VACCINES AND THEIR ADVERSE REACTION

V. Purushothaman

Director,Centre for Animal Health Studies
Tamil Nadu Veterinary and Animal Sciences University
Madhavaram Milk Colony, Chennai – 600 051.

History of Vaccine (Vacca – 'Cow')

- In 18th Century Edward Jenner coined the term Vaccine.
- Antigenic Preparation used to establish Immunity in humans and animals.
- After 200 years WHO aimed a mass vaccination against Smallpox to eradicate it
- 1980- WHO announced smallpox free world.

Vaccines

Types of Vaccines:

Inactivated:

Virulent Micro-organisms killed by heat or chemical. Short lived immune response may require booster dose.

Eg.,: Flu, Cholera and Hepatitis.

Live, attenuated:

Live micro-organism cultivated under condition that attenuates its virulence.

Eg.,: Yellow fever, Mumps, Measles and Rubella.

Toxoids:

Introducing inactivated toxins from micro-organisms.

Eg., : tetanus and diphtheria.

Synthetic Peptide Vaccine:

Vaccines are those which contain non infectious peptides corresponding to the epitopes responsible for immunity or protection

Eg: FMD vaccine, Bovine Rotavirus, Canine parvovirus polio etc.

DNA Vaccine:

Created from an infectious agent's DNA called *DNA vaccination*. It works by insertion (and expression, triggering immune system recognition) into human or animal cells, of viral or bacterial DNA.

07/06/2006 - PowerMed has demonstrated the immunogenicity of an influenza DNA vaccine.

Subunit:

Instead of whole or attenuated microorganisms a fragment of it can create immune response.

Eg: HBV containing surface protein of the virus expressed in yeast, Rabies and FMDV.

Corresponding author E.mail : dcahs@tanuvas.org.in

Antidiotype Vaccines:

Falls under the category of Subunit vaccine and are based on the concept of mimicking an antigenic epitope using an antibody.

Eg: Sendai Virus, Reo Virus, Polio, rabies, FMD.

Conjugate:

Outer polysaccharide coats linked or tagged with proteins or toxins (antigen).

Eg: *Haemophilus influenzae* type B vaccine.

Recombinant

Combining the physiology of one micro-organism and the DNA of the other, immunity can be created against diseases that have complex infection processes.

Eg: Hepatitis B.

Pharming: Edible Vaccines

- Foods specifically engineered to confer immunity to certain diseases.
- Example: already lab rats made immune to cholera from ingesting genetically modified potatoes.
- For human trials, same antigen produced in genetically modified bananas.

Developing Immunity

Natural immunity

Natural immunity develops after you've been exposed to a certain organism. Your immune system puts into play a complex array of defences to prevent you from getting sick again from that particular type of virus or bacterium.

Vaccine Induced Immunity

Immune system recognizes vaccine as foreign agents and destroys them by developing antibodies against it.

When it encounters a virulent version of the same, it acts on it and destroys it.

Vaccination schedule

- It is recommended to receive vaccinations as soon as their immune systems are sufficiently developed to respond to particular vaccines.
- With additional 'booster' shots often required to achieve 'full immunity'.
- Advisory Committee on Immunization Practices, which recommends schedule additions for the Center for Disease Control, recommends routine vaccination of children against: hepatitis A, hepatitis B, polio, mumps, measles, rubella, diphtheria, pertussis, tetanus, HiB, chicken pox, rotavirus, influenza, meningococcal disease and pneumonia.

Vaccine Controversies

Potential for adverse side effects in general:

Some refuse to immunize themselves or their children, because they believe certain vaccines' adverse side effects outweigh their benefits Since most people are vaccinated against contagious and potentially fatal diseases, the chances of someone who is not vaccinated becoming ill is a good deal smaller than it might be if their opinion was held by more people.

The main risk of rubella, for example, is to the fetuses of pregnant women, but this risk can be effectively reduced by the immunization of children to prevent transmission to pregnant women.

Efficacy of vaccines

Vaccines do not guarantee complete protection from a disease.

- Even after immunization the individual may get the disease due to inadequate response of the immune system to the vaccine-'low titre of antibodies'.
- Lowered immunity in general (diabetes, steroid use, HIV infection)
- The host's immune system does not have a B-cell capable of generating antibodies to that antigen v.
- Some organisms mutate.
- Adjuvant are typically used to boost immune response.

The efficacy or performance of the vaccine is dependent on a number of factors:

- The disease itself (for some diseases vaccination performs better than for other diseases)
- The strain of vaccine (some vaccinations are for different strains of the disease)
- Whether one kept to the timetable for the vaccinations
- some individuals are 'non-responders' to certain vaccines, meaning that they do not generate antibodies even after being vaccinated correctly
- other factors such as ethnicity or genetic predisposition
- In cases where a vaccinated animal does develop the disease vaccinated against, the disease is likely to be milder than without vaccination.

Adverse effects (known and suspected)

Some autoimmune diseases like Acute disseminated encephalomyelitis, Guillain-Barré syndrome, Transverse myelitis and multiple sclerosis are known to be connected to vaccines, which suggests other autoimmune disorders might also be vaccine-related.

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Economics of vaccine development

One challenge in vaccine development is economy.

- In many of the diseases, most demanding is a vaccine.
- Pharmaceutical firms and biotech companies have little incentive to develop vaccines for these diseases, because there is little revenue potential, the number of vaccines actually administered has risen dramatically in recent decades.

Preservatives

- To shelf life and reduce production and storage costs, thimerosal, a mercury-

containing organic compound, is used routinely until recent years as a preservative.

- Thimerosal was gradually being phased out in the U.S. (it has been phased out in other countries, e.g. Denmark in 1992), but may be used in some stages of manufacture.

Reverse Vaccinology - Moving forward in reverse-

- A genome-based approach to vaccine development.
- Possibility of using genomic information allows us to study vaccine development in silico, without the need of cultivating the pathogen.
- Reduces the time required for the identification of candidate vaccines.

Developing Vaccines in the 20th century

- Existing vaccine can be divided into two groups:

Living:

Induce immunity by mimicking natural infections using attenuated forms of pathogens.

Non living:

Vaccines use whole pathogen (killed bacteria, Parasites or viruses) or components of them (subunit vaccines).

Developing Vaccines in the year 2020 by reverse vaccinology

- Advantages:
  - o Fast access to virtually every antigen
  - o Non-cultivable can be approached
  - o Non abundant antigens can be identified
  - o Antigens not expressed in vitro can be identified.
  - o Non-structural proteins can be used
- Disadvantages:
  - o Non proteinous antigens like polysaccharides, glycolipids cannot be used.

Characteristic of Ideal Vaccine

- Impeccable safety profile
- Elicits high level of long lived efficacy
- Requires only a single dose
- Stimulates protection within 2 weeks of administration.
- Administrable without a needle or syringe.
- Can be manufactured in large scale with quality control by relatively uncomplicated and economical processes.
- Amenable to production in formulation thaat are resistant to high and low temperature ant therefore free from strict storage requirements.

Vaccines developed in TANUVAS

- **Live Attenuated PPR vaccine thermo stable PPR vaccine.**

PPR infected goat – mouth lesions

Sheep–ocular and nasal discharges

ORAL PELLET VACCINE TO CONTROL NEWCASTLE DISEASE IN VILLAGE CHICKENS

- Developed a lactose-starch pellet oral vaccine for controlling ND in village chickens
- The vaccine was found to be safe, pure and potent in lab and controlled field trials
- The vaccine seed was also tested as priming vaccine in broilers and found to give satisfying immunity in single dose.
- Molecular characterization studies also proved the low pathogenicity of seed correlating with ICPI value

Development of a safe and potent Anthrax Vaccine.

- The department is currently concentrating on developing a safe and potent anthrax vaccine for small ruminants.
- Improving the existing vaccine with different adjuvant.
- Development of a diagnostic kit for anthrax for easy diagnosis.
- Development of a recombinant anthrax vaccine.

Development of *E. coli* biofilm Vaccine

- Developed biofilm vaccine
- Use of chitosan and bentonite.
- To control calf mortality.

Development of vaccine for Sheep pasteurellosis.

- Separate vaccine for sheep pasteurellosis.
- Adjuvant vaccine.

Protective antigen of *Bacillus anthracis* for Diagnosis and vaccine development

- Anthrax toxin
- Action and Effect of anthrax toxin
- Diagnosis by protective antigen
- Vaccine development

About anthrax toxin

- **Two types of plasmid**
  - pXo1(184 Kilo base pairs)
  - pXo2(90 Kilo base pairs)
- **pXo1 codes three toxin**
  - Protective antigen(83 kilo Dalton)
  - Edema factor(85 kilo Dalton)
  - Lethal factor(90 kilo Dalton)
- **pXo2 codes for capsule**

Diagnosis by protective antigen

- **Production and purification of protective antigen**
  - Chemically defined medium:
    - R-medium
    - Casaminoacid medium
- **Analysis by SDS-PAGE**

Vaccine development

- Anthrax vaccine adsorbed(AVA) by different adjuvants
  - Aluminium hydroxide gel
  - Montanide
- Recombinant vaccine.