Antigens

Introduction:-

Molecules that can be recognized by the immunoglobulin receptor of B cells or by the T-cell receptor when complexed with major histocompatibility complex (MHC) are called antigens. The word antigen is a shortened form of the words antibody generator. Antigens are substances that react with antibodies, while immunogens are molecules that induce an immune response. In most cases, **antigens are immunogens**. 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. **All molecules that are immunogenic are antigenic, but not all antigenic molecules are considered immunogenic**. Thus, haptens can be said to lack immunogenicity.

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.Dosage and route of the antigen

1- 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.

2- Foreignness

To be immunogenic, a molecule must be recognized as non self ,i.e., foreign. The molecule is considered self or non self by the immune system depending on whether or not the molecule was exposed to the immune system during fetal development.

3- 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.

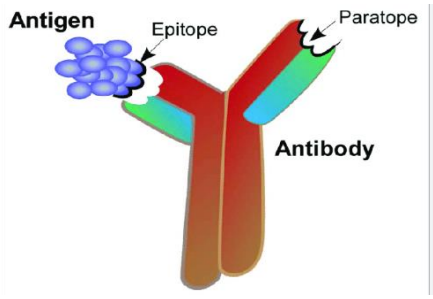
4-Stability

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 nonimmunogenic materials for reconstructive surgeries, such as breast implants.

Epitopes ❖

An **epitope**, also known as **antigenic determinant**, is the part of an antigen that is recognized by the immune system, specifically by **antibodies, B cells, or T cells**. The part of an antibody that binds to the epitope is called a **paratope.**

Epitopes are small chemical groups on the antigen molecule that can elicit and react with antibody. An antigen can have one or more determinants (epitopes).



B-cell epitopes

The part of the antigen that immunoglobulin or antibodies bind to is called a B-cell epitope. B-cell epitope can combine with its receptor only if the antigen molecule is in its native state.

T-cell epitopes

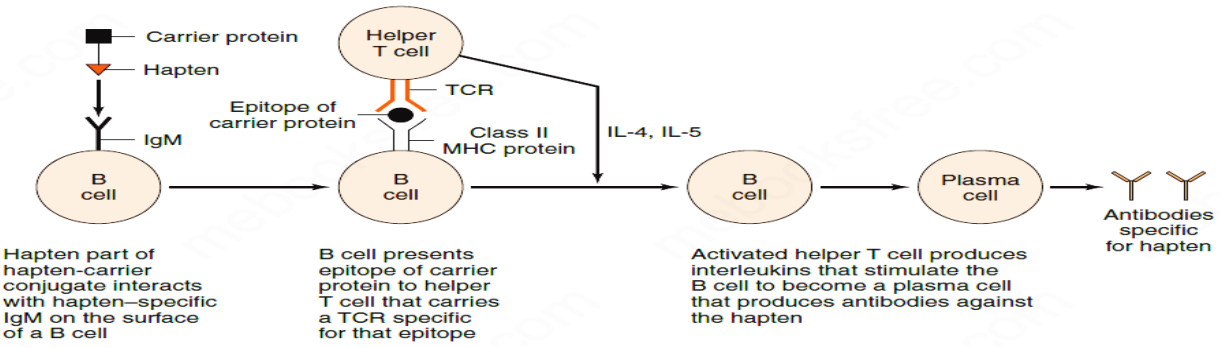
T cell epitopes are presented on the surface of an antigen-presenting cell, where they are bound to major histocompatibility complex (MHC) molecules. In humans, professional antigen-presenting cells are specialized to present MHC class II peptides, whereas most nucleated somatic cells present MHC class I peptides. T cell epitopes presented by **MHC class I** molecules are typically peptides between **8 and 11**

amino acids in length, whereas **MHC class II** molecules present longer peptides, **13–17 amino acids in length**.

❖ 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**, Moreover, haptens are 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. In this process, the haptens combine with an IgM receptor on the B cells. A peptide of the carrier protein is presented in association with class II MHC protein to the helper T cells. The activated helper T cells then produce interleukins, which stimulate the B cells to produce antibodies to hapten, the hapten–carrier molecule is bound to surface immunoglobulins on B cells via the hapten epitopes. The hapten–carrier molecule is then taken in, processed, and pieces of the carrier are presented by these B cells and TH cells.

The medically important concept that is related to the hapten–carrier protein model is that of **conjugate vaccines** such as the pneumococcal and meningococcal vaccines and the vaccine against *Haemophilus influenzae*. In these conjugate vaccines, the capsular polysaccharide is conjugated to a carrier protein. The capsular polysaccharide is not a hapten because it can induce IgM via the T-independent response.



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. Superantigens bind directly to conserved amino acid residues outside the antigen-binding groove on class II MHC molecules, thereby selectively stimulating T cells .Compared to a normal antigen-induced T-cell response **where 0.0001-0.001% of the body's T-cells are activated**, these

superantigens are capable of activating up to **20% of the body's T-cells**, leading to massive cytokine expression and immunomodulation.

Examples of superantigens.

1-Toxic shock syndrome toxin-1 (TSST-1), produced by some strain of Staphylococcus aureus.

2- Streptococcal pyrogenic exotoxin (Spe), produced by rare invasive strains of Streptococcus pyogenes (the group A beta streptococci).

3- ETEC enterotoxin, produced by enterotoxigenic E. coli (ETEC)

