# Antigens – Definition, Properties, and Classification

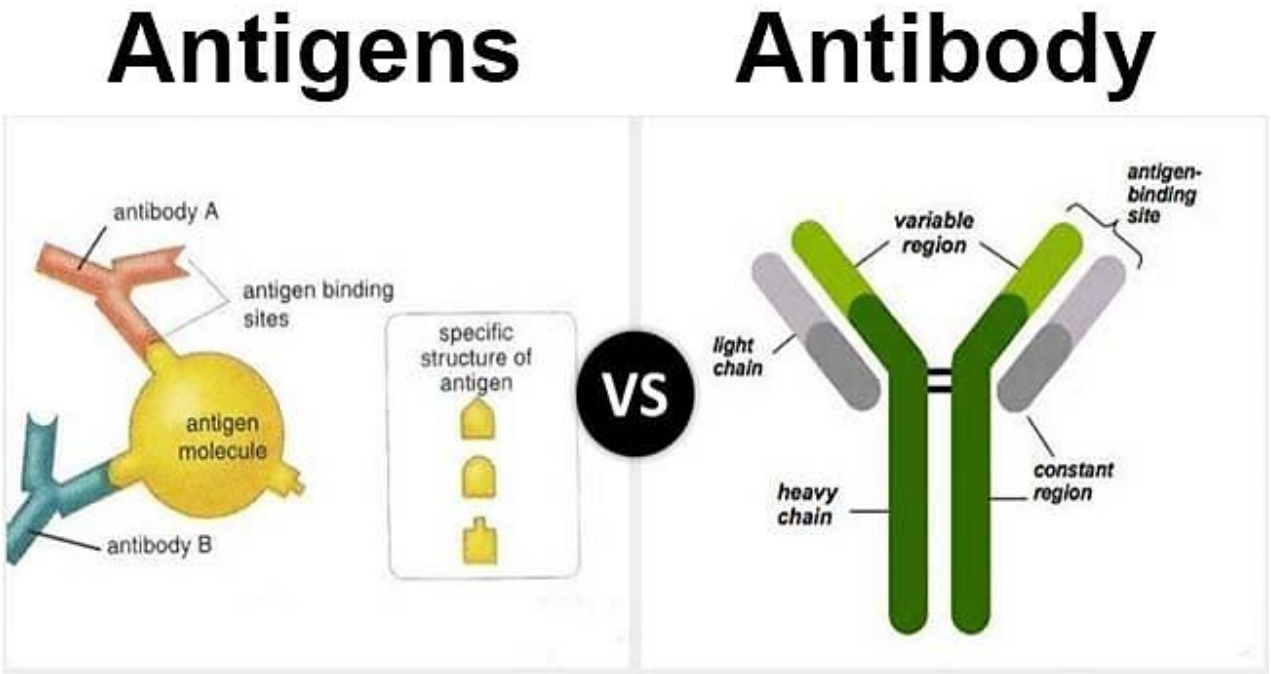
## Definition of Antigen

The term **antigen** is derived from "antibody generator," reflecting its ability to stimulate the production of antibodies. An **antigen (Ag)** is any substance, typically a protein or polysaccharide, that can be specifically recognized by components of the immune system, particularly **B cells** and **T cells**, leading to an immune response.

## Key points in defining an antigen:

- Must be recognized as **foreign (non-self)** by the immune system.
- Can induce the production of **specific antibodies** (humoral immunity) or activate **T cells** (cell-mediated immunity).

Includes **proteins, glycoproteins, lipids, polysaccharides**, and sometimes **nucl**



## Classification of Antigens

Antigens can be classified based on several criteria:

### A. Source

1. **Exogenous Antigens**: Enter the body from outside (e.g., microbes, pollen, toxins).
2. **Endogenous Antigens**: Generated within the body (e.g., viral proteins produced inside infected cells, tumor antigens).
3. **Autoantigens**: Normal body molecules that the immune system mistakenly recognizes as foreign in autoimmune diseases.
4. **Alloantigens**: Found in genetically different members of the same species (e.g., blood group antigens, transplant antigens).

### B. Chemical Nature

1. **Proteins**: Highly immunogenic due to complex structure; examples include bacterial toxins.
2. **Polysaccharides**: Moderate immunogenicity; examples include bacterial capsules.
3. **Lipids**: Poorly immunogenic unless bound to proteins (forming glycolipids or lipoproteins).
4. **Nucleic acids**: Generally weak immunogens; often require carriers to elicit a response.

### C. Immunogenicity and Reactivity

1. **Complete Antigens (Immunogens)**: Can induce an immune response independently and react with antibodies. Example: tetanus toxoid.
2. **Haptens (Incomplete Antigens)**: Cannot elicit an immune response alone; must bind to a carrier molecule. Example: penicillin.

## Properties of Antigens: it is essential for predicting immune responses.

### A. Immunogenicity

The ability to **stimulate an immune response** depends on:

- Molecular size (larger molecules are more immunogenic) and compex.
- Foreignness (difference from host molecules)
- Degradability (must be processed for presentation by MHC molecules)

### B. Antigenicity

The ability to **react specifically with antibodies or T-cell receptors**. Note that **all immunogens are antigenic, but not all antigens are immunogenic** (e.g., haptens).

### C. Specificity

Each antigen possesses unique **antigenic determinants (epitopes)** recognized by specific antibodies or T cells. A single antigen may contain multiple epitopes.

### D. Valency

Refers to the **number of antigenic determinants** on a molecule capable of binding to antibodies. Polyclonal responses can target multiple epitopes on the same antigen.

### E. Cross-reactivity

Some antigens share similar epitopes with others, leading to cross-reactions. Example: antibodies against cowpox virus can react with smallpox virus (basis of vaccination).

**F. Complexity**

Protein antigens are usually more complex and highly immunogenic than polysaccharides or lipids.

## Mechanisms of Antigen Recognition

- **B-cell recognition**: Direct binding of antigens to **B-cell receptors (BCRs)**; mainly protein or polysaccharide antigens.
- **T-cell recognition**: Requires processing and presentation by **Major Histocompatibility Complex (MHC)** molecules.
- **Antigen-presenting cells (APCs)**: Dendritic cells, macrophages, and B cells capture and process antigens, presenting them to T cells.

## Factors Affecting Antigenicity

1. **Foreignness** – more difference from host = stronger response.
2. **Size** – molecules >10 kDa are typically immunogenic.
3. **Chemical composition** – proteins > polysaccharides > lipids in immunogenicity.
4. **Structural complexity** – highly branched or folded molecules stimulate stronger immune responses.
5. **Route of administration** – subcutaneous and intradermal routes are more immunogenic than oral.
6. **Dose** – intermediate doses often elicit the best response.

## Clinical Relevance of Antigens

- **Vaccine design**: Selecting strong immunogenic antigens to produce protective immunity.
- **Autoimmune diseases**: Immune system attacks self-antigens.
- **Allergic reactions**: Overreaction to harmless environmental antigens (allergens).
- **Transplantation**: Alloantigens influence graft rejection.

# Cell and T-Cell Epitopes

An **epitope**, also called an **antigenic determinant**, is the specific portion of an antigen recognized by the immune system.

## 1. B-Cell Epitopes

A **B-cell epitope** is the part of an antigen that is recognized and bound directly by a **B-cell receptor (BCR)** or by an antibody in solution. The binding triggers **B-cell activation**, leading to antibody production.

### Characteristics

1. **Recognition**: in their **native three-dimensional conformation**, meaning they do not require processing by antigen-presenting cells (APCs).
2. **Types of B-cell Epitopes**:
    - **Linear (Sequential) Epitopes**: Composed of consecutive amino acids in a protein's primary sequence. Example: peptide fragments in vaccines.
    - **Conformational (Discontinuous) Epitopes**: Formed by amino acids brought together by the protein's three-dimensional folding. Most natural protein epitopes are conformational.
3. **Size**: Typically 5–20 amino acids for peptides or small patches on larger molecules.
4. **Accessibility**: Must be exposed on the surface of the antigen to allow BCR or antibody binding.

### Examples

- The **hemagglutinin protein of influenza** contains conformational epitopes recognized by neutralizing antibodies.

- **Bacterial polysaccharides** can serve as B-cell epitopes, particularly in capsular vaccines.

**Clinical Relevance**

- **Vaccine development** relies heavily on identifying B-cell epitopes to elicit effective humoral immunity.
- **Monoclonal antibody therapies** target specific B-cell epitopes for neutralization of pathogens or cancer cells.

## 2. T-Cell Epitopes

A **T-cell epitope** is a peptide fragment of an antigen presented on the surface of **antigen-presenting cells (APCs)** bound to **Major Histocompatibility Complex (MHC) molecules**, recognized by **T-cell receptors (TCRs)**. T-cell recognition is essential for **cell-mediated immunity** and the activation of B cells.

**Characteristics**

1. **Processing Requirement**: **process** into short peptides (typically 8–25 amino acids) by APCs.
2. **Presentation**:
   - **MHC Class I**: Presents intracellularly derived peptides (usually 8–11 amino acids) to **CD8+ cytotoxic T cells**.
   - **MHC Class II**: Presents extracellularly derived peptides (usually 13–25 amino acids) to **CD4+ helper T cells**.
3. **Linear Epitopes**: are **always linear**, as the protein is degraded into peptides for MHC presentation.
4. **Specificity**: The TCR recognizes both the **peptide** and the **MHC molecule**, making T-cell recognition highly specific.

**Examples**

- Viral peptides from influenza matrix protein recognized by CD8+ T cells.

- Bacterial antigens processed and presented to CD4+ T cells, triggering cytokine release and B-cell help.

**Clinical Relevance**

- **Vaccine design**: Identifying T-cell epitopes ensures robust cellular immunity, critical for intracellular pathogens like viruses and some bacteria.
- **Autoimmune diseases**: Aberrant recognition of self-peptides as T-cell epitopes can trigger tissue damage.
- **Transplantation**: Recognition of alloantigens as T-cell epitopes leads to graft rejection.

## 3. Comparison of B-Cell and T-Cell Epitopes

| Feature | B-Cell Epitopes | T-Cell Epitopes |
|---|---|---|
| **Recognition** | BCR or antibody | TCR + MHC molecule |
| **Structure** | Linear or conformational | Always linear (peptide) |
| **Requirement for processing** | Not required | Required (processed by APCs) |
| **Location** | Surface-exposed | Presented on MHC molecules |
| **Size** | 5–20 amino acids | 8–25 amino acids |
| **Role** | Humoral immunity | Cellular immunity |