Course: Immunology

Lecturer: Dr. Weam Saad

Lecture: Antigens

Antigens

Definitions:

Antigen (Ag): Any foreign substance that enters human body and is able to generate specific immune response.

Immunogen - A protein that induces a complete specific immune response, meaning induction of immune system to produce specific antibodies and memory cells.

Hapten: a type Ag or foreign substance that cannot induce a complete immune response alone, but with adding a carrier molecule **(adjuvant)** can become a complete Ag and it is able to react with the specific Abs that result after immune response induction, e.g. gelatin is not a good Ag, but after adding the tyrosine (adjuvant) it became a good immunogenic Ag.

Epitope: it is a part of an Ag can be recognized by immune cells.

Antigenic determinant: A cluster (group) of epitopes.

Multivalent Ag: Ag has multiple epitopes.

Monovalent Ag: Ag has one epitope.

Surface Ag: it is the Ag on the surface of microorganism. e.g. somatic O Ag and flagella H Ag of *Salmonella sp.*

Factors influencing immunogenicity of any Antigen:

A. Properties of good Immunogen:

1. **Foreignness** - The immune system normally distinguish between self and non-self, so that only foreign molecules are immunogenic.
2. **Size** - In general, the larger size Ag molecule the more immunogenic it is.
3. **Chemical Composition** - In general, the more complex the substance is chemically the more immunogenic it will be. The antigenic determinants are created by the primary sequence of residues (or amino acids) in the polymer and by the secondary, tertiary or quaternary structure of the molecule.

4. **Physical form** - In general particulate antigens are more immunogenic than soluble Ag, and denatured antigens more immunogenic than the native and other forms.
5. **Degradability** - Antigens that are easily phagocytosed are generally more immunogenic. Because the immune response needs the antigen to be phagocytosed, processed and presented to helper T-cells by an antigen presenting cell (APC). Also stable Ag is good in immunogenicity because its epitopes will be stable and can be recognized be immune cells.

B. Biological factors affecting the immune System response to Antigens (Ag):

1. **Genetic Factors** - Some substances are immunogenic in one species but not in another. Also, some substances are immunogenic in a person but not in others.
2. **Age -** Age can also influence immunogenicity. Usually the children and the very old people have a suppressed ability of immune response to an immunogen.

C. Method of Ags Administration:

1. **Dose** - The dose of administration of an immunogen can influence its immunogenicity. Optimal dose will start the immune response.
2. **Route** - Generally the subcutaneous route is better than the intravenous or intra gastric routes. The route of antigen administration can affect the nature of the response
3. **Adjuvants** - Substances that can enhance or increase the immune response to an immunogen are called adjuvants. The use of adjuvants has many side effects such as fever and inflammation.

Chemical Nature of Antigens:

A. Proteins –most good antigens are proteins. They are good immunogens, may be pure proteins or they may be glycoproteins or lipoproteins. In general, proteins are usually very good immunogens.

B. Polysaccharides - Pure polysaccharides and lipopolysaccharides are good immunogens.

C. Nucleic Acids - Nucleic acids are usually poorly immunogenic, they may become immunogenic when they are single stranded or when complex with proteins.

D. Lipids - In general lipids are non-immunogenic (haptens). Some glycolipids and phospholipids can stimulate T-cells directly and produce a cell-mediated immune response.

Types of antigens according to the specific immune response type that they produce:

1. T-dependent Antigens
2. T-independent Antigens

Adjuvants (from Latin adjuvane, to help) are substances that, when mixed with an antigen and injected with it, enhance the immunogenicity of that antigen. Adjuvants are often used to boost the immune response when an antigen has low immunogenicity or when only small amounts of an antigen are available. They help in:

1. Staying of Antigen for long time.
2. Induction of stimulatory signals.
3. Increase local inflammation.
4. Stimulate the nonspecific proliferation of lymphocytes.

Freund's adjuvant is a solution of antigen emulsified in oil and used as an immunopotentiator (booster). These adjuvants are in two types;

1. Freund's complete adjuvants composed of inactivated and dried *Mycobacterium tuberculosis* and water in oil emulsion.
2. Freund's incomplete adjuvant is without mycobacterial components (just the water in oil emulsion).

Immunization

The importance of active immunization is to prevent infectious diseases using prepared vaccine.

Types of Vaccines

A wide variety of immunizing agents were developed. The following are some examples:

1. **Killed vaccines** are generally safe, but not effective like attenuated vaccines.

a. **Killed bacteria**, such as the traditional pertussis vaccine prepared with killed *Bordetella pertussis* (for whooping cough), the typhoid vaccine prepared with acetone-inactivated *Salmonella typhi*, and the cholera vaccine, prepared with killed *Vibrio cholerae*.

b. **Killed viruses**, such as Salk's polio vaccine, containing a mixture of the three known types of poliovirus، after inactivation with formalin. This vaccine has been as successful in the eradication of poliomyelitis as Sabin's attenuated oral vaccine. Its main advantage is safety, but is not as effective as the oral vaccine.

2. **Component vaccines**, which are safer than killed vaccines, but have problem in efficacy:
   a) **Bacterial polysaccharides**, such as those used for *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae* type b, and a vaccine for typhoid fever made of the Vi capsular polysaccharide.
   b) **Inactive toxins** (toxoids), such as tetanus and diphtheria toxoids which are formalin-inactivated toxins that have lost their active site but maintained their immunogenic determinants and induce antibodies able to neutralize the toxins.
   c) **Recombinant bacterial antigens**. A recombinant vaccine of *Rickettsia rickettsii* (antigen produced in *E. coli* used for this bacteria and the disease Rocky Mountain spotted fever).
   d) **Mixed component vaccines**. e.g. For save vaccines for whooping cough, a mixture of inactivated pertussis toxin used to replace the killed pertussis vaccine.
   e) **Conjugate vaccines.** Most polysaccharide vaccines have poor immunogenicity in infants because of the fact that polysaccharides

tend to induce T-independent responses with little memory. This problem solved when the polysaccharide is conjugated to an immunogenic protein like a hapten-carrier conjugate. The first conjugate vaccines is the polyribositolribophosphate (PRP) of *Haemophilus influenzae* type b (HiB) for children of less than 5 years of age.

f) **Viral component vaccines** use the viral component .The best example is the hepatitis B vaccine, prepared from the particles of hepatitis virus outer coat protein (hepatitis B surface antigen or HBs Ag) isolated from chronic carriers. Also, some of HIV vaccines are component vaccines (contain envelope glycoproteins).

g) **Synthetic peptide vaccines**. The use of synthetic peptides for vaccination is easy to manufacture and save in neutralizing specific antibodies e.g. malaria vaccine.

h) **DNA vaccines**. Used recently by intramuscular injection of non-replicating plasmid DNA encode for the hemagglutinin (HA) or nucleoprotein (NP) of influenza virus induce humoral and cellular protective immune response.

3. **Attenuated vaccines**. Attenuated vaccines are very efficient, but in rare cases can cause the disease, they are designed to prevent and protect people especially people have weak immune system or immunocompromised individual. Most antiviral vaccines are made of attenuated viruses in the laboratory, including the classic smallpox vaccine, the oral polio vaccine, and mumps-rubella-measles vaccine, the attenuated bacteria, e.g. new bacterial vaccine against typhoid fever is based on the use of an attenuated strain of *Salmonella typhi* that grows poorly and is non-pathogenic but induces protective immunity in 90% of the individuals.

4. **Recombinant organisms.** Recombinant technology is used to delete the genes coding for virulence factors from bacteria, or to add genetic information to attenuate viruses or attenuate bacteria. Experimental vaccines for AIDS were developed by adding parts of the envelope coding gene of HIV into the vaccinia virus genome.

Examples for important vaccines:

1) **BCG vaccine:** (Bacillus Calmette-Guerin) vaccine:
   Vaccine used against tuberculosis, usually given to healthy babies. Live attenuated bacteria. Given by injection percutaneous.
2) **MMR vaccine**: (Mumpus, Measles and Rubella) vaccine:
   Vaccine used against three diseases composed of combination or mixture of live attenuated viruses of three diseases. Given by injection (usually I.M.in hand).
3) **DPT Vaccine**: the **Triple vaccine** or Diphtheria, Pertussis and Tetanus vaccine:
   This vaccine is a type of component vaccine, composed of diphtheria and tetanus toxoids and killed bacteria of pertussis (whooping cough). Given by injection (usually I.M.in hand)