Antigens

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Antigens

- The immune system recognizes components of the body it protects as “self” and foreign matter as “nonself” or antigens.
- The vast majority of antigens are proteins, or proteins with side chains.
- Lipids and nucleic acids are only antigenic when combined with proteins or polysaccharides.

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Antigens

- **Microbes:**

capsules, cell walls, flagella, pili, toxins, coats of viruses,

- **Nonmicrobes:**

Pollen, egg white , red blood cell surface molecules, serum proteins, and surface molecules from transplanted tissue.

- **Hapten**:

Small foreign molecule that is not antigenic by it self.

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Tolerogen

An antigen that invokes a specific immune non-responsiveness due to its molecular form. If its molecular form is changed, a tolerogen can become an immunogen.

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Allergen

is a substance that causes the allergic reaction. The (detrimental) reaction may result after exposure via ingestion, inhalation, injection or contact with skin.

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Exogenous antigens

Antigens that have entered the body from the outside (inhalation, ingestion, or injection). By endocytosis or phagocytosis,

- are taken into the antigen-presenting cells (APCs) and processed into fragments.

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Endogenous antigens

Antigens that have been generated within the cell, as a

- result of normal cell metabolism,

- viral or intracellular bacterial infection.

Autoantigens

- is usually a normal protein or complex of proteins (sometimes DNA or RNA) that is recognized by the IS of patients suffering from a specific autoimmune disease.

- Under normal conditions not be the target of the IS, but due to mainly genetic and environmental factors the normal immunological tolerance for such an antigen has been lost in these patients.

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Tumor antigens

presented by the MHC I molecules on the surface of tumor cells.

Sometimes be presented only by tumor cells and never by the normal ones. In this case, they are called tumor-specific antigens (TSAs) and typically result from a tumor specific mutation.

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Immunogenicity

The term immunogen is often used synonymously with the term antigen

* **Immunogen :**
  A foreign substance, when introduced into the body, stimulate formation of specific antibodies or sensitized lymphocytes

* **Antigens:**

Antigens bind to a receptor but do not induce the activation of the lymphocytes.

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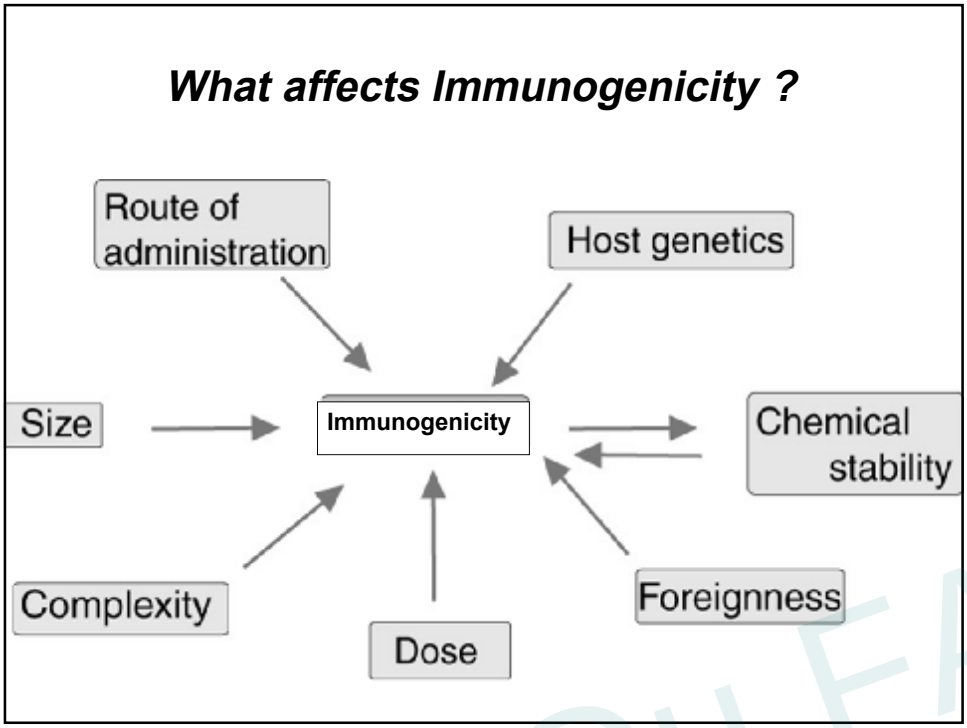
What affects Immunogenicity ?



Factors that influence the immunogenicity of proteins

Parameter	Increased immunogenicity	Decreased immunogenicity
Size	Large	Small (MW<2500)
Dose	Intermediate	High or low
Route	Subcutaneous > intraperitoneal > intravenous or intragastric	
Composition	Complex	Simple
Form	Particulate	Soluble
	Denatured	Native
Similarity to self protein	Multiple differences	Few differences
Adjuvants	Slow release	Rapid release
	Bacteria	No bacteria
Interaction with host MHC	Effective	Ineffective

Figure A-2 Immunobiology, 6'e. (© Garland Science 2005)

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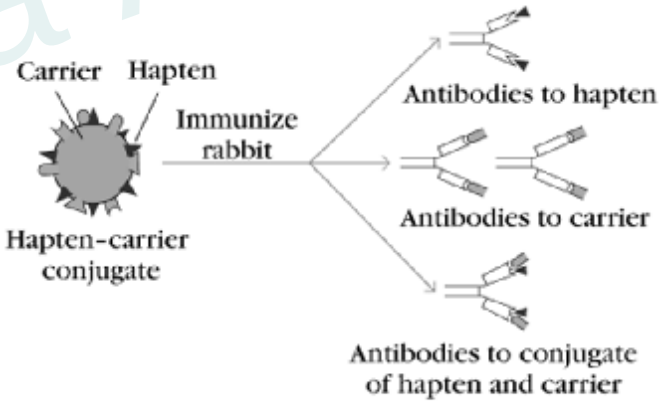
Haptens

- Low molecular weight substances
- Antigenic, can react with the products of a specific immune response
- not immunogenic by itself, become immunogenic, if couple to a larger carrier molecule (albumin, globulins)
- simple chemicals and drugs: penicillin, sulphonamid, aspirin, cosmetic, tranquillizers, neomycin skin ointment



Injection with:	Antibodies formed:
Hapten (DNP)	None
Protein carrier (BSA)	Anti-BSA
Hapten-carrier conjugate (DNP-BSA)	Anti-DNP (major) Anti-BSA (minor) Anti-DNP/BSA (minor)

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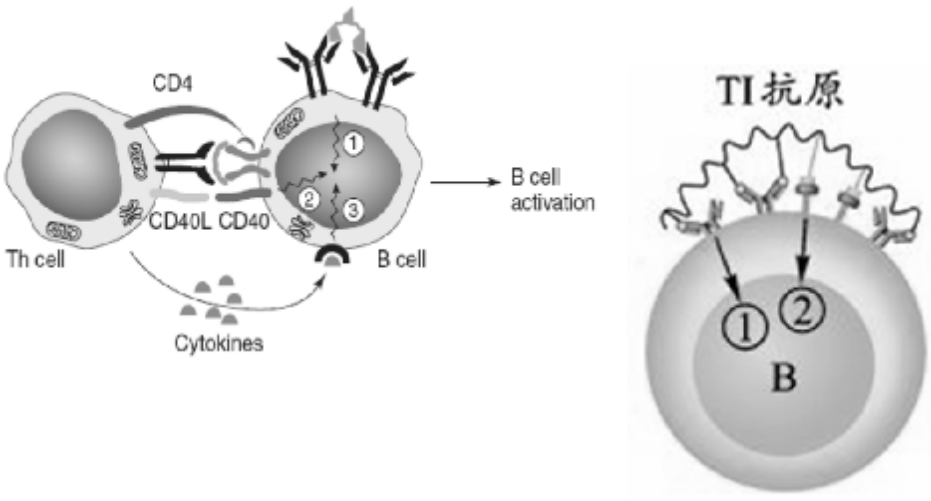
Antigens Recognition

- depends on T and B cells:
  T-dependent (TD) antigens
- A small number of antigens can activate B cells without MHC class II-restricted T cell help:
  T-independent (TI) antigens

Classification of Antigens of Antigens



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Antigenic determinants recognized by B cells and Ab

- **Composition**
  - Proteins, polysaccharides, nucleic acids, haptens
  - Sequence (linear) determinants
  - Conformational determinants
- **Size**
  - 4-8 residues
- **Number**
  - Limited (immunodominant epitopes)
  - Located on the external surface of the Ag (exposed)

Antigenic determinants recognized by T cells

- **Composition**
  - Proteins (some lipids)
  - Sequence determinants
    - Processed
    - MHC presentation
- **Number**
  - Limited to those that can bind MHC

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mitogens

- Phytohemagglutinin (PHA), a lectin isolated from red kidney beans; mitogen for T
- Concanavalin-A, extracted from castor beans, mitogen for T
- Pokeweed mitogen. A mitogen for B and T cells

They activate the T cells regardless of their antigen specificity.

Superantigens

- ❑ Activate multiple clones of T-lymphocytes
- ❑ Have the ability to bind both class II MHC and TCR β chain
- ❑ Act as a clamp between the two, providing a signal for T-cell activation
- ❑ Not processed by APC
- ❑ Active at very low concentration causing release of large amounts of cytokines, pathological effects
- ❑ It does not lead to acquired immunity, not specific for the pathogen

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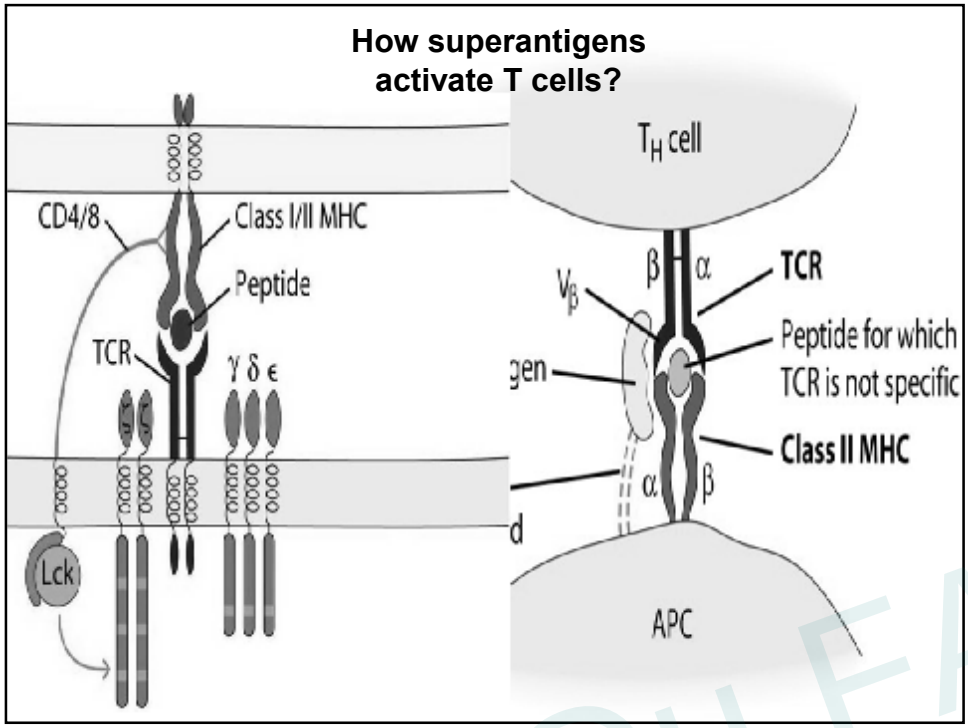

Superantigens

are mostly of bacterial origin and include:

- Staphylococcal enterotoxins
responsible for some types of acute food poisoning

- Toxic shock syndrome toxin
responsible for tampon sepsis-induced shock

- Exfoliative dermatitis toxin.

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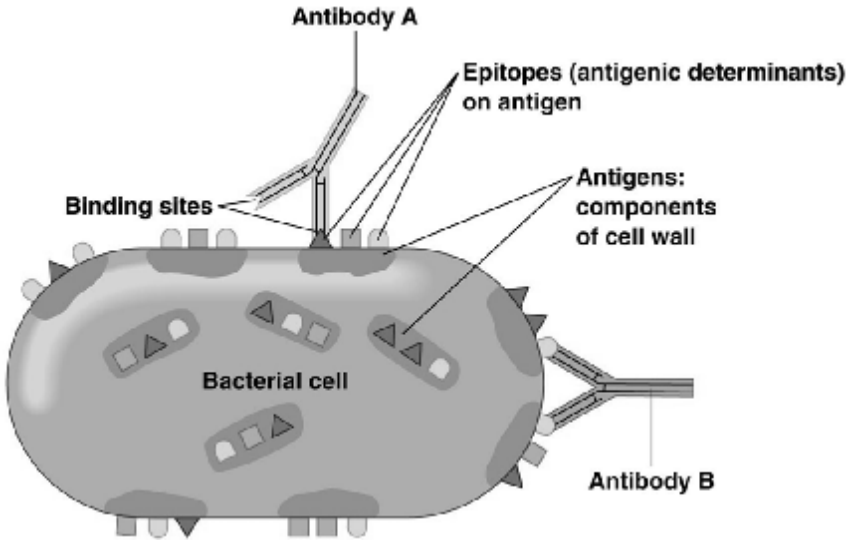
Antigens

- Antibodies do not recognize the whole antigen
- They interact with specific regions called the antigenic determinants **(Epitopes).**
- Most antigens have many different types epitopes on
- The immune system may produce **several distinct antibodies against** a single antigen.

Antigenic Determinants



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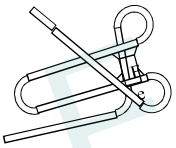
Antigenic epitopes

Epitope,or,**Antigenic determinants,** are the portions of antigen molecules that physically interact with **paratopes** (combining sites) of immune response molecules and therefore actually "determine" antigen specificity



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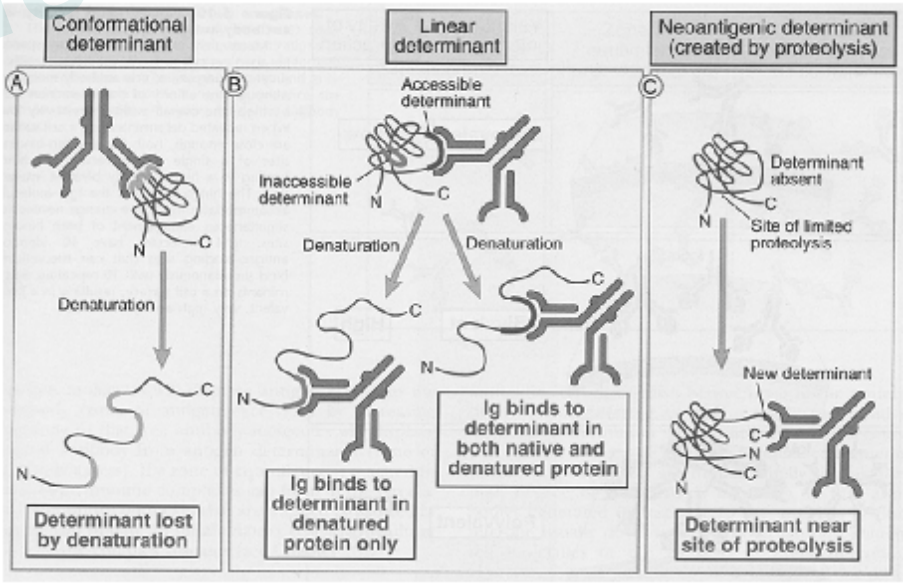
Antigenic epitopes



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Types of Epitopes

1. **Linear epitopes**

♣ **continuous** and found in polysaccharides as well as in both native (nondenatured) and denatured proteins, especially fibrillar proteins.

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2. Conformational epitopes

♣ Discontinuous (involve multiple subunits, often located far apart in the primary sequence of the antigen molecule) and are thus found only in native (globular) proteins.

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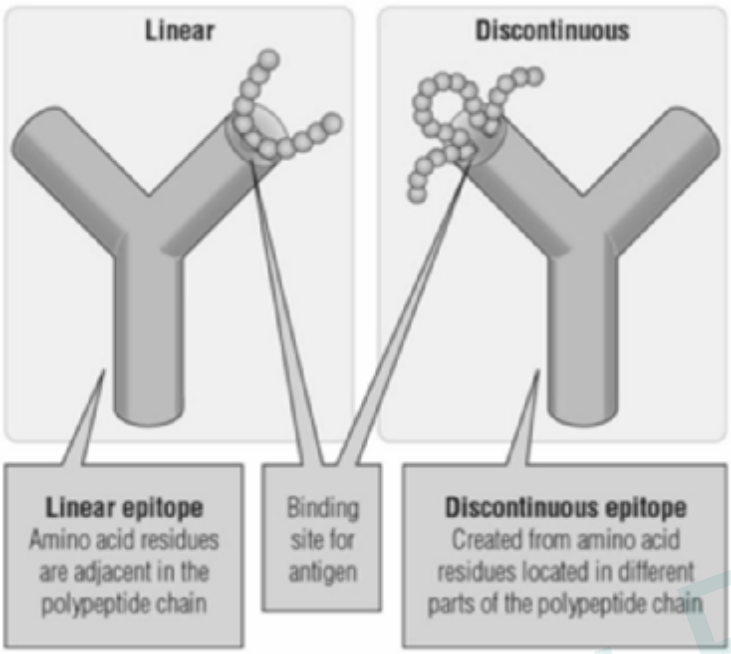

Cross-reactivity

one epitope is shared by two antigens,

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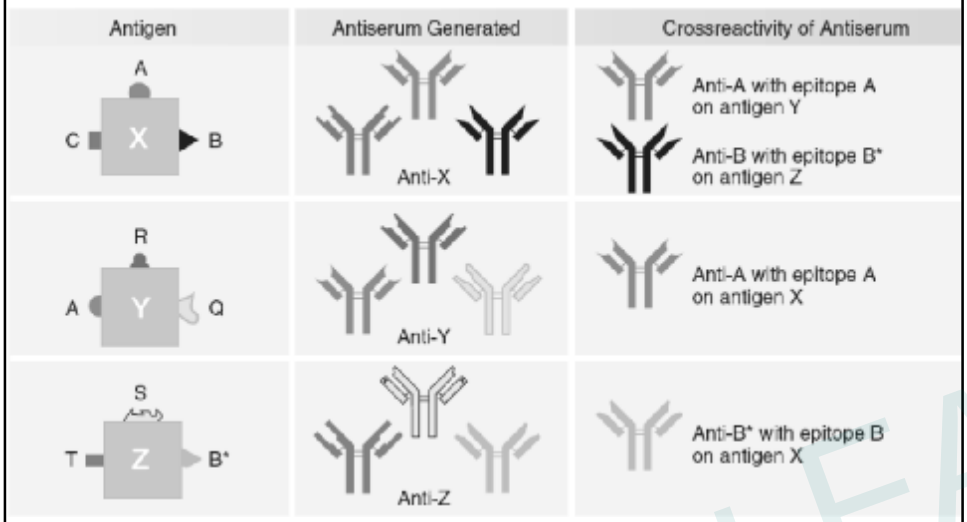
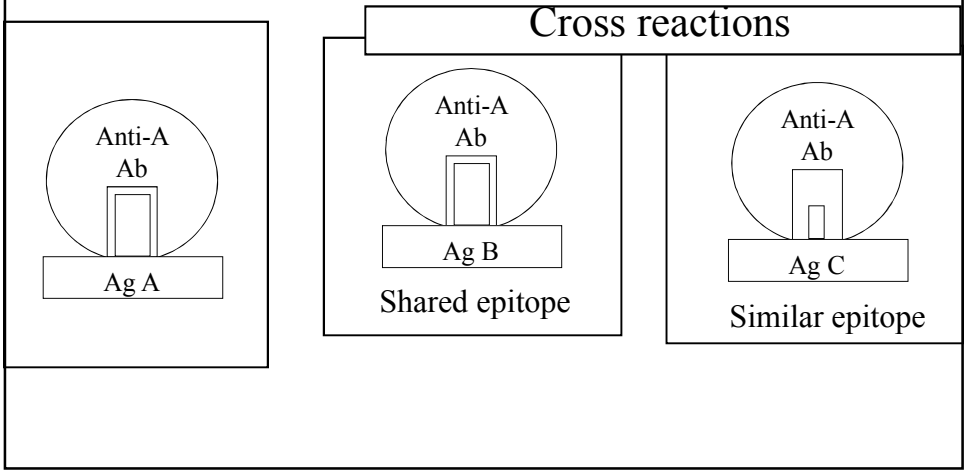
Antibody Cross-reactivity



Cross Reactivity



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adjuvants

8 Adjuvant

- **Adjuvant:** The Latin "adjuvans" means to help, particularly to reach a goal.
- *An adjuvant is a substance that helps and enhances the pharmacological effect of a drug or increases the ability of an antigen to stimulate the immune system.*

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how adjuvants augment the immune response?

- ✓ Antigen persistence is prolonged.
- ✓ Co-stimulatory signals are enhanced.
- ✓ Local inflammation is increased.
- ✓ The nonspecific proliferation of lymphocytes is stimulated.

Adjuvants that enhance immune responses

Adjuvant name	Composition	Mechanism of action
Incomplete Freund's adjuvant	Oil-in-water emulsion	Delayed release of antigen; enhanced uptake by macrophages
Complete Freunds adjuvant	Oil-in-water emulsion with dead mycobacteria	Delayed release of antigen; enhanced uptake by macrophages; induction of co-stimulators in macrophages
Freunds adjuvant with MDP	Oil-in-water emulsion with muramyldipeptide (MDP), a constituent of mycobacteria	Similar to complete Freund's adjuvant
Alum (aluminum hydroxide)	Aluminum hydroxide gel	Delayed release of antigen; enhanced macrophage uptake
Alum plus *Bordetella pertussis*	Aluminum hydroxide gel with killed *B. pertussis*	Delayed release of antigen; enhanced uptake by macrophages; induction of co-stimulators
Immune stimulatory complexes (ISCOMs)	Matrix of Quil A containing viral proteins	Delivers antigen to cytosol; allows induction of cytotoxic T cells

Figure A-4 Immunobiology, 6/e, © Garland Science 2005

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