The antigens

Antigens. The word antigen is a shortened form of the words "antibody generator." Antigens are substances that react with antibodies,

Immunogens are molecules that induce an immune response. In most cases, antigens are immunogens, and the terms are used interchangeably.

The antigens that are not immunogenic but can take part in immune reactions are termed as **haptens**.

The term **immunogenicity** means the ability of an antigen to elicit an immune reaction in the form of a B-cell or T-cell response.

B cells + antigen → effector B cells + memory B cells
↓
(plasma cells)

T cells + antigen → effector T cells + memory T cells
↓
(e.g., CTLs, T_Hs)

Determinants of Antigenicity:

A number of factors have been identified that make a substance immunogenic. Some of the important determinants of antigenicity include:

1. Molecular size
2. Foreignness
3. Chemical-structural complexity
4. Stability
5. Other factors

Molecular Size

In general, protein molecules with large molecular weight are highly antigenic. Substances with molecular weights of about 100,000 Da and more are highly immunogenic, while substances with molecular weights of less than 5000 Da are generally not immunogenic.

Foreignness:

To be immunogenic, a molecule must be recognized as nonself, i.e., foreign. The molecule is considered self or nonself by the immune system depending on whether or not the molecule was exposed to the immune system during fetal development. **Foreignness implies ability of the host to tolerate self-antigens**. Tolerance to self-antigens develops by contact with them in the initial phases of the development of immune system, particularly during the development of lymphocytes.

Chemical-Structural Complexity:

Proteins are the most potent immunogens followed by polysaccharides. Nucleic acids and lipids are not efficient in eliciting a good immune reaction, although they may act as haptens. Structural complexity of a protein contributes to its immunogenicity. Chains of single amino acids or single sugars are poorly immunogenic, but if different amino acids or sugars are combined in the same molecule, the immunogenicity is greatly enhanced. Therefore, the structure of protein plays an important role in its immunogenicity, especially in inducing cellular immunity.

Stability:

Highly stable and nondegradable substances (e.g., some plastics,metals, or chains of D-amino acids) are not immunogenic This is because internalization, processing, and presentation by antigen-presenting cells (APCs) are always essential to mount an immune response. Therefore, very stable substances (such as silicon) have been successful as non-immunogenic materials for reconstructive surgeries, such as breast implants. On the other hand, if a substance is very unstable, it may break up before an APC can be internalized, and hence become immunogenic. In addition, large, insoluble complexes are more immunogenic than smaller, soluble ones. This is because macrophages find it easier to phagocytose, degrade, and present the insoluble complexes than the soluble complexes.

Biological system

Biological system also plays an important role in determining the immunological efficiency of an antigen. Some substances are immunogenic in one individual but not in others

Dosage and route of the antigen:

The **dose of antigen** and the **route** by which it comes into contact with the immune system also influence immunogenicity of the antigen. Very low doses of antigen do not stimulate immune response, either because too few lymphocytes are contacted or because a nonresponsive state is elicited. Conversely, an extremely high dose also fails to elicit tolerance. Repeated administration of antigens (booster doses) may be required to enhance immune response of the host to certain antigens. This is particularly important in case of vaccines where a prerequisite immune level needs to be attained.

Adjuvants

Adjuvants are the substances that when mixed with an antigen and injected with it boost the immunogenicity of the antigen. Adjuvants increase both the strength and the duration of immune response.

Antigenic Specificity

Antigenic specificity of the antigen depends on antigenic determinants or epitopes.

Epitopes

An epitope is defined as the immunologically active region of an immunogen that binds to antigen-specific membrane receptors on lymphocytes or secreted antibodies. The interaction between cells of the immune system and antigens takes place at many levels and the complexity of any antigen is mirrored by its epitope. There are two types of epitopes: B-cell epitopes and T-cell epitopes.

B-cell epitopes: B-cell epitopes are antigenic determinants recognized by B cells. The B-cell epitope is about six or seven sugar residues or amino acids long. B-cell epitopes tend to be hydrophilic and are often located at bends in the protein structure.

T-cell epitopes:T cells recognize amino acids in proteins but do not recognize polysaccharide or nucleic acid antigens. This is the reason why polysaccharides are considered as T-independent antigens and proteins as T-dependent antigens

Comparison of antigen recognition by T cells and B cells

Characteristic	B cells	T cells
Interaction with antigen	Involves binary complex of membrane Ig and Ag	Involves ternary complex of T-cell receptor, Ag, and MHC molecule
Binding of soluble antigen	Yes	No
Involvement of MHC molecules	None required	Required to display processed antigen
Chemical nature of antigens	Protein, polysaccharide, lipid	Mostly proteins, but some lipids and glycolipids presented on MHC-like molecules
Epitope properties	Accessible, hydrophilic, mobile peptides containing sequential or nonsequential amino acids	Internal linear peptides produced by processing of antigen and bound to MHC molecules

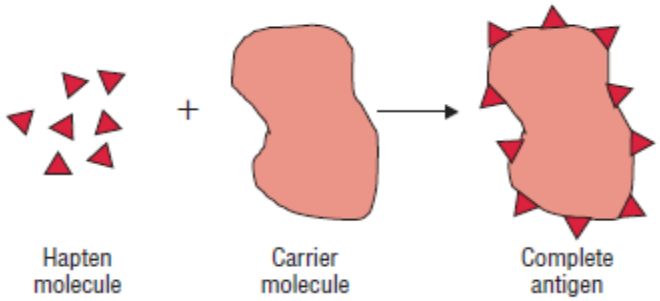
Histocompatibility Antigens

Histocompatibility antigens are the cellular determinants specific for each individual of a species. These antigens are associated with the plasma membrane of tissue cells. Human leukocyte antigen (HLA) is the major histocompatibility antigen that determines the homograft rejection. Therefore, HLA typing is absolutely essential before carrying out transplantation of tissue or organ from one individual to another.

Haptens

Haptens are small organic molecules that are antigenic but not immunogenic. They are not immunogenic because they cannot activate helper T cells. Failure of hapten to activate helper T cells is due to their inability to bind to MHC proteins; they cannot bind because they are not proteins and only proteins can be presented by MHC proteins. Moreover, haptens are univalent hence cannot activate B cells by themselves. The haptens,

however, can activate B cells when covalently bound to a “carrier” protein. When bound with a carrier molecule, they form an immunogenic hapten–carrier conjugate.



Hapten–carrier conjugate.

Superantigens

Superantigens are a class of molecules that can interact with APCs and T lymphocytes in a nonspecific way. The superantigens act differently by interacting with MHC class II molecules of the APC and the T-lymphocyte receptor. This interaction results in the activation of a larger number of T cells (10%) than conventional antigens (1%), leading to massive cytokine expression and immunomodulation. Examples of superantigens are staphylococcal enterotoxins, toxic shock syndrome toxin, exfoliative toxins, and also some viral proteins.