Antigens

Dr. Imran Riaz Malik
Immunology

- **Antigens are defined as substances that bind to specific antibodies.**

- **Immunogens are those substances that elicit a response from the immune system.**

- **Not all antigen produce an immunogenic response, but all immunogens are antigens.**

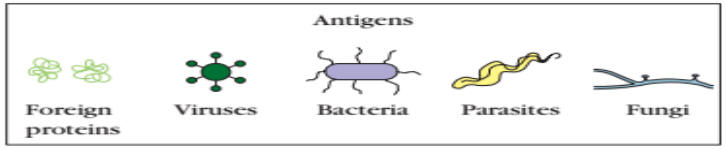
- **Antigens are usually proteins or polysaccharides.**

- **This includes parts of bacteria, viruses and other microorganisms.**

- **Lipids and nucleic acids are antigenic only when combined with proteins and polysaccharide.**

- **Non-microbial expogenous antigens include pollen, egg white, and proteins from transplanted tissues and organs or on the surface of transfused blood.**

VISUALIZING CONCEPTS



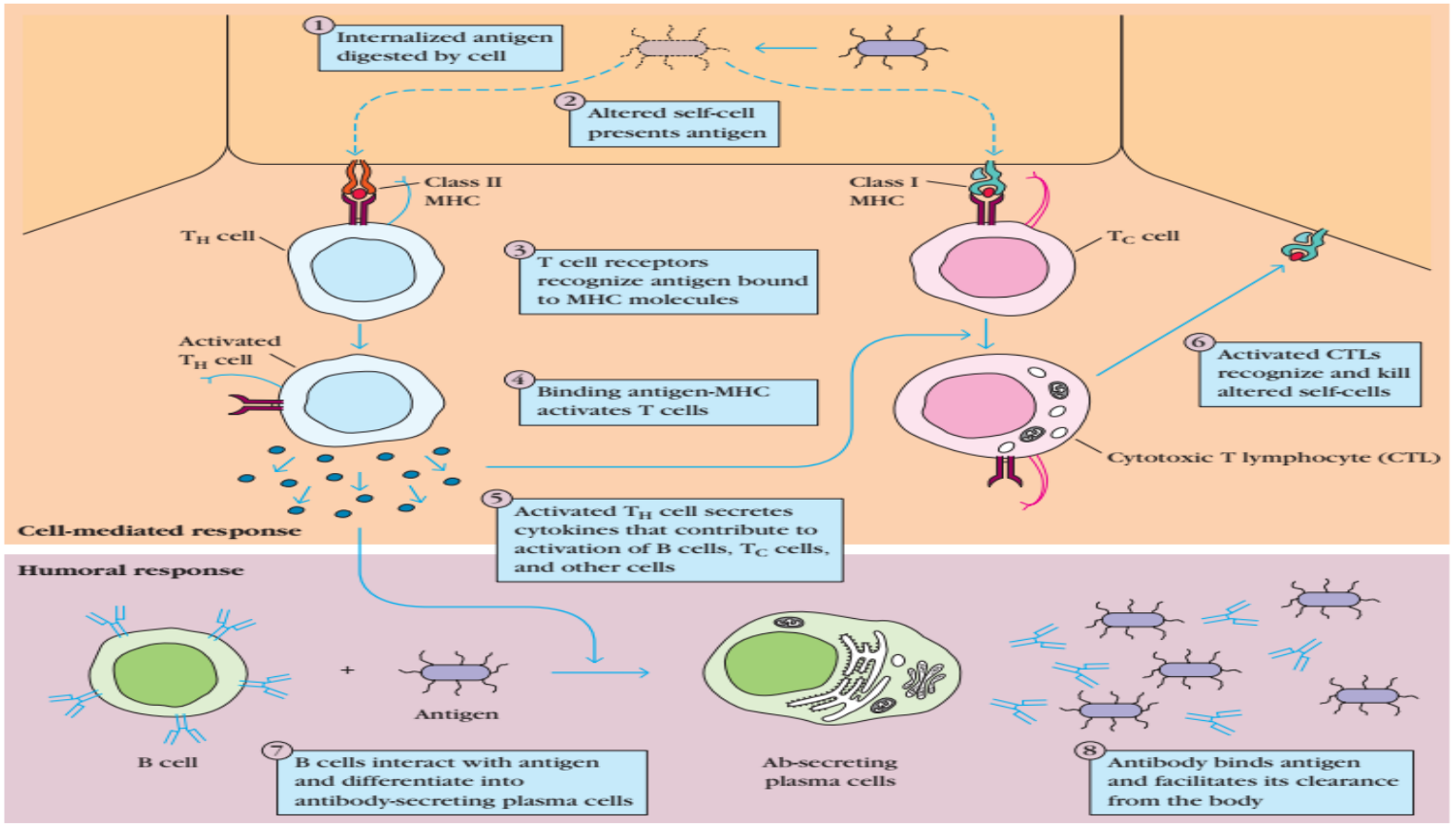


FIGURE 1-7 Overview of the humoral and cell-mediated branches of the immune system. In the humoral response, B cells interact with antigen and then differentiate into antibody-secreting plasma cells. The secreted antibody binds to the antigen and facilitates its clearance from the body. In the cell-mediated response, various subpopulations of T cells recognize antigen presented on self-cells. T_H cells respond to antigen by producing cytokines. T_C cells respond to antigen by developing into cytotoxic T lymphocytes (CTLs), which mediate killing of altered self-cells (e.g., virus-infected cells).

Factors influencing immunogenicity of an antigen

- **Foreignness**
- **Molecular Size**
- **Chemical composition and complexity**
- **Ability to be processed and presented with MHC**

- **Tolerogen is a substance that does not evoke immune response due to its molecular form. If its molecular form is changed, a tolerogen can become an immunogenic.**

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

- **Exogenous antigens are antigens that have entered the body from the outside, for example by inhalation, ingestion or injection.**

- **By endocytosis or phagocytosis, these antigens are taken into the antigen presenting cells and processed into fragments.**

- **APCs then present the fragments to T helper cells(CD4+) by the use of MHC class II molecules on their surface.**

- **Some T cells are specific for the peptide: MHC complex. They become activated and start to secrete cytokines.**

- **Endogenous antigens are antigens that have been generated within the cell, as a result of normal cell metabolism, or because of viral or intracellular bacterial infection.**

- **The fragments are then processed on the cell surface in the complex with MHC class I molecules.**

- **If activated cytotoxic CD8+ recognize them, the T cells begin to secrete various toxins that cause the lysis or apoptosis of the infected cell.**

- **Self reactive T cells are deleted as a result of tolerance (also known as negative selection).**

- **An autoantigen is usually a normal protein or complex of protein(and sometimes DNA or RNA) that is recognized by the immune system of patients suffering from a specific autoimmune disease.**

- **Due to mainly genetic and environmental factors, the normal immunological tolerance for such antigen has been lost in these patients.**

- **A native antigen is an antigen that is not yet processed by an APC to smaller parts. T cells cannot bind native antigens, but require that they be processed by APCs, whereas B cells can be activated by native antigens.**

- **Tumor antigens or Neoantigens are those antigens that are presented by MHCI or MHCII molecules on the surface of tumor cells.**

- **If these antigens are presented only by tumor cells they are called tumor specific antigens (TSAs) and , in general result from a tumor specific mutation.**

- **More common are antigens that are presented by both tumor cells and normal cells, and they are called tumor associated antigens (TAAs).**

- **Superantigens (SAgs) are secreted proteins (exotoxins) that exhibit highly potent lymphocyte transforming activity directed toward T lymphocytes.**

- **Compared to a normal antigen induced T cell response where 0.0001-0.001% of the body's cells are activated, SAgs are capable of activating upto 20% of the body's T cells.**

- **This causes a massive immune response that is not specific to any particular epitope on the SAg.**

- **Since one of the fundamental strengths of the adaptive immune system is its ability to target antigens with high specificity, SAgs produce an immune response that is effectively useless.**

- **Microbes produce SAgs as a defense mechanism to aid them in evading the immune system.**

Immunogenicity of an antigen is influenced by three main factors of a biological system:

- **Genotype of recipient**
- **Dose and route of antigen administration**
- **Boosters**
- **Administration of adjuvants**
- **Intravenous, Intradermal, Subcutaneous, Intraperitoneal, Intramuscular.**

- **An adjuvant is an agent that may stimulate the immune system and increase the response to a vaccine, without having any specific antigenic effect in itself.**
- **Known adjuvants include oils, aluminum salts and virosomes.**

- **Adjuvants accomplish this task by mimicking specific sets of evolutionary conserved molecules which include liposomes, LPS, components of bacterial cells walls, and endocytosed nucleic acids such as double stranded dsRNA, ssDNA, and unmethylated CG dinucleotide containing DNA.**

Virosomes

- **Aluminum salts are unfavorable, since they develop their effect by inducing local inflammation, which is also the basis for the extended side effect pattern of this adjuvant.**

- **In contrast, the adjuvant capabilities of virosomes are independent of any inflammatory reaction.**

- **Virosomes containing a membrane bound haemagglutinin and neuraminidase derived from the influenza virus.**

- **It facilitates the uptake into antigen presenting cells(APC) and induce a natural processing pathway.**

TABLE 3-2 POSTULATED MODE OF ACTION OF SOME COMMONLY USED ADJUVANTS

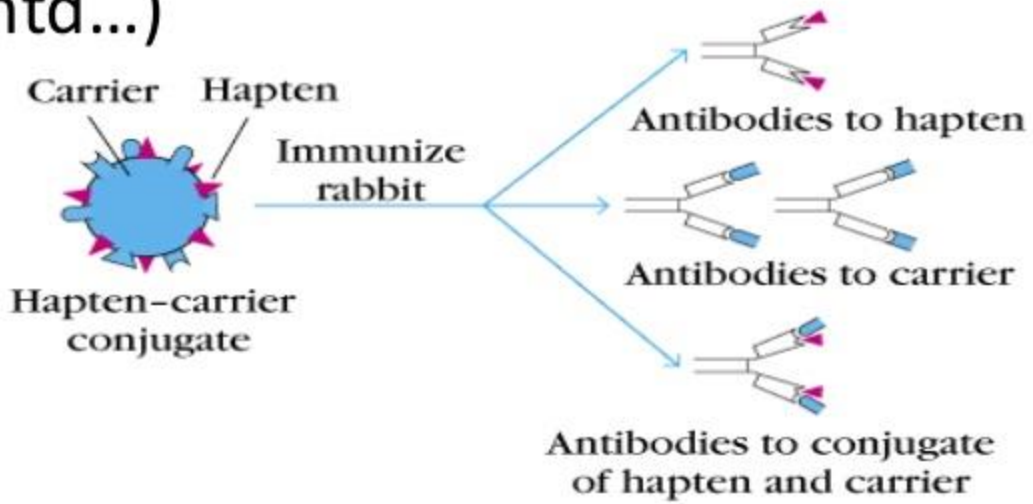
Adjuvant	Postulated mode of action			
	Prolongs antigen persistence	Enhances costimulatory signal	Induces granuloma formation	Stimulates lymphocytes nonspecifically
Freund's incomplete adjuvant	+	+	+	−
Freund's complete adjuvant	+	++	++	−
Aluminum potassium sulfate (alum)	+	?	+	−
Mycobacterium tuberculosis	−	?	+	−
Bordetella pertussis	−	?	−	+
Bacterial lipopolysaccharide (LPS)	−	+	−	+
Synthetic polynucleotides (poly IC/poly AU)	−	?	−	+

- **A hapten is a small molecule which can elicit an immune response only when attached to a large carrier such as a protein.**

- **Some haptens can induce autoimmune disease. An example is hydralazine, a blood pressure lowering drug which occasionally can produce drug induced lupus erythematosus in certain individuals.**

- **other haptens that are commonly used in molecular biology applications include fluorescein, biotin, digoxigenin, and dinitrophenol.**

Pioneering work of Karl Landsteiner (contd…)



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)