Tikrit University
College of Veterinary Medicine

Lect. 9-Immunology

Subject name: Antigens
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Lecturers link

Antigen

The adaptive immune system, uses receptors that can bind and respond to almost all the foreign macromolecules present in an invading microorganism. These foreign macromolecules are called antigens .

- **Antigen is a substance which when introduced into the tissues of a susceptible animal, it stimulates the formation of specific neutralizing substances or antibody which it reacts specifically in some observable way or produced Cytokines or both antibody and Cytokines**
- **The ability of a material to induce an immune response is referred to as immunogenicity and such material is called as immunogen.**
- ***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.**

What Makes a Good Antigen?

- **The best antigens are large, complex, and foreign. However, their ability to stimulate an immune response is also determined by their route of administration, by the amount of antigen administered, and by the genetic makeup of the immunized animal.**
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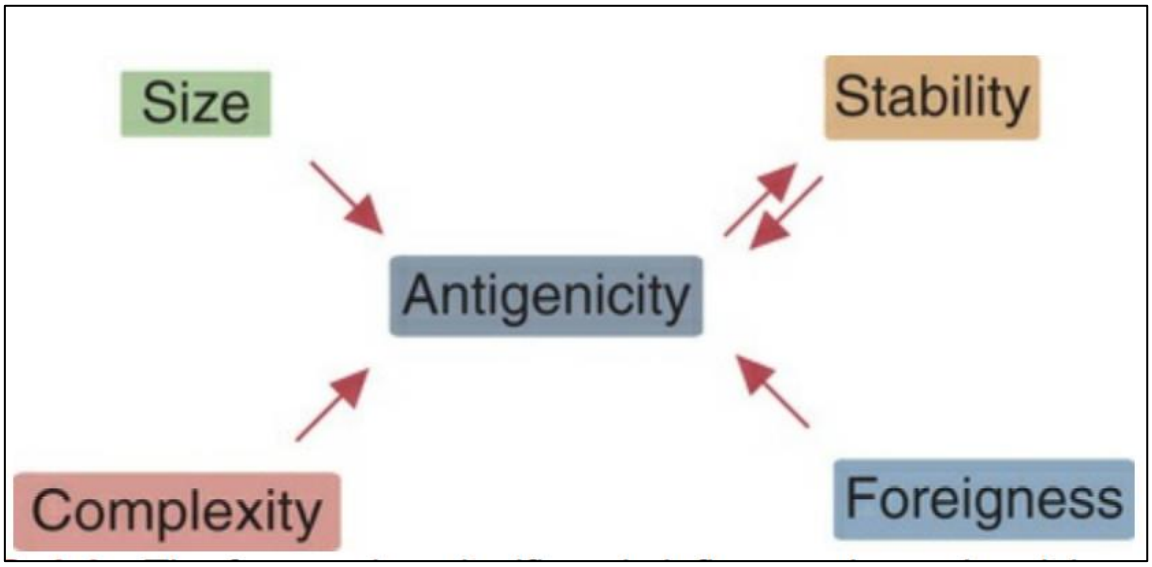
- **Simple polysaccharides, such as starch or glycogen, are not good antigens simply because they are often degraded before the immune system has time to respond to them.**
- **Lipids tend to be poor antigens because of their wide distribution, relative simplicity, structural instability, and rapid metabolism.**
- **Mammalian nucleic acids are very poor antigens because of their relative simplicity and flexibility, and because they are very rapidly degraded. Microbial nucleic acids, on the other hand, have a structure very different from that found in eukaryotes As a result, they can stimulate potent immune responses.**
- **Proteins are the most effective antigens because they have properties that best trigger an immune response.**

FACTORS DETERMINING ANTIGENICITY



1. **Foreignness**

<u>The immunogenicity of a molecule also depends on its degree of foreignness</u>

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

2. **COMPLEXITY**

<u>Good antigens have complex structure. Large complex molecules can be readily taken up by macrophages. Complex proteins are good immunogen containing many different amino acids, especially aromatic ones, are better antigens than large.</u> Repeating polymers, such as lipids, carbohydrates, and nucleic acids are poor antigens, but <u>complex bacterial lipopolysaccharides are good antigen .</u>

3. **STABILITY**

<u>Structural stability is an important feature of good antigens, especially those that trigger antibody responses. Antigen molecule must be stable and rigid.</u> 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.

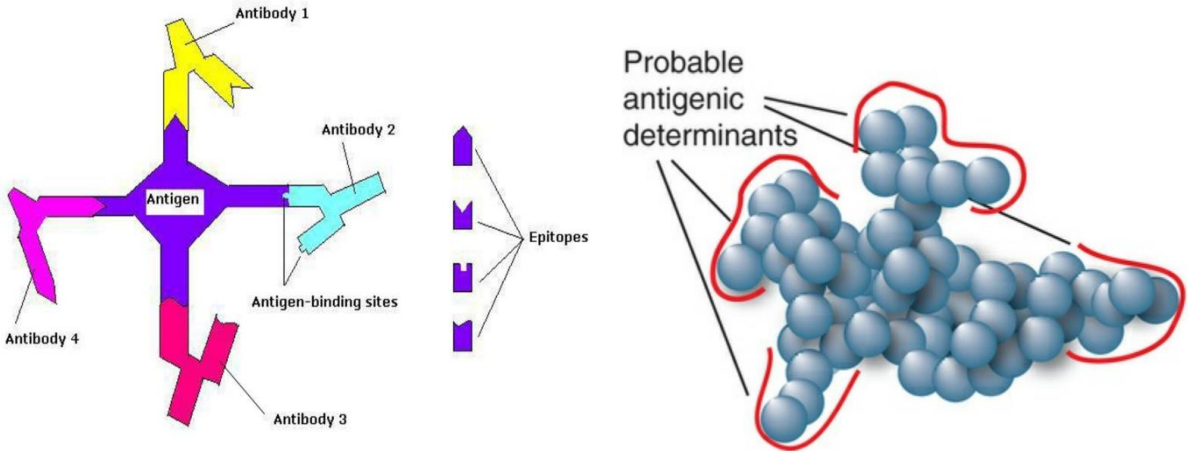
4. MOLECULAR SIZE

Foreign proteins make the best antigens, especially if they are big (greater than 1000 Da is best). 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 a good antigen. Many of the major antigens of microorganisms such as the clostridial toxins, bacterial flagella, virus capsids, and protozoan cell membranes are large proteins.

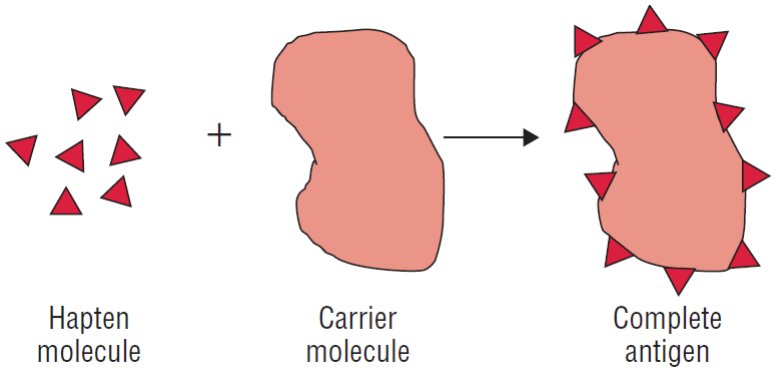
5. Others factor

a) **EPITOPES**

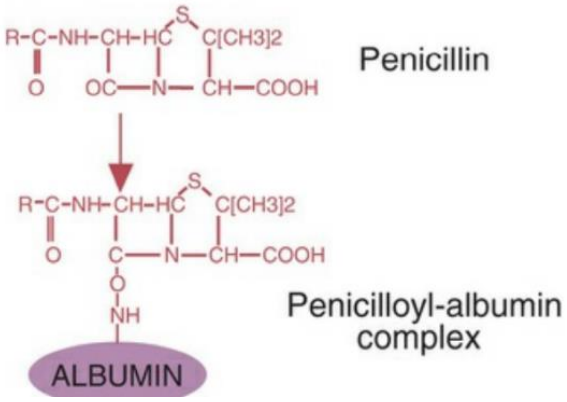
- **Large molecules have regions on their surface that bind to lymphocyte antigen receptors and against which immune responses are therefore directed. These regions, usually on the surface of the molecule, are called epitopes, or antigenic determinants. In a large, complex protein molecule, many different epitopes may be recognized by lymphocytes, but some are much more immunogenic than others. Thus animals may respond to a few favored or ideal epitopes, and the remainder of the molecule may be ignored. Such favored epitopes are said to be immunodominant.**
- **The presence of multiple identical determinants in an antigen is referred to as polyvalency or multivalency.**



b) **Haptens : Small molecules, such as many drugs or hormones of less than 1000 Da, are far too small to be appropriately processed and presented to the immune system. As a result, they are not immunogenic. however, these small molecules that can function as epitopes only when molecules are chemically linked to other larger molecules are called haptens (in Greek, haptein means "to grasp or fasten").**



- **The antibiotic penicillin is a small nonimmunogenic molecule. Once degraded within the body, however, it forms a very reactive "penicilloyl" group, which can bind to serum proteins such as albumin to form penicilloyl-albumin complexes). The penicilloyl hapten can be recognized as a foreign. In some individuals and so provokes an immune response, resulting in penicillin allergy.**



c) **Cross-reactivity**

Cross-reactivity between antigens occurs when an antibody directed against one specific antigen is successful in binding with another, different antigen. Identical or similar epitopes may sometimes be found on apparently unrelated molecules. As a result, antibodies directed against one antigen may react unexpectedly with an unrelated antigen. In another situation, the epitopes on a protein may differ in only minor respects from those on the same protein obtained from an animal of a related species.

Types of Antigens

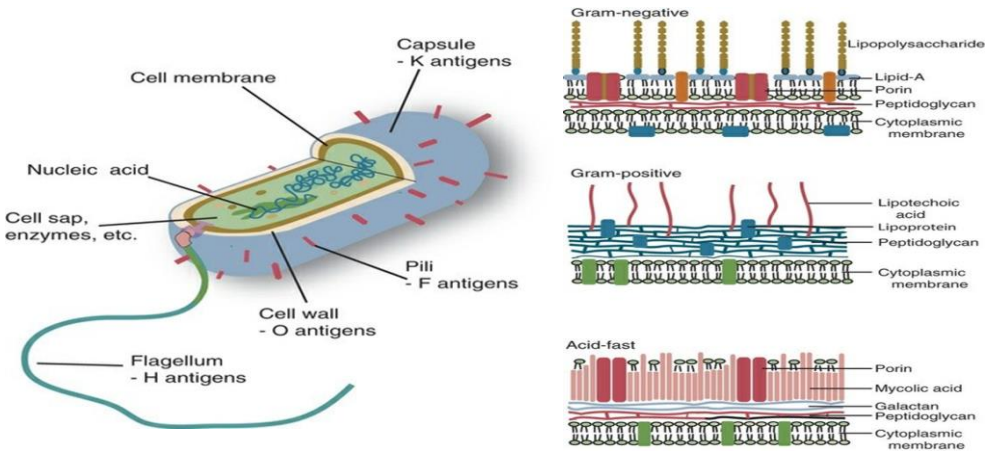
1. Autoantigens

In some situations (and not always abnormal ones), an animal may display immune responses against normal body components. These are called autoimmune responses. Antigens that induce autoimmunity are called autoantigens. They can include hormones, such as thyroglobulin; structural components, such as basement membranes; complex lipids, such as myelin; intracellular components, such as the mitochondrial proteins, nucleic acids, or nucleoproteins; and cell surface proteins, such as hormone receptors.

2. Microbial antigens:

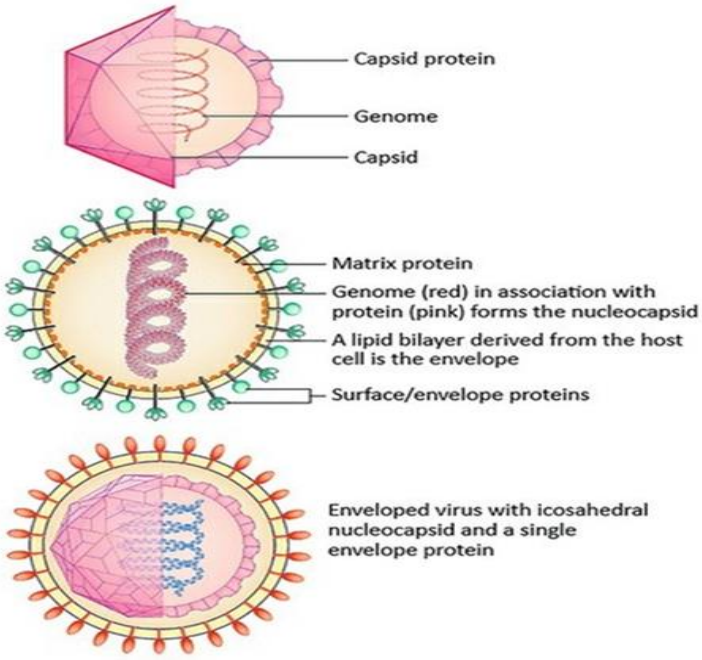
a) Bacterial antigen

- **Cellular antigens:**
  - **The major components of the bacterial surface include the cell wall and its associated protein structures, the capsule, the pili, and the flagella**
  - **The cell wall of Gram-positive organisms compose of peptidoglycan and also contain lipoteichoic acids (Fig.2). lipoteichoic acids has antigenic properties being able to stimulate specific immune response**
  - **Most of the antigenicity of Gram-negative bacteria is associated with the lipopolysaccharide. This consists of an oligosaccharide attached to a lipid (lipid A) and to a series of repeating trisaccharides. The structure of these trisaccharides determines the antigenicity of the organism. These polysaccharide antigens are called O antigens.**
  - **These antigens serve as pathogen-associated molecular patterns (PAMP)and are recognized by pattern-recognition receptors such as the Toll-like receptors. The major cells expressing TLRs are antigen-presenting cells (APCs). Activation of TLRs in APCs can affect maturation of these cells and T helper 1 (Th1) cell differentiation for processing more specific immune mechanisms.**
  - **Bacterial capsules consist mainly of polysaccharides that are usually good antigens are called K antigens. Pili and fimbriae they are classified as F or K antigens. also ,Flagellar antigens are collectively called H antigens.**
- **Soluble antigens Some soluble substances produced by the bacteria, which are excreted into the environment. For example, the exotoxins such as Clostridium tetani toxin.**



b) **Viral Antigens**

Viruses usually have a relatively simple structure consisting of a nucleic acid core covered by a protein layer . This protein layer is termed the capsid, and consists of multiple subunits called capsomeres. <u>Capsid protein and envelope (consists of lipoprotein and glycoprotein) are good antigens</u> well capable of stimulating antibody responses. When a virus infects an animal, its proteins are processed, recognized, and trigger adaptive immune responses. Examples, HN protein (glycoprotein) of Newcastle disease virus

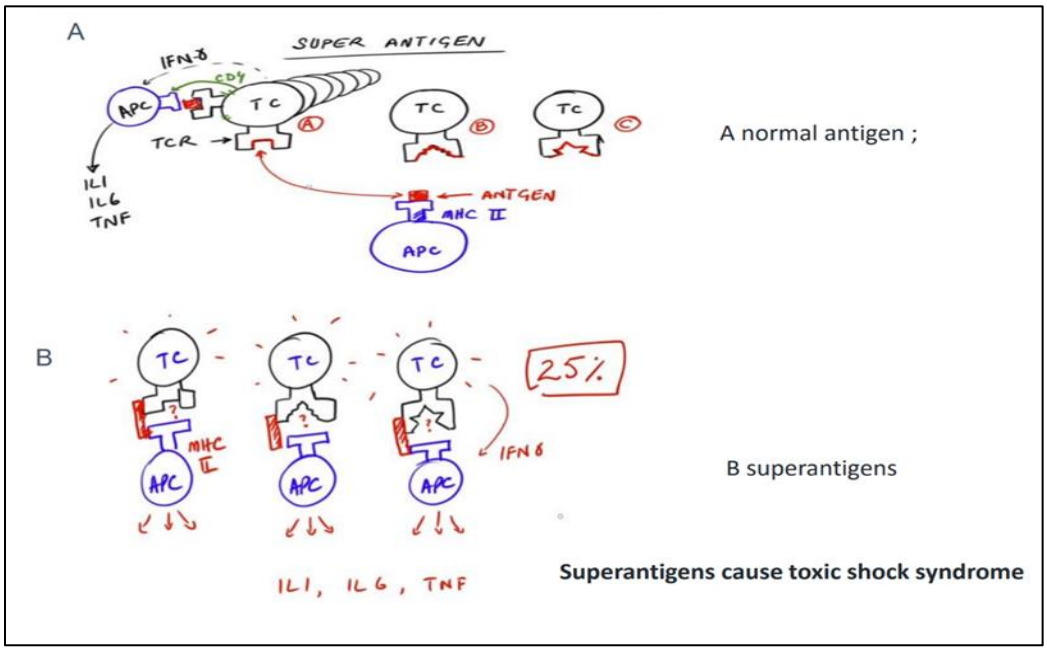


The structure of some viruses. The antigenic proteins include the capsids and envelope proteins. (Courtesy Dr. S. Payne.)

c) Other Microbial Antigens **In addition to bacteria and viruses, animals may be invaded by fungi, protozoan parasites, arthropods, and even parasitic worms (helminths).** **Each of these organisms consists of many different structures composed of proteins, carbohydrates, lipids, and nucleic acids. Many of these molecules can serve as antigens and trigger adaptive immunity. These organisms are not always successful in protecting an animal or eliminating the invader.**

d) **Super antigen**

Fewer than 1 in 10,000 T cells can bind and respond to any specific foreign antigen. However, some microbial molecules called superantigens are unique in that they may stimulate as many as one in five T cells. All superantigens come from microbial sources such as streptococci, staphylococci, and mycoplasma, and from viruses such as rabies. they bind the T cell and the antigen presenting cell together. Because of this strong binding, superantigens trigger a powerful T cell response. Some superantigens may stimulate the secretion of so many cytokines that they trigger a toxic shock syndrome.



3. Cell surface antigen

Mammalian cell surface contain protein molecules within lipid bilayer. These proteins may act as antigen when injected into another animal of same species or different species. Important cell surface antigens are

a) **Blood group antigen: Blood groups are mainly named according to the species-specific antigens present on the surface of erythrocytes. Theses antigens play a key role in inducing immune-mediated reactions and can cause complications while transfusing blood from different blood groups. RBC of group A carry antigen A, group B carry antigen B, O group have neither A nor B antigen and group AB carry both A and B antigen**
b) **Major histocompatibility complex (MHC) molecules: The major histocompatibility complex (MHC) is a collection of genes coding for MHC molecules found on the surface of all nucleated cells of the body. Antigens can only trigger an adaptive immune response after binding to MHC molecules. The MHC molecules are divided into three types, Class I, Class II and Class III.**
c) **Cluster of differentiation (CD): The cluster of differentiation (CD) is a protocol used for the identification of cell surface molecules present on leukocytes. CD molecules often act as receptors or ligands important to the function of immune cells. Some CD proteins play a role in cell.**