Antigens

Kusum Shrestha
Assistant Professor
School of Health and Allied Sciences
Pokhara University

Introduction

ANTIGEN

Antigen is defined as any substance that satisfies two distinct immunologic properties—immunogenicity and antigenicity.

1. **Immunogenicity:** It is the ability of an antigen to induce immune response in the body (both humoral and/or cell mediated).
   - B cells + antigen → effector B cells (plasma cell) + memory B cells
   - T cells + antigen → effector T cells (helper T cell or cytotoxic T cell) + memory T cells
2. **Antigenicity (immunological reactivity):** It is the ability of an antigen to combine specifically with the final products of the above two responses (i.e., antibodies and/or T cell-surface receptors).

contd

- The substance *that* satisfies the first property, i.e. immunogenicity (inducing specific immune response) is more appropriately called **"immunogen"** rather than **using the word "antigen”**
- All molecules having immunogenicity property, also show antigenicity, but the reverse is nor true (e.g. haptens- which are antigenic, but not immunogenic)

Epitope

- Epitope or antigenic determinant is the smallest unit of antigenicity
- *It* is defined as a small area present on antigen comprising of few (four *to* five) amino acids or monosaccharide residues, *that* is capable of sensitizing T and B cells and reacting with specific site of T cell receptor or an antibody.
- The specific site of an antibody *that* reacts with the corresponding epitope of an antigen is called **paratope.**
- Epitopes are of two types. They may be linear(sequential) and conformational(non sequential)
- In general, T cells recognize sequential epitopes, while B cells bind to the conformational epitopes

Hapten

- Low molecular weight molecules that lack immunogenicity but retain antigenicity or immunological reactivity
- Haptens can become immunogenic when combined with a larger protein molecule called carrier
- Classified as complex hapten(two or more epitopes) and simple(only one epitope)

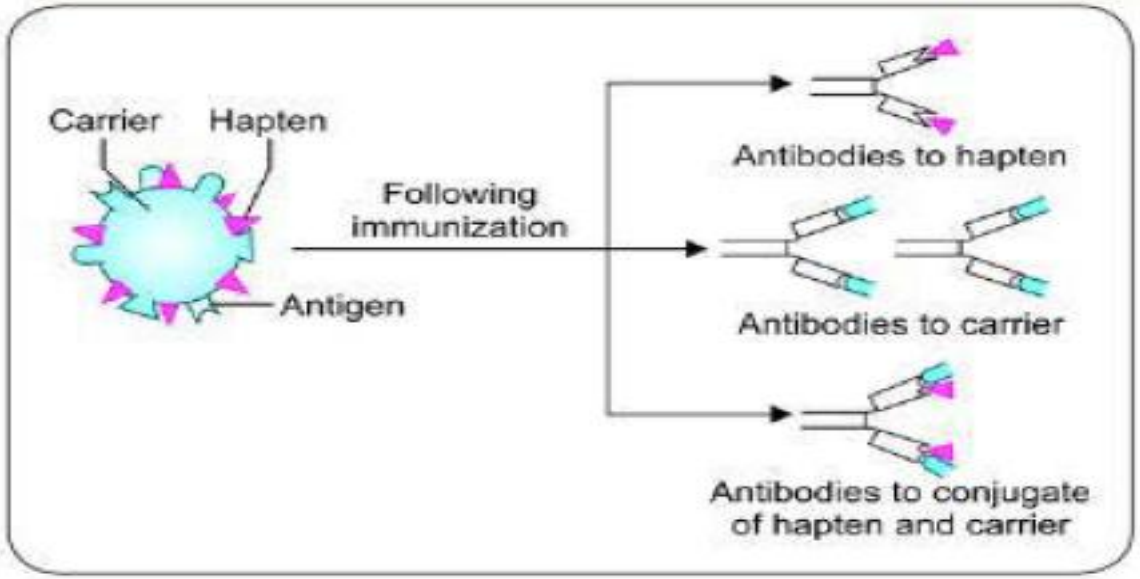

Fig. 10.1: Types of antibodies produced against a hapten-carrier conjugate

Classification of antigen

- Based on host-antigen relationship, antigens can be classified into two groups

1)Self or auto antigen

2)Non-self or foreign antigen

❖Biological class(on the basis of inducing antibody formation)

1) T dependent antigen
2) T independent antigen
3) Superantigen

Self or auto antigen

1. **Self or auto antigens:** They belong to the host itself; hence they are not immunogenic. Hosts do not react to their own antigens by exhibiting a mechanism called **immunological tolerance** (chapter 17). However, sometimes, the self-antigens are biologically altered (e.g. as in cancer cells) and can become immunogenic.

Non self or foreign antigen

2. **Non-self or foreign antigens:** They are immunogenic and are of three types based on their phylogenetic distance to the host.
   - **Alloantigens** are species specific. Tissues of all individuals in a species contain species-specific antigens.
   - **Isoantigens** are type of antigens which are present only in subsets of a species, e.g. blood group antigens and histocompatibility antigens. The histocompatibility antigens are highly specific as they are unique to every individual of a species.
   - **Heteroantigens:** Antigens belonging to two different species are called heteroantigens, e.g. antigens of plant or animal or microorganisms, etc. A **heterophile antigen** is a type of heteroantigen that exists in unrelated species

T dependent antigen

T Dependent (TD) Antigens

Most of the normal antigens are T cell dependent, they are processed and presented by antigen-presenting cells (APCs) to T cells which leads to T cell activation. The activated T cells secrete cytokines that in turn stimulate the B cells to produce antibodies.

T independent antigen

T Independent (TI) Antigens

There are a few antigens such as **bacterial capsule, flagella** and **LPS** (lipopolysaccharide) that do not need the help of T cells and APCs. They directly bind to immunoglobulin receptors present on B cells and stimulate B cells polyclonally. It leads to increased secretion of non-specific antibodies hypergammaglobulinemia.

Superantigen

Superantigens

Superantigens are the third variety of biological class of antigens, recently described in the last decade. The unique feature of superantigens is, they can activate T cells directly without being processed by antigen-presenting cells (APCs).

TABLE 10.2: Superantigens

Bacterial superantigen
Staphylococcal toxin: ▪ Toxic shock syndrome toxin-1 (TSST-1) ▪ Exfoliative toxin ▪ Enterotoxins
Streptococcal pyrogenic exotoxin (SPE)-A and C
Mycoplasma arthritidis mitogen-I
▪ *Yersinia enterocolitica* ▪ *Yersinia pseudotuberculosis*
Viral superantigen
Epstein-Barr virus associated superantigen
Cytomegalovirus associated superantigen

Factors affecting immunogenicity

- Size of the antigen
- Chemical nature of antigen
- Susceptibility of antigen to tissue enzyme
- Structural complexity
- Foreignness to host
- Genetic factor
- Optimal dose of antigen
- Route of administration
- Repeated dose of antigen
- Multiple antigens

Size and chemical nature of antigen

- **Size of the antigen:** Larger is the size; more potent is the molecule as an immunogen. It is found that molecules of more than 10,000 Dalton molecular weight only can induce immune response (e.g. hemoglobin). Substances of molecular weight between 5000-10,000 Dalton are poor immunogens (e.g. insulin).
- **Chemical nature of the antigen:** Proteins are stronger immunogens than carbohydrates followed by lipids and nucleic acids.

Susceptibility of antigen to tissue enzyme

Susceptibility of antigen to tissue enzymes: Only substances that are susceptible to the action of tissue enzymes are immunogenic. Degradation of the antigen by the tissue enzymes produces several immunogenic fragments having more number of epitopes exposed. Molecules that are not susceptible to tissue enzymes such as polystyrene latex or synthetic polypeptides composed of **D-amino acids** are not antigenic; while polypeptides consisting of **L-amino acids** are antigenic

Structural complexity

Structural complexity: Simple homopolymers made up of single amino acid lack immunogenicity. Polymers made up of two or more amino acids are immunogenic. More so, addition of aromatic amino acids increases immunogenicity. Complex proteins containing 20 amino acids and with four level of structural organization are strongly immunogenic; e.g. hemoglobin.

Foreignness to host

- **Foreignness to the host:** This is one of the key factor which determines immunogenicity. Higher is the phylogenetic distance between the antigen and the host; more is the immunogenicity.
  - Self-antigens are not immunogenic; whereas, heteroantigens and alloantigens are immunogenic; the degree of immunogenicity increases with the distance.
    - Plant antigens are more immunogenic than animal antigens to humans.
    - Bovine serum albumin is more immunogenic to chicken than to goat.
  - Isoantigens are not immunogenic to those individuals who possess these antigens; but for other individuals they are immunogenic.

Genetic factor

Genetic factor: Different individuals of a given species show different types of immune responses towards the same antigen. This is believed to be due to the genetic differences between the individuals.

- Responders are the individuals who produce antibody faster.
- Slow responders are the individuals who produce antibody slowly and may need repeated antigenic exposures.
- Non-responders are the individuals who do not produce antibody in spite of repeated antigenic exposures.

Optimal dose of antigen: An antigen is immunologically active only in the optimal dose range. A too little dose fails to elicit immune response and a too large dose leads to development of immunological tolerance

Route of antigen administration: In general, the immune response is better induced following parenteral administration of an antigen; however it also depends on the type of antibody produced.

Site of injection may influence immunogenicity- The hepatitis B vaccine is more immunogenic following deltoid injection than gluteal injection. This may be due to the paucity of antigen presenting cells (APCs) in gluteal fat.

Repeated dose of antigen

Repeated doses of antigens: Repeated doses of antigens over a period of time are needed to generate an adequate immune response. This is due to the role of memory cells in secondary immune response. However, after a certain doses of antigens, no further increase in antibody response is seen.

Multiple antigens: When two or more antigens are administered simultaneously, the effects may vary. The antibody response to one or the other antigen may be equal or diminished (due to antigenic competition) or enhanced

Effect of prior administration of antibody

- **Effect of prior administration of antibody:** The immune response against a particular antigen is suppressed if its corresponding antibody was administrated prior to that.
  - The primary immune response is more susceptible to get suppressed than the secondary immune response.