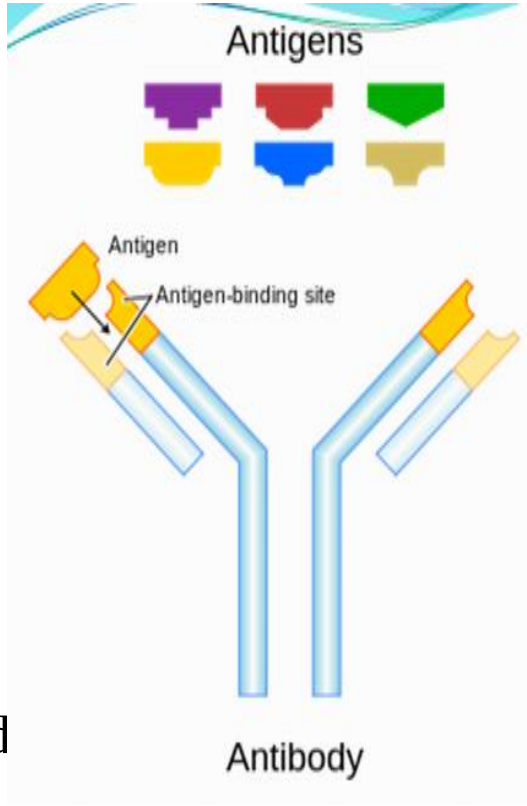
Lecture 3:

Antigen



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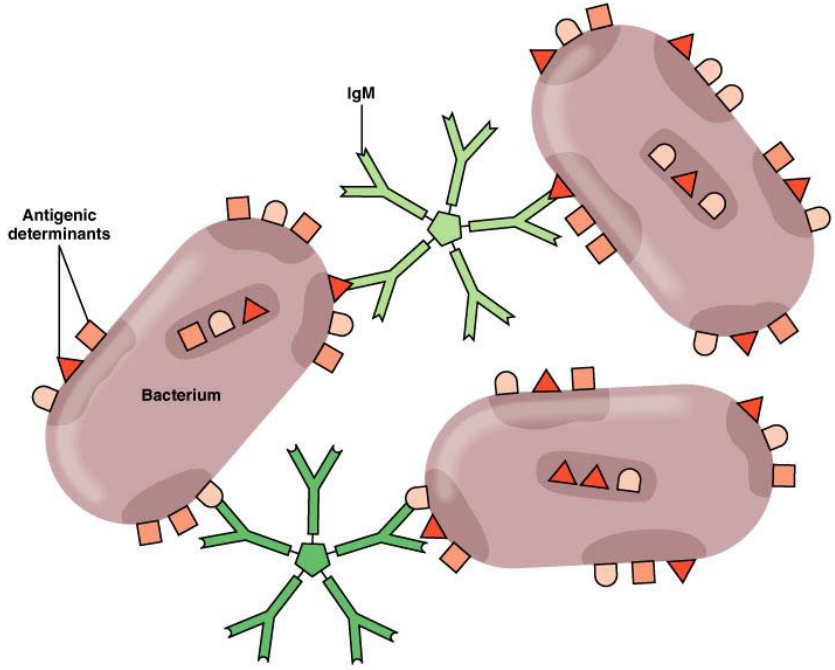
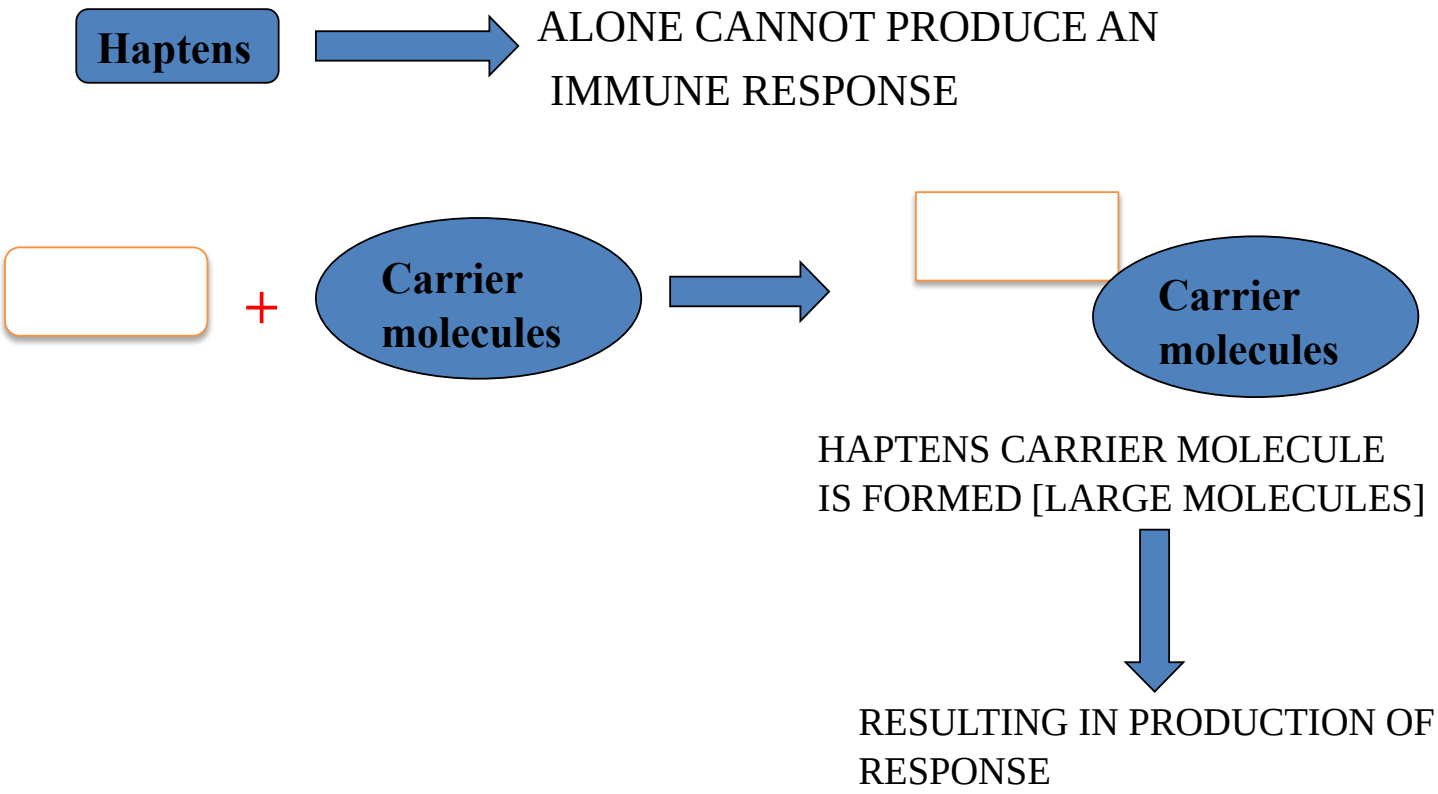
Antigens

- Antigens (**Immunogen**) are foreign molecules that trigger a specific immune response and stimulate the immune system to produce antibodies.
- Each antigen has a distinct surface feature or epitope.
- Include components of bacterial cell walls, capsules, pili, and flagella, as well as proteins of viruses, fungi, and protozoa.
- An antigen may be a substance from the environment, such as chemicals, food, spores, pollen, or dust.
- Antigens can be proteins, lipids, carbohydrates, or nucleic acids

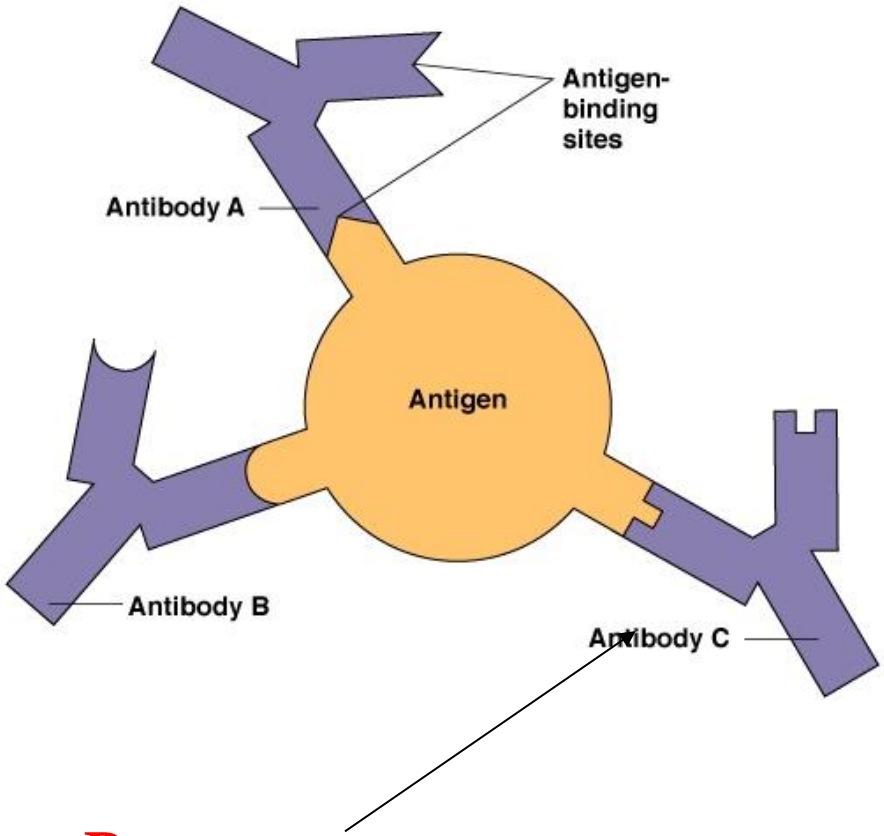


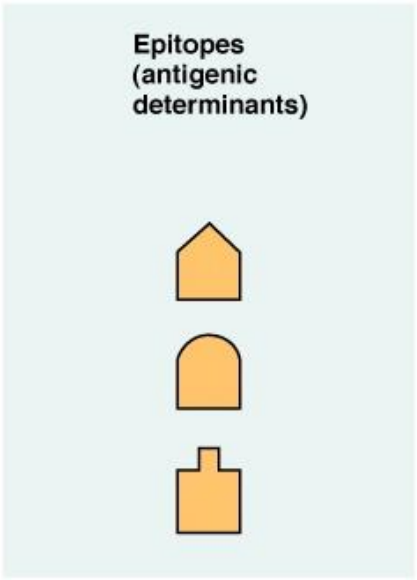
Hapten

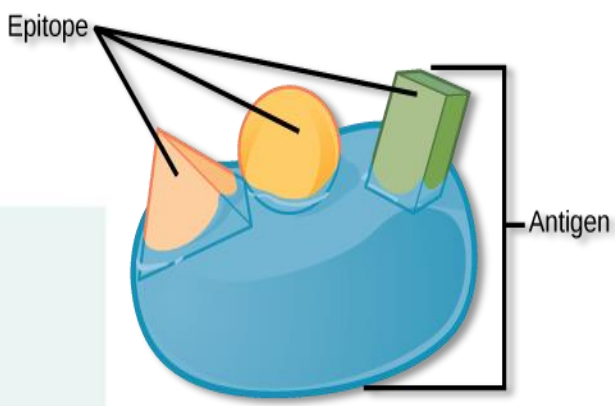
A small organic non-immunogenic substance, which can react with the products of a specific immune response. Haptens can not induce an immune response when administered by themselves unless coupled to a carrier molecule. Haptens have the property of **antigenicity** but not immunogenicity.



- **Epitope** is an immunologically active region of an antigen (immunogen) that binds to antigen-specific membrane receptors on lymphocytes or to secreted antibodies.
- It is also called **antigenic determinants.**



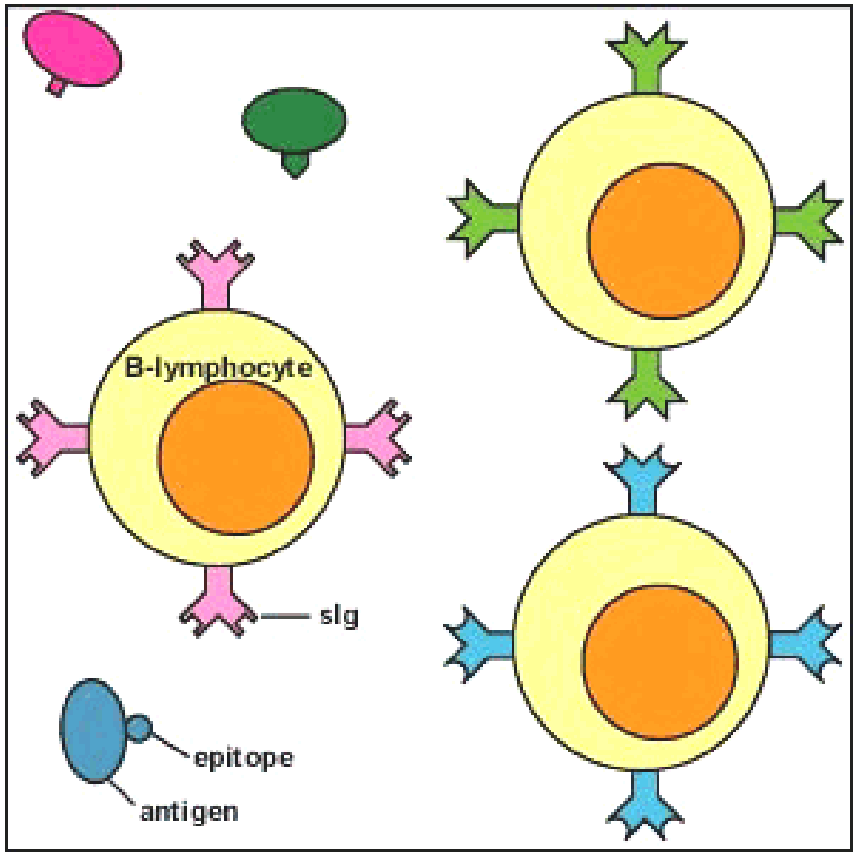




Paratope

The combining area on the antibody molecule, corresponding to the epitope

Antigen reacting only with particular B lymphocyte



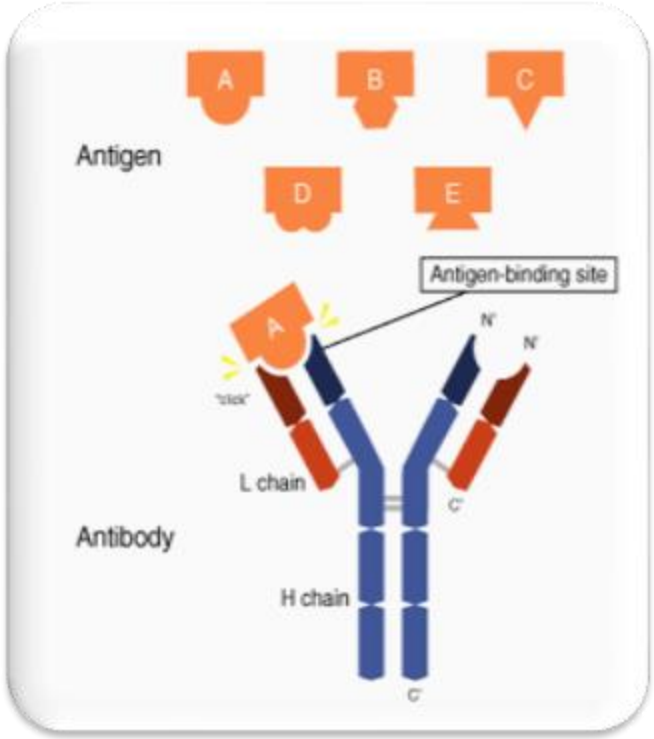
B-lymphocytes have sIg molecules on their surface that recognize epitopes directly on antigens. Different B-lymphocytes are programmed to produce different molecules of sIg, each specific for a unique epitope.

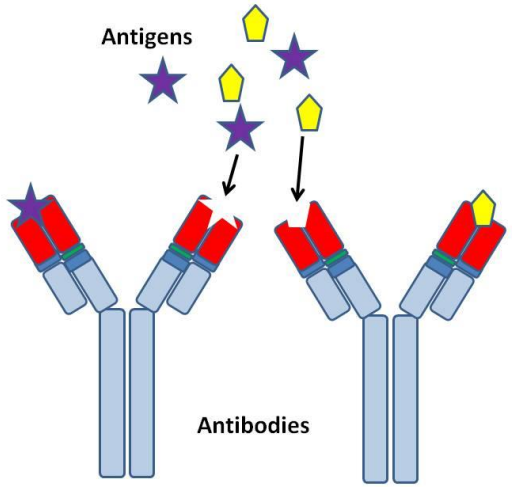
Isoantigens are antigens found in some but not all members of a species. A species may be grouped depending on the presence of different antigens in its members e.g. human erythrocyte antigen based on which individuals can be classified into different blood groups.

Types of Antigens

Antigens can be of three types;

1. Exogenous Antigens
2. Endogenous Antigens
3. Autoantigens





1. Exogenous Antigens

Exogenous antigens are antigens that can enter the body from the outside, for example, by inhalation, ingestion/eating, or injection.

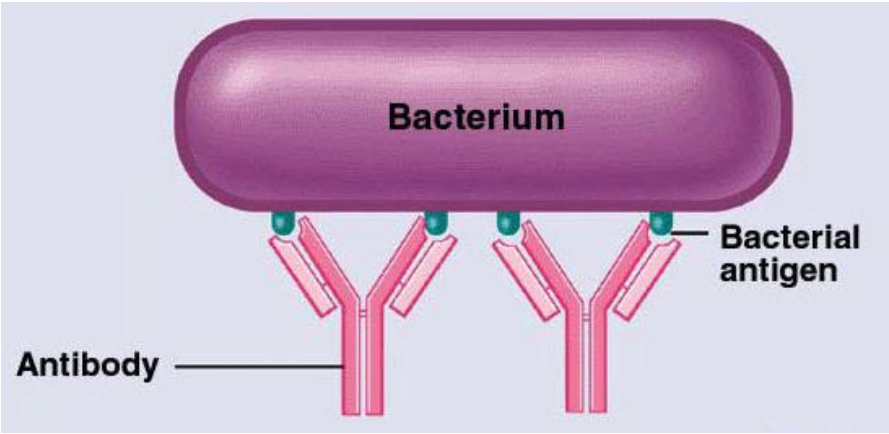
1- Bacterial antigens:

a. Antigens related to bacterial cells

- Somatic antigen (O -Antigen): Part of cell wall
- Capsular antigen (K-Antigen): Usually polysaccharide
- Flagellar Ag (H- Antigen): A protein made of flagellin
- Fimbrial Ag: Surface antigens in bacteria

b. Antigen secreted by bacteria:

- Exotoxins
- Enzymes



1. Exogenous Antigens

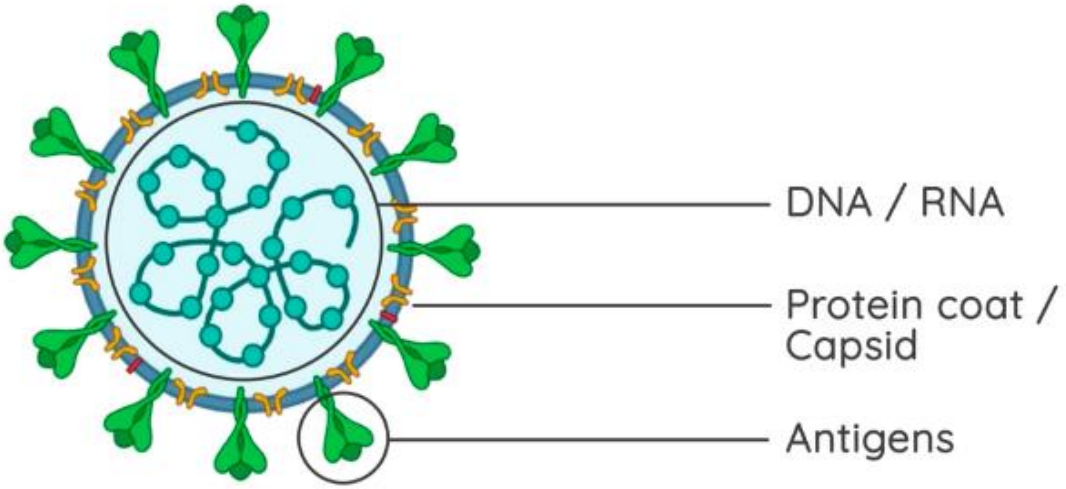
2-Viral antigens

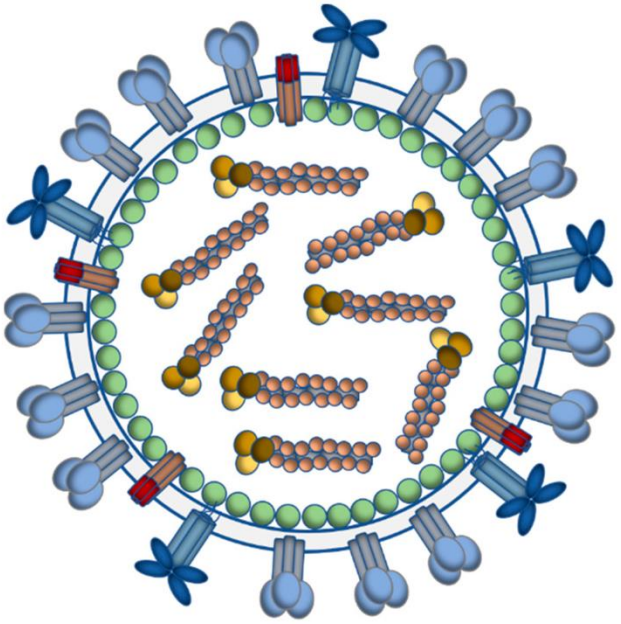
a. Protein coat viral antigens.

b. Soluble antigens (soluble nucleoproteins as in influenza)

❖ The antigens enter the body by various routes. They come in contact with various antigens-presenting cells i.e. macrophages.

✓ By endocytosis or phagocytosis, these antigens are taken into the antigen-presenting cells (APCs) and processed into fragments.





2. Endogenous antigens

- Antigens that have been generated within cells as the results of intracellular bacterial, viral infection or in various autoimmune conditions.
- Found within the cytosol of human cells such as viral proteins, proteins from intracellular bacteria, and tumor antigens.

Processing of the endogenous antigens:

The fragments of the processed antigens are presented on the surfaces of antigens-presenting cells along with an MHC I or MHC II.

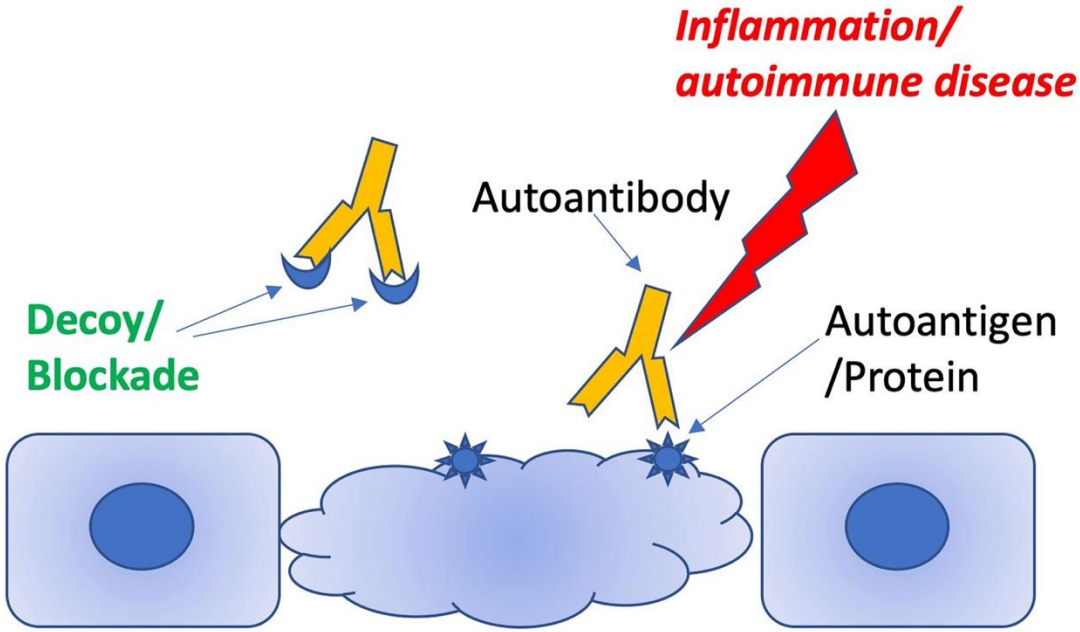
Some examples of endogenous antigens.

Human tissue antigens: Blood group antigens: A, B and Rh antigens.

3. Autoantigens

- Autoantigen is usually a normal protein or complex of proteins (and sometimes DNA or RNA) that is recognized by the immune system of patients suffering from a specific autoimmune disease.

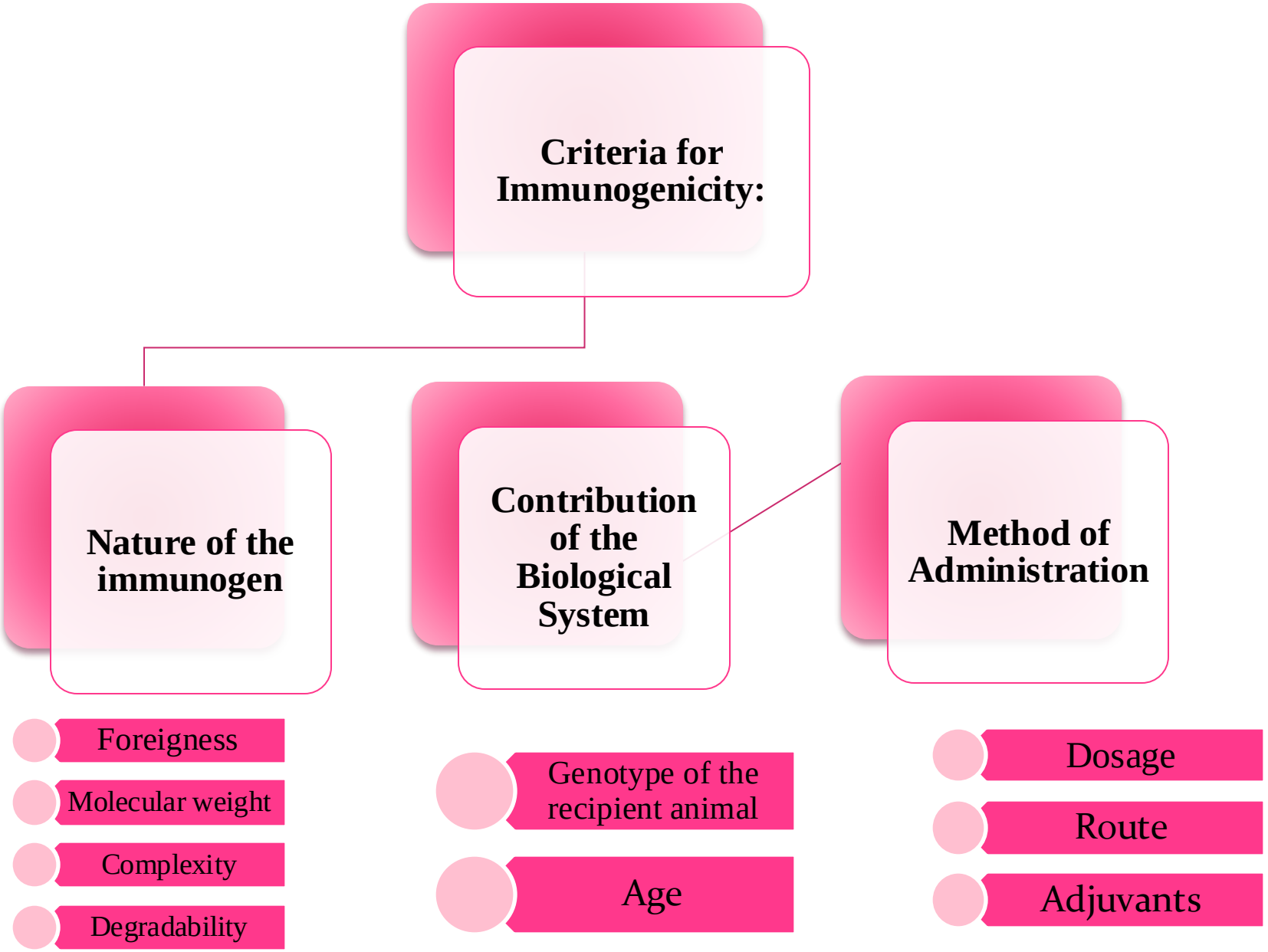
- These antigens should under normal conditions not be the target of the immune system, but due to mainly genetic and environmental factors the normal immunological tolerance for such an antigen has been lost in these patients.

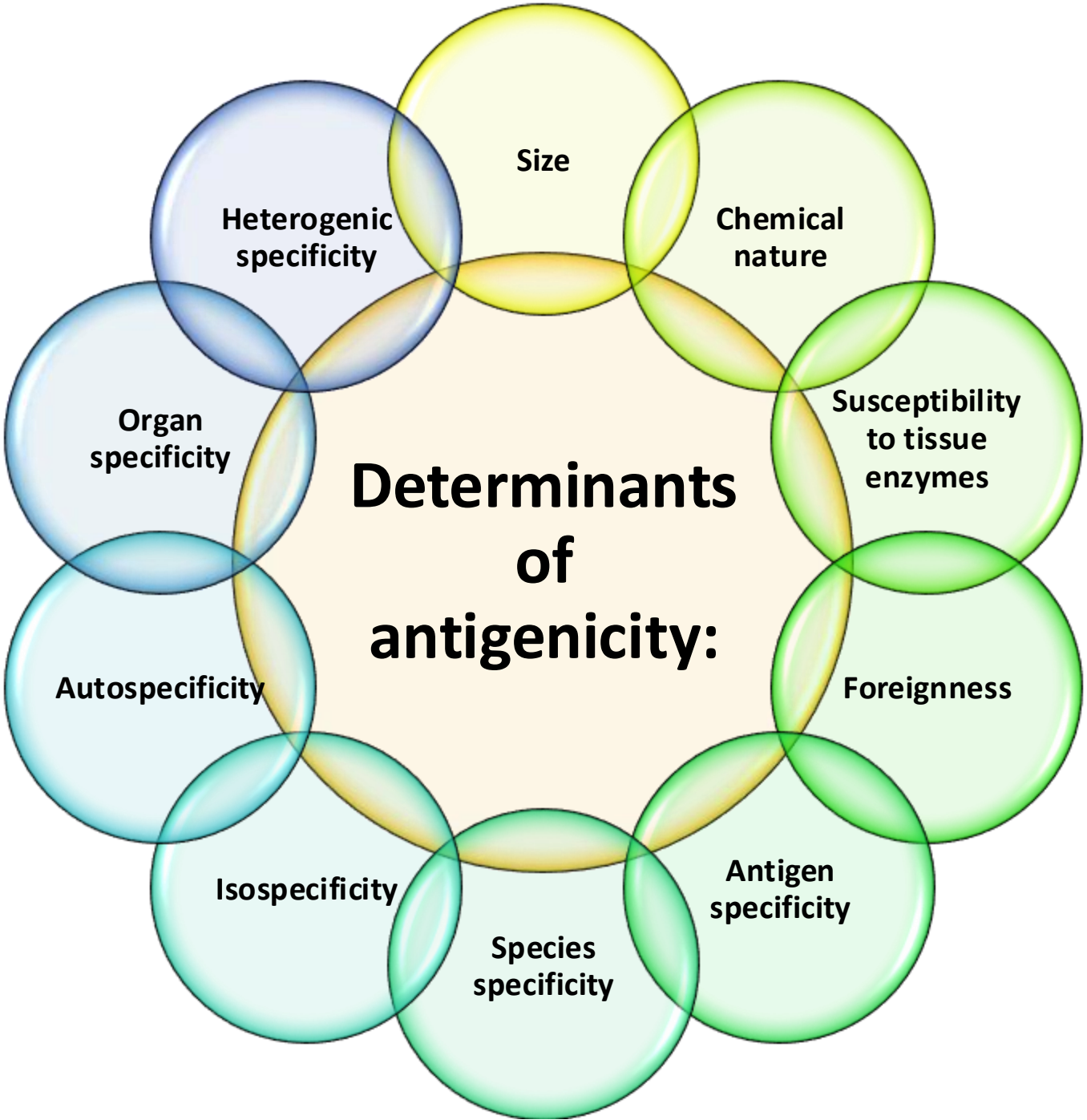


Tumor antigens

- Tumor antigens are those antigens that are presented by the MHC I **(Major Histocompatibility Complex I)** molecules on the surface of tumor cells.
- These antigens can sometimes be presented only by tumor cells and never by the normal ones.
- In this case, they are called tumor-specific antigens (TSAs) and typically result from a tumor specific mutation.

Characteristics of Antigen




Determinants of antigenicity:
Size
Chemical nature
Susceptibility to tissue enzymes
Foreignness
Antigen specificity
Species specificity
Isospecificity
Autospecificity
Organ specificity
Heterogenic specificity

Factors that influence the immunogenicity of proteins

Parameter	Increased immunogenicity	Decreased immunogenicity
Size	Large	Small (MW<2500)
Dose	Intermediate	High or low
Route	Subcutaneous > intraperitoneal > intravenous or intragastric	
Composition	Complex	Simple
Form	Particulate	Soluble
	Denatured	Native
Similarity to self protein	Multiple differences	Few differences
Adjuvants	Slow release	Rapid release
	Bacteria	No bacteria
Interaction with host MHC	Effective	Ineffective

Property of antigens/ Factors Influencing Immunogenicity

1. Foreignness

- An antigen must be a foreign substances to the animal to elicit an immune response.
- Self-responsive cells are eliminated during lymphocyte maturation, leaving only cells that respond to non-self, so-called "foreign" epitopes.

2. Molecular Size

- The larger the molecule the more immunogenic it is likely to be.
- The most active immunogens tend to have a molecular mass of 14,000 to 600,000 Dalton.
- Examples: tetanus toxoid (50000 Da), egg albumin (42700 Da), thyroglobulin (662000) are highly antigenic.

3. Chemical Nature and Composition

- In general, the more complex the substance is chemically the more immunogenic it will be.
- The antigenic determinants are created by the primary sequence of residues in the polymer and/or by the secondary, tertiary, or quaternary structure of the molecule.
- Antigens are mainly proteins and some are polysaccharides.
- Chemical nature of antigens:
  - Proteins: The vast majority of immunogens are proteins. proteins(Glycoproteins or Lipoproteins) are usually very good immunogens.
  - Polysaccharides: Pure polysaccharides and lipopolysaccharides are good immunogens.
  - Lipids: Lipids are not generally immunogenic (or antigenic) unless they are complexed with proteins or polysaccharides.
  - Nucleic acid: Nucleic acids are usually poorly immunogenic.
  - Nucleoproteins
  - Glycoproteins
  - Steroid hormones
  - Bacterial cells, viruses

4. Degradability

- Antigens that are easily phagocytosed are generally more immunogenic.
- This is because for most antigens (T-dependent 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).

5. Genetic Factors

- Some substances are immunogenic in one species but not in another
- Similarly, some substances are immunogenic in one individual but not in others (i.e. responders and non-responders).
- The species or individuals may lack or have altered genes that code for the receptors for antigen on B-cells and T-cells. Or
- They may not have the appropriate genes needed for the APC to present antigen to the helper T cells.

6. Age

Age can also influence immunogenicity. Usually, the very young and the very old have a diminished ability to mount an immune response in response to an immunogen.

7. Physical form

In general, particulate antigens are more immunogenic than soluble ones, and denatured antigens are more immunogenic than the native form.

- Antigenic determinants

- Recognize broad molecular patterns found in pathogens but not in the host.
  - Called PAMPS (Pathogen Associated Molecular Patterns)
  - Receptors for PAMPS are called PRRs (pattern recognition receptors).
- Lack a high degree of specificity
- A particular PRR can recognize a molecular pattern that may be present on a number of different pathogens enabling the receptor to recognize a variety of different pathogens.

Method of Administration

1. Dosage

Too low a dose of Antigen will fail to activate enough lymphocytes for a response whereas too high a dose can overwhelm the system and cause the lymphocytes to enter a nonresponsive state.

2. Route

Generally, the subcutaneous route is better than the intravenous or intragastric routes.

3. Adjuvants

Substances that can enhance the immune response to an immunogen are called adjuvants. The use of adjuvants, however, is often hampered by undesirable side effects such as fever and inflammation.

Biological classes of antigens:

A. Thymus-dependent antigen(TD-Ag)

T-independent antigens are antigens that can directly stimulate the B cells to produce antibodies without the requirement for T-cell help. In general, polysaccharides are T-independent antigens. Complex proteins, immunogenic over a wide range of doses memory cells present, rapidly metabolized, Ag process needed, Abs of all classes produced).

B. Thymus-lndependent antigen(TI-Ag)

T-dependent antigens are those that do not directly stimulate the production of antibodies without the help of T cells. Proteins are T-dependent antigens. Flagella, LPS, capsules, dose-dependent immunogenicity, no memory cells, slowly metabolized, no Ag processing, Ab response restricted to IgM and IgG3)

Biological classes of antigens:

- Thymus-dependent antigen(TD-Ag)

  Thymus-independent antigen(TI-Ag)

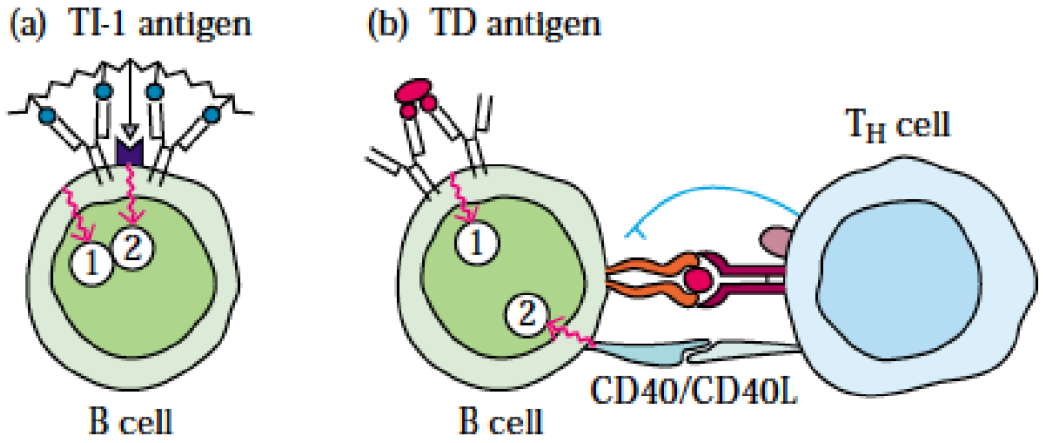


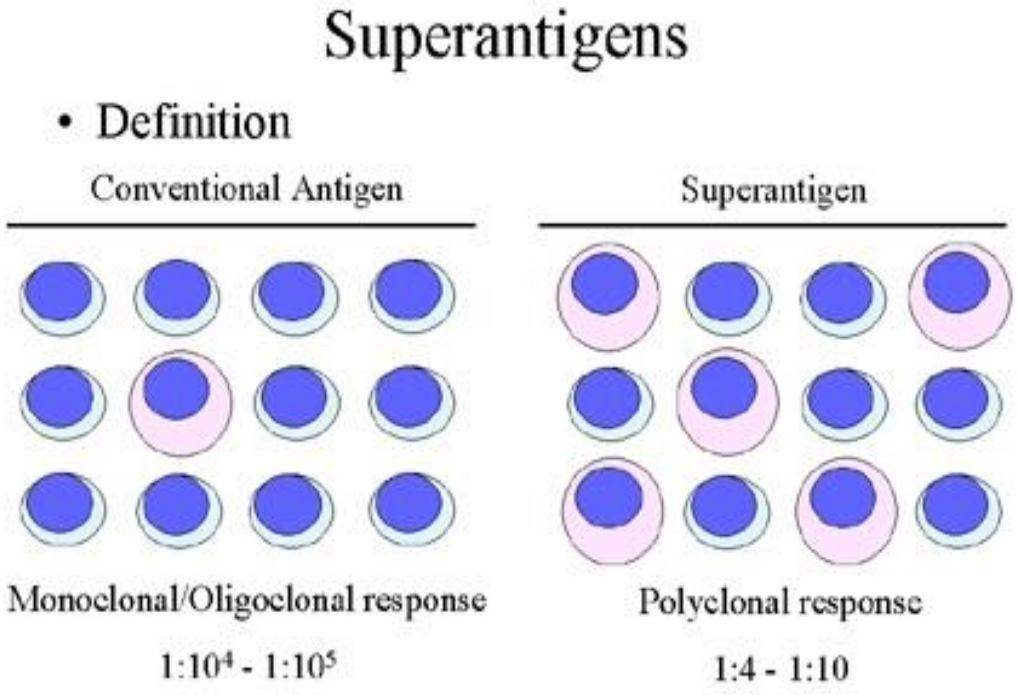
FIGURE 11-6 An effective signal for B-cell activation involves two distinct signals induced by membrane events. Binding of a type 1 thymus-independent (TI-1) antigen to a B cell provides both signals. A thymus-dependent (TD) antigen provides signal 1 by crosslinking mIg, but a separate interaction between CD40 on the B cell and CD40L on an activated T_H cell is required to generate signal 2.

- **Property differences between of T-dependent and T-independent antigens**

T-dependent antigen	T-independent antigens
Different Ag determinants	Same Ag determinants
Usually Protein	Usually Polysaccharide
Easley degraded	Resistant to degradation
Monoclonal Activation	Type1: Polyclonal activation Type2: Monoclonal activation

SUPERANTIGENS

When the immune system encounters a conventional T-dependent antigen, only a small fraction (1 in 10^4 -10^5) of the T cell population can recognize the antigen and become activated (monoclonal/oligoclonal response). However, some antigens polyclonally activate a large fraction of the T cells (up to 25%). These antigens are called **superantigens** .



Examples of **Superantigens** include:

1- Staphylococcal enterotoxins (food poisoning)

2- Staphylococcal toxic shock toxin (toxic shock syndrome)

3- Staphylococcal exfoliating toxins (scalded skin syndrome)

4- Streptococcal pyrogenic exotoxins (shock).

The diseases associated with exposure to superantigens are, in part, due to hyperactivation of the immune system and subsequent release of biologically active cytokines by activated T cells.