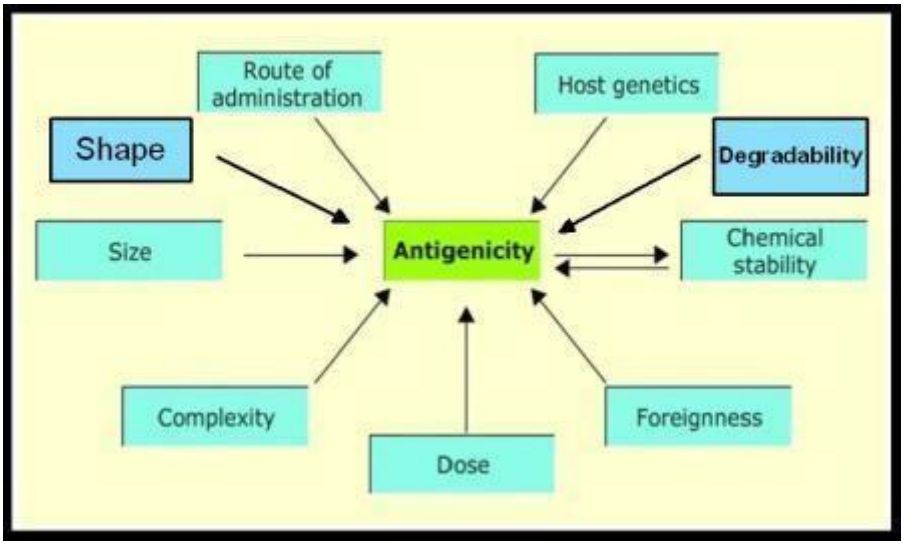
ANTIGEN

ANTIGEN - AN INTRODUCTION

- Antigen is a substance which when introduced into the tissues of a susceptible animal, it stimulates the formation ofspecific neutralizing substances or antibody with which it reacts specifically in some observable way or produced lymphokines or both antibody and lymphokines.
- The ability of a material to induce an immune response is referred to as immunogenicity and such material is called asimmunogen.
- *Immunogenicity* is the ability to induce a humoral and/cell mediated immune response.
- *Antigenicity* is the ability of a molecule to be recognized by an antibody or lymphocyte.
- All molecules possessing the property of immunogenicity also possess antigenicity but the reverse is not true.
- Molecules vary in their ability to act as antigens and stimulate immune response.

FACTORS DETERMINING ANTIGENICITY

- Molecular size
- Complexity
- Shape
- Stability
- Degradability
- Foreignness
- Genotype of the recipient animal
- Dosage and route of administration
- Adjuvants



MOLECULAR SIZE

- Foreign proteins are some of the best antigens.
- In general, the larger the molecular weight, the better are their antigenic properties.
- For example, ovalbumin (mol. wt. 40,000 Da). But there are some exceptions e.g. natural protein glucagon (2600 Da) is agood antigen.
- Penicillin and aspirin are not good antigen since their molecular weight is less than 1000 dalton.

COMPLEXITY

- Good antigens have complex structure.
- Large complex molecules can be readily taken up by macrophages.
- Complex proteins are good immunogen than large repeating polymers such as the lipids, carbohydrates and nucleic acids.
- Proteins vary in their antigenic power. Bacterial exotoxins and egg albumin are powerful antigens.
- Haemoglobin is a weak antigen.
- Protamines, histones and gelatin are almost devoid of antigenicity.
- More complex carbohydrate is immunogenic, especially if bound to proteins e.g. cell wall antigens of gram-negativebacteria.

SHAPE

- A good antigen should have a fixed shape to trigger higher antibody response.
- The immune system must recognize its shape.
- The highly flexible molecules that have no fixed shape are poor antigen.
- The surface area displays significant determinant sites for good immune response.

STABILITY

- Antigen molecule must be stable and rigid. For example, gelatin, a protein known for its instability is a poor antigen but they become stable when amino acid residue like tyrosine or tryptophan are incorporated which cross link the peptide chain.
- Similarly, flagellin is a weak antigen and its stability and antigenicity are enhanced by polymerization.

DEGRADABILITY

- All foreign materials are not capable of stimulating immune response e.g., stainless steel pin, plastic heart valves etc.
- The macromolecule which are degradable in nature can act as antigen. Plastic bags are inert organic polymers, not degradable and they are not antigen.
- The antigen molecule should be degraded and processed to form suitable to trigger immune response.

FOREIGNNESS

- Antigens are foreign substances.
- The defense cells of the body, normally do not respond to its own molecule (self-antigen).
- In general, the antigenicity of a substance is related to the degree of its foreignness.
- Antigen from other individual of the same species is less antigenic than from other species.
- Antigens from related species are less antigenic than those from unrelated (distinct) species.
- Antibodies are not usually produced against the body's own components.
- In exceptional cases autoantibodies are produced against own tissues (antigen).

GENOTYPE OF THE RECIPIENT ANIMAL

- The genetic control of the immune response is confined to the genes within the MHC.
- The MHC gene products function to present processed antigen to T cell thus playing a central role in determiningimmunogenicity.

DOSAGE AND ROUTE OF ADMINISTRATION

- An insufficient dose will not evoke an immune response either because it fails to activate enough lymphocytes or because it induces a non-responsive state.
- An excessively high dose also can fail to induce a response because it causes lymphocytes to enter a non responsive state.
- For inducing strong immune response, repeated administrations (boosters) are required.

- Antigens are generally administered parenterally i.e. by routes other than the digestive tract.

ADJUVANTS

- Adjuvants [adjuvare (Latin) = to help]. Adjuvants are substances that when mixed with an antigen and injected, it serves to enhance the immunogenicity.
- They are often used to boost the immune response when an antigen has low immunogenicity or when only small amountof antigen is available. Ajuvants augment the immune response by one or more of the following effects.
    - Prolong antigenic persistence
    - Enhance co-stimulatory signal
    - Induce granuloma formation
    - Stimulate lymphocyte proliferation nonspecifically.
- e.g: Alum, Aluminium hydroxide,Bacterial LPS, Saponin, IL-12, Montanide, Freund's adjuvant etc.
- Freund's incomplete adjuvant contains a mineral oil and an emulsifying agent such as mannide monooleate.
- Freund's complete adjuvant contains in addition heat killed Mycobacteria and it is more potent than incomplete adjuvant.

HAPTEN

- Haptens are usually non-protein substances of low molecular weight having very little or no antigenic property but acquireantigenicity when they are coupled to a protein (carrier molecule).
- Haptens are incapable of inducing antibody formation by themselves but can react specifically with antibodies.They are called partial antigen.
- The term hapten is derived from Greek *haptein* mean 'to fasten'.

- A chemical to be tested as a determinant of specificity was attached to an aromatic amine such as aniline (aniline, p-aminobenzoic acid, p- amino benzene sulphonic acid, p-amino phenyl arsonic acid), then diazotized and coupled to a protein.
- The resulting product was called a *conjugated antigen* or *azoprotein*.
- It is possible to study the immune response of a well-defined chemical by conjugating to a protein molecule.
- Hapten may be complex or simple molecule.
- *Complex hapten* is large molecular weight, polyvalent compound.
- When they combine with antibody prepared against the complete antigenic complex (new antigen) a visible precipitationis formed.
- *Simple hapten* is a low molecular weight, univalent compound. When they combine with antibody prepared against complete antigenic complex, no visible precipitation is formed.
- Examples: Penicillin, Dinitro Phenyl (DNP) etc.

ANTIGENIC DETERMINATS OR EPITOPES

- An antigen will evoke immune response in a specific host.
- The antigenic specificity is determined by *Epitopes*, the smallest unit of antigenicity.
- Epitopes are some specific areas or chemical groupings with steric (spatial) configuration present on the surface of antigen molecule.
- Epitopes are capable of sensitizing an immunocyte and reacting with its complementary site on the specific antibody orTCR.
- The combining area on the hypervariable region of antibody molecule that corresponds to epitopes is called *paratope* ***or*** *idiotope*. On T cells the recognition site is termed as *Agretope*.
- Epitopes and paratope determined the specificity of immunological reaction.
- Epitopes are also called antigenic determinants.
- Most epitopes have 6 to10 amino acids (T cell epitopes) or 10-15 amino acids (B-cell epitopes)