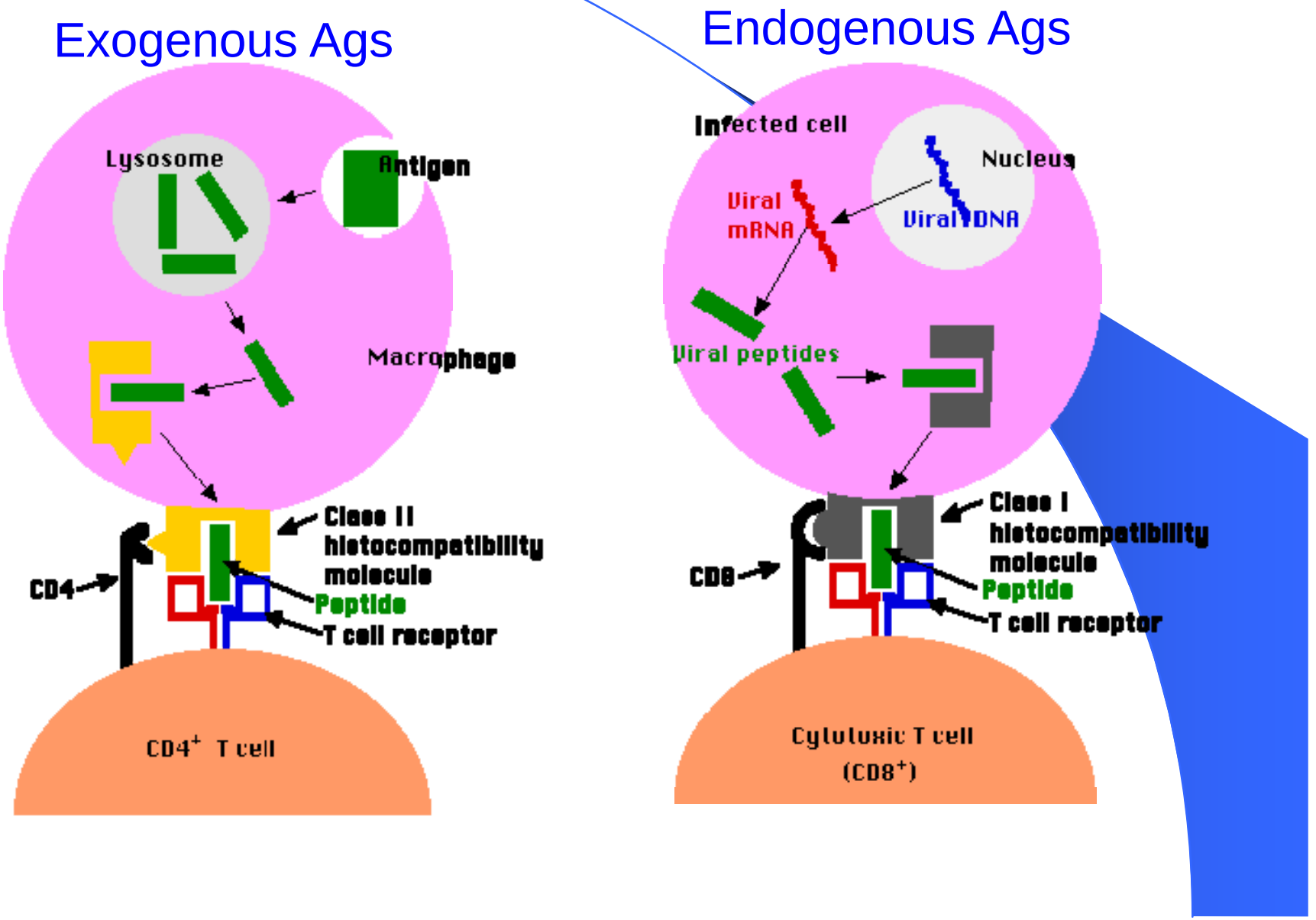
2. Origin of Antigens

- Ags can be classified on the basis of their origin:

1. Exogenous Ags – from outside
   - enter the body by inhalation, ingestion or injection.
   - these are taken by the APCs and degraded into small peptides. APCs then present them to helper T cells by using MHC type II molecules.

2. Endogenous Ags – generated within the cell as a
   - result of normal cell metabolism, or
   - because of viral or intracellular pathogenic infection.
   - The fragments are presented along with MHC type I molecules to cytotoxic T cells.

Antigen processing & presentation



3. Source of an Antigen

- Xenoantigen – foreign Ag, from different species e.g. bacteria, viruses
- Alloantigen – different individual from same species e.g. blood group Ag
- Autoantigen – same individual e.g. lens protein, tumor cells
- Heterophile antigen – Common/ related Ags shared by different species

  e.g. M protein of streptococus bears common antigen determinant with basement membrane of kidney

4. Biological Classes of Ags

- Depending on the ability to induce Ab formation, Ags are classified as:

1. T cell dependent (TD) ags
2. T cell independent (TI) ags

T cell Dependent (TD) Ags

- Ags that require T cells to generate an immune response
- Structurally complex e.g. RBCs, S.proteins
- Immunogenic over a wide dose range and do not cause tolerance.
- Produce immunological memory
- Requires processing by APCs.
- Rapidly metabolised

T cell Independent (TI) Ags

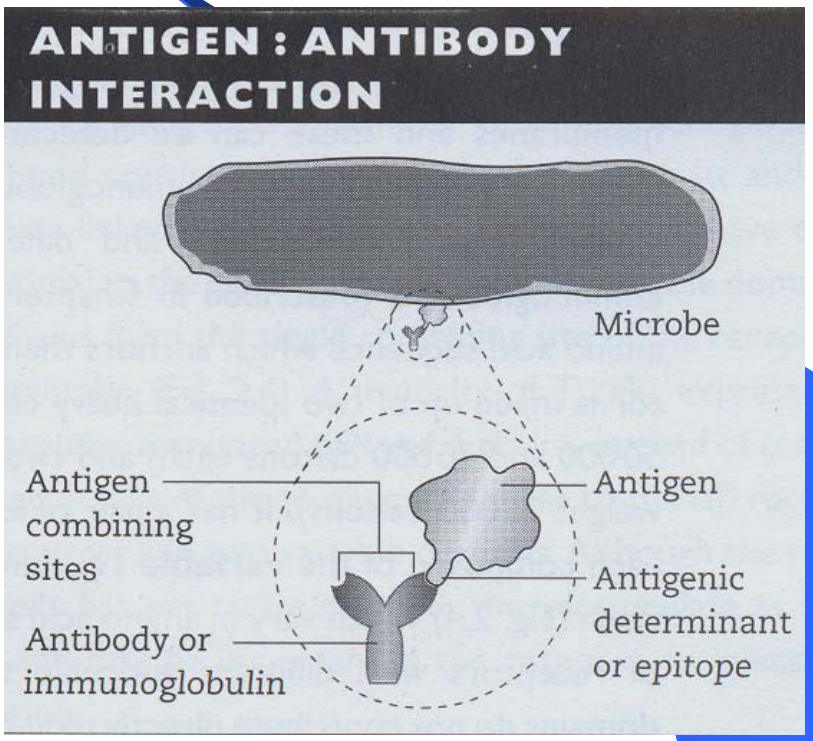
- Directly stimulate Ab production by B cells, without the participation of T cells.
- Structurally simple, being composed of a limited no. of repeating epitopes. e.g. Pneumococcal capsular polysaccharide, bacterial LPS, flagellar protein
- Immune response is dose dependent.

  Too little - non immunogenic

  Too much - tolerance
- Do not produce immunological memory.
- Do not require processing by APCs.
- Remain in the body for long periods

Epitope or Antigenic determinant

- Smallest unit of antigenicity.
- Small area/ part on the Ag which combines with its complementary site either on the specific Ab or T cell receptor.



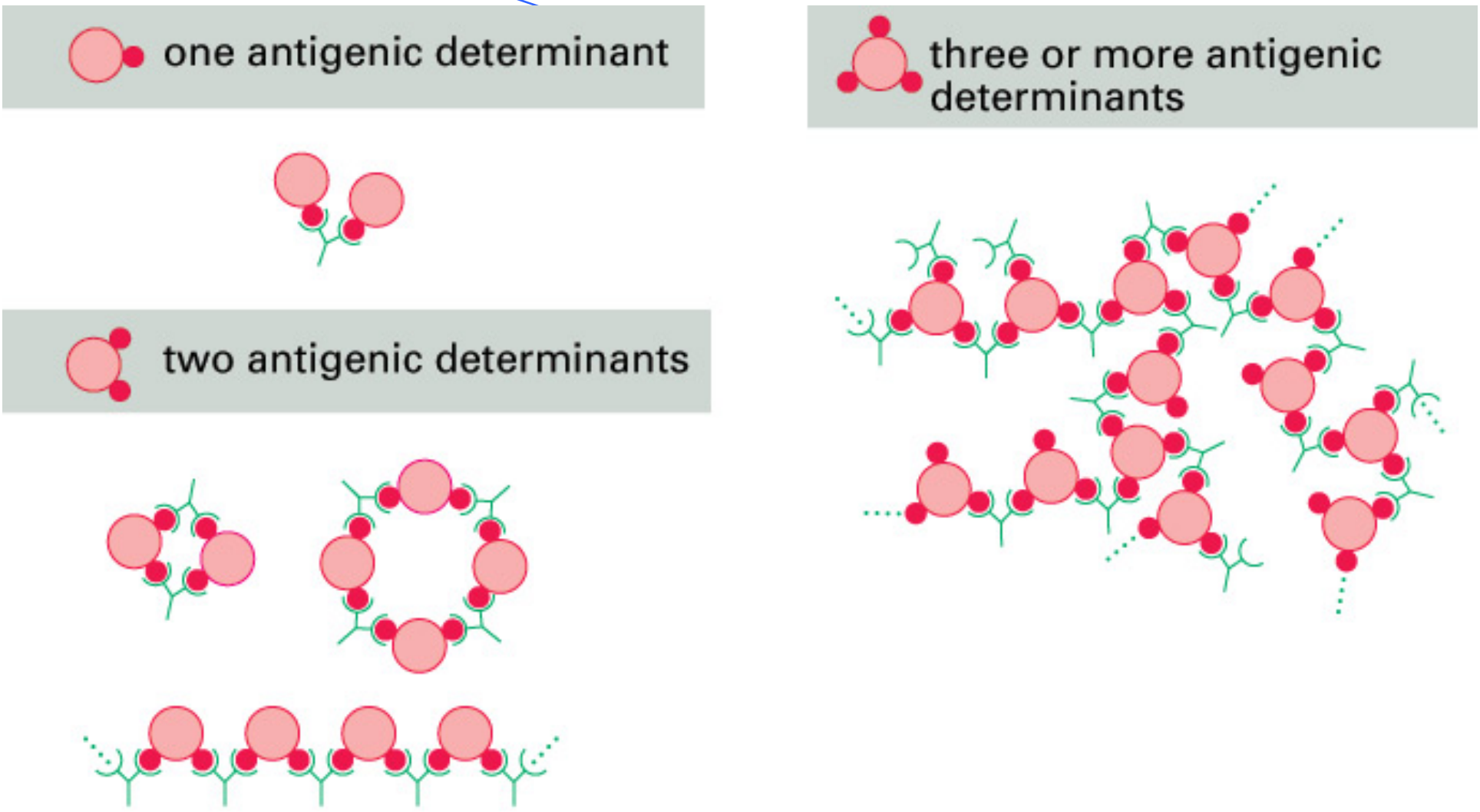
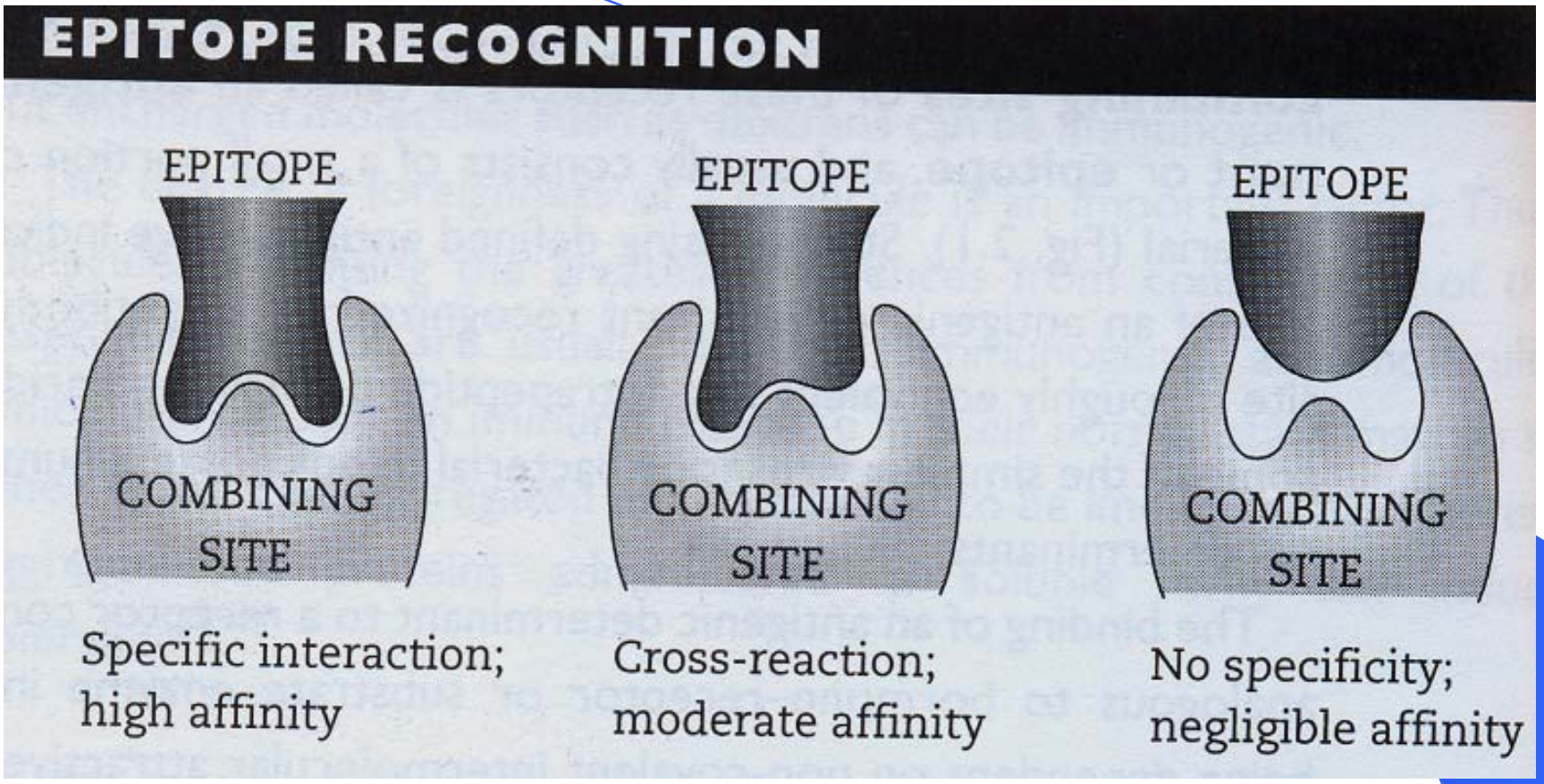


Figure 24–19. Molecular Biology of the Cell, 4th Edition.



Interaction between epitopes of different shapes & Ag combining site on the Ab

Determinants of Antigenicity

- Properties which make a substance antigenic:
  1. Size
  2. Nature of Ag
  3. Foreignness
  4. Susceptibility to tissue enzymes.
  5. Exposure to the Ag.
  6. Antigenic specificity

1. Size

- Large molecules are highly antigenic.
- Low mol.wt. (<5000) substances are weakly antigenic or non antigenic.
- Can be made antigenic by absorbing them on large inert particles like bentonite or kaolin.

2. Nature of the Ag

- Macromolecular proteins are the most potent immunogens.
- Polysaccharides, glycoproteins, synthetic polypeptides, lipids and nucleic acids are less immunogenic

Proteins – high MW and structural complexity (excellent)

Lipids – relative simplicity and lack of structural stability (interior)

Nucleic Acid – relative simplicity, molecular flexibility and rapid degradation (poor)

Antigenicity can be enhanced by conjugating to a protein.

Physical form

Particular > Soluble

Denature > Native

3. Foreignness

- Ags which are ‘foreign’ to the individual induce an immune response.

- Antigenicity is related to the degree of foreignness - Ags from other individuals of the same species are less antigenic than those from other species.

4. Susceptibility to tissue enzymes

- Substances which are rapidly metabolised & are susceptible to the action of tissue enzymes behave as more potent Ags.

- Ags are degraded into fragments of appropriate size containing the epitope.

- Degradation is brought about by phagocytosis & the intracellular enzymes.

5. Exposure to the Ag

- Dose of the immunogen : optimum dose

  * Lower or higher than the optimum can induce tolerance (inability to induce an immune response)

- Route of administration

  Subcutaneous > Intravenous > Intragastric

- Immune response can be increased by mixing the Ag with a powerful adjuvant.

Adjuvants

I. Definition

Adjuvant is certain substance which can non-specifically enhance the Immune response or change the type of Immune response when it is injected before or together with the antigens.

II. Classification of adjuvant

organic adjuvants: BCG

inorganic adjuvants: $Al(OH)_3$

synthesized adjuvants: polyI:C

complex adjuvants

Common adjuvant:

Incomplete Freund′s adjuvant

Complete Freund′s adjuvant

Freund's adjuvant is a solution of antigen emulsified in mineral oil and used as an immunopotentiator (booster).

- The Freund's Complete Adjuvant is composed of inactivated and dried mycobacteria (usually *M. tuberculosis*), whereas the **incomplete form** lacks the mycobacterial components (hence just the water in oil emulsion).

- It is named after Jules T. Freund.

III. Mechanisms of adjuvant

- Change the chemical and physical characteristic of Ag
- Improves the Ag process and presentation ability of macrophages
- Non-specifically stimulate proliferation of lymphocytes

7. Antigenic Specificity

- The specificity of natural tissue Ags can be considered under different categories as species, iso-, auto- and organ specificities.

Species Specificity

- Tissues of all individuals in a species contain some species specific Ags.
- Forensic applications - identification of the species of blood & of seminal stains.

Isospecificity

- Ags found in some but not all members of a species. e.g.
  1. Human Erythrocyte Ags
     - different blood groups.
     - Important in blood transfusion, disputed paternity cases
  2. Histocompatibilty Ags –
     - tissue specific Ags : cellular determinants specific to each individual of a species.
     - Important in tissue/ organ transplantation

Autospecificity

- Self Ags are ordinarily non-antigenic but there are some exceptions.

1. Ags that are not normally found free in circulation or tissue fluids e.g. lens protein confined within its capsule.

2. Ags that are absent during embryonic life & develop later e.g. sperms

Organ Specificity

- Some organs such as the brain, kidney & lens protein of different species, share the same Ag. Such Ags are called organ specific Ags.

e.g. Following Antirabic vaccination using sheep brain vaccines, neuroparalytic complications are seen due to sharing of brain specific Ags by sheep & human beings.

Sheep brain Ags – Immune response – Nervous tissue damage.

Heterogenetic (heterophile) Specificity

- Same or closely related Ags may occur in different species, classes & kingdoms - Heterophile Ags

  e.g Weil – Felix reaction in typhus fever,

  Paul Bunnell test in Infectious mononuclosis.

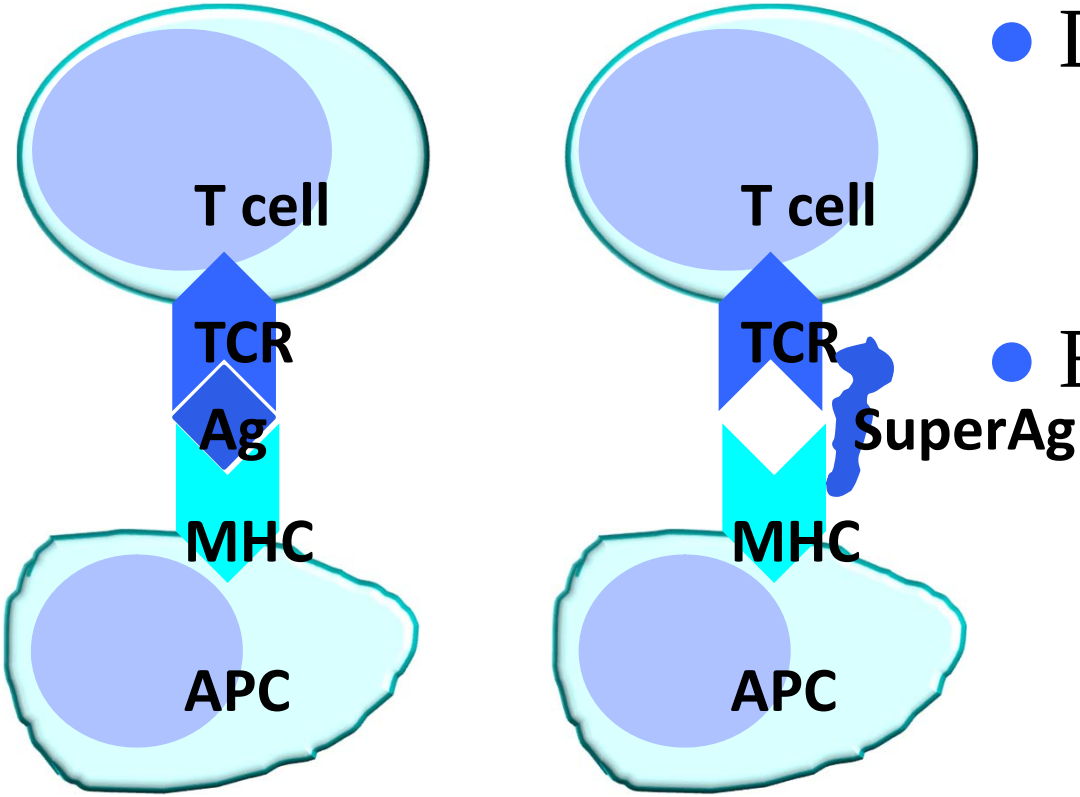
- Weil-Felix :- sharing of carbohydrate hapten by certain strains (OX strain) of Proteus & Rickettsiae.

- Antigenic specificity is not absolute. Cross reactions can occur between Ags due to :

1. Stereochemical similarities
2. Sharing of identical antigenic determinants by different Ags.

   e.g. Streptococcal infection & Rheumatic Fever

Superantigens



- Definition
  - Polyclonal T cell response
- Examples
  - Staphlycoccal enterotoxins
  - Toxic shock toxin

THANKYOU