Viral vaccines

Objectives
1- Define active immunity.
2- Describe the methods used for the preparation of attenuated live & killed virus vaccines.
3- Comparison of Characteristics of Killed and Live Viral Vaccines.
4- List the future prospects as novel approaches to vaccine development.
5- Discuss passive & passive-active immunity.

- Prevention of viral diseases can be achieved by the use of vaccines that induce active immunity or by administration of preformed antibody that provides passive immunity.

Active immunity

Currently available viral vaccines

1. Attenuated live-virus vaccines
2. Killed- virus vaccines

Attenuated live-virus vaccines

Live-virus vaccines utilize virus mutants that antigenically overlap with wild-type virus but are restricted in some step in the pathogenesis of diseases. This can be achieved by:
1. Serial passages in embryonated eggs or in cell cultures (usually from a species different from the natural host). This procedure resulted in the chance selection of strains of viruses which have greatly reduced virulence for man (e.g. Measles, Mumps, and Rubella vaccines).

2. Temperature-sensitive mutants: grow at low temperature but not at high temperature. Virus will grow in the cooler, upper airways (33\degree C) where it causes few symptoms and induces antibodies, but it will not grow in the warmer (37\degree C), lower airways where it can cause pneumonia. e.g. influenza virus vaccine.

3. Cold-adaptation: the virus is encouraged to grow at 25 \degree C (e.g. Influenza virus vaccine).

4. Recombinant vaccines (Genetic reassortment): Recombination by reassortment only occurs between viruses with segmented genomes e.g. influenza viruses. Cells are co-infected with an attenuated laboratory donor virus and a virulent wild-type influenza virus isolate. The desired reassortant vaccine virus will contain the surface genes from the wild-type virulent virus and other viral genes that confer attenuation from the attenuated donor virus.
Live Vaccines

- Also called **attenuated** vaccines

**Killed - virus vaccines:**

Inactivated (killed - virus) vaccines produced by inactivation of viral infectivity whilst retaining its immunogenicity. Purity & potency combined with adequate antigenicity are the key words for inactivated vaccines.

**Inactivation of viral infectivity by:**

- Mild formalin, B-propiolactone, ethylenimines.

Killed-viral vaccines are now available as either:

a) **Whole virus vaccines.**

b) **Subunit vaccines** (purified component vaccines): subunit vaccines were separated from purified virus by detergent then centrifugation.
This vaccine contains only those viral components needed to stimulate protective antibody.
### Comparison of Characteristics of Killed and Live Viral Vaccines

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Killed Vaccine</th>
<th>Live Vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of doses</td>
<td>Multiple</td>
<td>Single</td>
</tr>
<tr>
<td>Need for adjuvant</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Duration of immunity</td>
<td>Shorter</td>
<td>Longer</td>
</tr>
<tr>
<td>Effectiveness of protection (more closely mimics natural infection)</td>
<td>Lower</td>
<td>Greater</td>
</tr>
<tr>
<td>Immunoglobulins produced</td>
<td>IgG</td>
<td>IgA and IgG</td>
</tr>
<tr>
<td>Mucosal immunity produced</td>
<td>Poor</td>
<td>Yes</td>
</tr>
<tr>
<td>Cell-mediated immunity produced</td>
<td>Poor</td>
<td>Yes</td>
</tr>
<tr>
<td>Residual virulent virus in vaccine</td>
<td>Possible</td>
<td>No</td>
</tr>
<tr>
<td>Reversion to virulence</td>
<td>No</td>
<td>Possible</td>
</tr>
<tr>
<td>Excretion of vaccine virus and transmission to nonimmune contacts</td>
<td>No</td>
<td>Possible</td>
</tr>
<tr>
<td>Interference by other viruses in host</td>
<td>No</td>
<td>Possible</td>
</tr>
<tr>
<td>Stability at room temperature</td>
<td>High</td>
<td>Low</td>
</tr>
</tbody>
</table>
New approaches to vaccine design

Molecular biology and modern technologies are combining to devise novel approaches to vaccine development.

1. Synthetic peptides

Viral nucleic acid can be readily sequenced and the amino acid sequence of the gene products predicted. Also the technology for synthesis of peptides in vitro has been refined. It is now possible to synthesize short peptides that correspond to antigenic determinants on a viral protein.

The immune response induced by synthetic peptides is considerably weaker than that induced by intact protein.

2. Purified proteins produced using cloned genes:

Viral genes can be easily cloned into plasmids and this cloned DNA then expressed in:

a. Bacteria E. Coli
b. Yeast cells
c. Mammalian cells

**Vectors**: plasmid, or DNA mammalian virus.

Gene coding for immunizing proteins of the influenza virus, herpes simplex virus, and rabies virus have been synthesized in bacteria. A recombinant hepatitis B virus vaccine contains viral protein synthesized in yeast cells or mammalian cell lines.
Purified proteins produced using cloned genes
3. **Recombinant Vaccinia virus as vaccines** the concept is to use recombinant DNA techniques to insert the gene coding for the protein of interest into the genome of an avirulent virus that can be administered as the vaccine (the prototype vector is vaccinia virus).
4. **Edible vaccines**: Whereby transgenic plants synthesizing antigens from pathogenic viruses may provide new cost-effective ways of delivering vaccines.

5. **Naked DNA vaccines**

Recombinant plasmids carrying the gene for the protein of interest are injected into hosts and the DNA produces the immunizing protein.

6. **Administration of vaccine locally** to stimulate antibody at the portal of entry (such as aerosol vaccines for respiratory disease viruses).

**Passive immunity**

Immunity acquired by an individual by the transfer of preformed antibodies. These antibody preparations are often called immune globulins.

The main advantage of passive immunity is that it provides immediate protection. The main disadvantage is that it does not provide long-term protection i.e., it active only for a few weeks to a few months.

Immune globulin preparations against rabies virus, hepatitis A virus, hepatitis B virus and Varicella-zoster virus are in common use.
Passive-active immunity:

Consists of administering both immune globulins and a viral vaccine. This provides both immediate as well as long-term protection (e.g. Protection against rabies in an unimmunized person who has been bitten by a potentially rabid animal. Persons exposed to hepatitis B virus percutaneously or by contamination of mucosal surfaces.

Summary

1-Active immunity can be elicited by vaccines containing killed viruses, purified protein subunits, or live attenuated viruses.

2-In general live virus vaccines are preferable to killed vaccines.

3-There are some potential problems with live viral vaccines, the most important of which is reversion to virulence & should not be given to immunocompromised individuals or to pregnant women.

4-Many methods of novel approaches to vaccine development avoid the incorporation of viral nucleic acid in the final product. The ultimate success of these new approaches remains to be determined.

5-Passive immunity is provided by the administration of preformed antibody (immune globulins).

6-Passive-active immunity is induced by giving both immune globulins & viral vaccine.