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A CASE REPORT

New generation vaccines for livestock diseases

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Abstract : Vaccine is a biological preparation that improves immunity to a particular disease. A vaccine typically contains an agent that resembles a disease-causing microorganism, and is often made from weakened or killed forms of the microbe. The agent stimulates the body's immune system to recognize the agent as foreign, destroy it and remember it, so that the immune system can more easily recognize and destroy any of these microorganisms that it later encounters. Vaccines can be prophylactic (e.g. to prevent or ameliorate the effects of a future infection by any natural or wild pathogen), or therapeutic (e.g. vaccines against cancer are also being investigated). Different kinds of vaccines from conventional to molecular types are nowadays manufactured to combat infections. But it is the owner of livestock who should determine the potential form of the same which may prove helpful as prophylactic measure against various diseases. Judgment about the effectiveness of a vaccine type depends upon its compatibility, administration route and dose, cost effectiveness and maintenance of proper cold chain. The immune system recognizes vaccine agents as foreign, destroys them and remembers them. When the virulent version of an agent comes along the body recognizes the protein coat on the virus, and thus is prepared to respond, by neutralizing the target agent before it can enter cells and by recognizing and destroying infected cells before that agent can multiply to vast numbers. Proper schedule of administration, route of administration, effectiveness, maintenance of cold chain and cost efficiency are some of the primary governing factors for use of any vaccine.

Key words : Diseases, Effectiveness, Livestock, Vaccines

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INTRODUCTION

Vaccine is a biological preparation that improves immunity to a particular disease. A vaccine typically contains an agent that resembles a disease-causing microorganism, and is often made from weakened or killed forms of the microbe. The agent stimulates the body's immune system to recognize the agent as foreign, destroy it and remember it, so that the immune system can more easily recognize and destroy any of these microorganisms that it later encounters.

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Types:

Vaccines are dead or inactivated organisms or purified products derived from them. There are several types of vaccines currently in use. These represent different strategies used to try to reduce risk of illness, while retaining the ability to induce a beneficial immune response. Viral vaccines are classified majorly as live virus vaccines, inactivated virus vaccines and protein vaccines.

Live virus vaccines:

Naturally occurring virulent virus vaccines: There are some examples of this type of vaccines. Virulent herpes turkey virus is used in chickens to control Marek's disease. Herpes turkey virus is antigenically similar to Marek's disease virus and is not pathogenic to chickens. Pigeon po virus may be used as first dose in chickens against fowl pox. This is preferred

especially for layers to avoid any reaction. Goat tissue vaccine (GTV) was available previously to control rinderpest in cattle, vaccination was done with virulent rinderpest virus along with rinderpest hyperimmune serum to minimize reaction (serum-virus simultaneus vaccine). To control rotavirus infection in pigs, bovine rotavirus can be used as vaccine. In some diseases, virulent virus can be ginven by unnatural routes. In case of infectious laryngotracheitis (ILT) of chickens virulent virus is given by cloacal route. Orf live virus is injected in sheep in inguinal region. To control contageous bovine pleuropneumonia (CBPP), the injection of live organisms is given in caudal fold region of tail.

Attenuated live virus vaccines: There are some naturally available less virulent viruses of Newcastle disease of poultry. These strains are F-strain (isolated in England), B-1 and La Sota strains (isolated in USA) and CDF-66 strain (Isolated in India). Except CDF-66 strain, all other strains are poorly antigenic. Indian strains of infectious bronchitis virus of poultry are less pathogenic. All these starins are used in young chicks as vaccines to avoid post-vaccination reactions.

Virulent viruses can be attenuated by serial passages in embryonated chicken eggs, cell cultures or laboratory animlas. These viruses loose virulence for the original host, but maintain their antigenicity. Some vaccines contain live, attenuated microorganisms. Many of these are live viri that have been cultivated under conditions that disable their virulent properties, or which use closely-related but less dangerous organisms to produce a broad immune response, however some are bacterial in nature. They typically provoke more durable immunological responses and are the preferred type for healthy adults. Examples include the viral diseases yellow fever, measles, rubella, and mumps and the bacterial disease typhoid. The live Mycobacterium tuberculosis vaccine developed by Calmette and Guérin is not made of a contagious strain, but contains a virulently modified strain called BCG used to elicit immunogenicity to the vaccine.

Large numbers of such vaccines are available. Some of the examples are GTV and tisue culture vaccines of rinderpest, R_2B vaccine of Newcastle disease, fowl pox and sheep pox vaccines. In siome diseases, temperature sensistive mutant strains are used as vaccines. A large number of viral inactivated vaccines are used in animals and birds. The examples are IBR, FMD, sheep pox, equine influenza and hog cholera vaccines.

Attenuated live virus vaccines can also be obtained by employing the tchnique of genetic engineering. In the viral genome, the gene which is responsible for virulence, is excised and removed. The virus without the gene respnsible for virulence can be usd as attenuated live virus vaccine. Pseudorabies virs vaccine for swine has been obtained by removing thymidine kinase (TK) gene which is responsible for its virulence.

Virus vectored vaccine:

This is a new approach of immunization in human beings and animlas. In this approach, the genes of viruses respinsible for protective antigens are introduced in the genome of large viruses which can be used as vectors. Viruses used as vecors may be fowl pox, vaccinia, herpes and adenoviruses. It should be ensured that the vectored vaccine replicates and does not cause any untoward reaction in the vaccinated animal. As an example, the gene of rabies virus responsible for protective antigens has successfully been incorporated into the genome of vaccinia virus which has been used as a vaccine to immunize animals gainst rabies.

Under normal circumstances, virulent viruses cannot be used as vaccines. To make them safe for animal vaccination, the viruses are inactivated by physical and chemical agents. Physically, heat or ultraviolet rays are used to kill the viruses. These agents should inactivate the virus without denaturing the proteins acting as antigens. The pH and ionic environment of the medium also affects the rate of heat inactivation of the viruses.

Commonly used chemical agents for virus inactivation are formldehyde, beta-propiolactone, and ethylamine. Formaldehyde in a proper dilution, say 1:4000 is used for inactivation of the virus at 37^{o}C until there is no residual infectivity and it maintains antigenicity and immunogenicity. Beta-propiolactone is considered to be a good inactivating agentas it is hydrolysed completely within hours to non-toxic products. The drawbacks of inactivated vaccines are the use of alrgerand repeated doses to maintain immunogenicity (Ganguly *et al.,* 2012).

Killed vaccines:

Killed vaccines are the vaccines containing killed microorganisms. These are previously virulent microorganisms which have been killed with chemicals or heat. Examples are the Influenza (flu), cholera, bubonic plague, polio and hepatitis A vaccines.

Experimental viral protein vaccines:

Virus subunit vaccine:

Whole virion does not act as antigen but only the epitope portion on the protein surface of the virus acts as antigen for antibody production. It is desirable to include only the antigenic or the epitopic portion of the virus surface in the vaccine and discard the remaining portion of the virus. Protein subunit of micro-organism (which would constitute a 'whole-agent' vaccine), the epitope portion of it can induce an immune response. Examples include the subunit vaccine against hepatitis B virus that is composed of only the surface proteins of the virus (previously extracted from the blood serum of chronically infected patients, but now produced by recombination of the viral genes into yeast), the virus-like particle (VLP) vaccine against human papillomavirus (HPV)

that is composed of the viral major capsid protein, and the hemagglutinin and neuraminidase subunits of the influenza virus. Such subunit vaccines have been used against human rabies, measles, FMD and hepatitis B viruses. The types of vaccines are highly specific in nature. One of the disadvantages of sub-unit vaccines is that it is lowly immunogenic and needs an adjuvant.

DNA vaccine:

Viral genes or antigenic proteins are excised and cloned in prokaryotic cells by recombinant DNA technology. When these genes are expressed in prokaryotic cells, the resultant proteins are harvested from host cells and used as vaccine in the concerned species of animals. Experiments of these type of vaccine have been carried out with VP-1 protein of FMD virus. Avian flu vaccine was developed by reverse genetics techniques.

Synthetic peptide vaccine:

The amino acid sequences of viral peptides are determined first and then antigenic sites (epitopes) are located on the poteins. It is then possible to synthesize short peptides coresponding to antigenic determinanats to which neutralizing antibodies bind. Synthetic peptides used as vaccines produced neutralizing antibodies against some viruses including the virus of FMD and rabies.

Anti-idiotypic vaccines:

When an antigen is administered in the body, it generates an antibody response. This antibody in turn acts as antigen and generates an immune response and produces antibody known as idiotypic antibody which is the mirror image of the antigen These idiotypes act as antigens and elicit production of anti-idiotypic antibodies (Ganguly *et al*., 2012).

Experimental vaccines:

A number of innovative vaccines are also in development and in use.

Dendritic cell vaccines combine dendritic cells with antigens in order to present the antigens to the body's white blood cells, thus stimulating an immune reaction. These vaccines have shown some positive preliminary results for treating brain tumors.

Recombinant vector vaccines prepared by combining the physiology of one micro-organism and the DNA of the other.

DNA vaccination is new type of vaccination created from an infectious agent's DNA, has been developed. It works by insertion and expression, triggering immune system recognition of viral or bacterial DNA into human or animal cells. Some cells of the immune system that recognize the proteins expressed will mount an attack against these proteins and cells expressing them. Because these cells live for a very long time, if the pathogen that normally expresses these proteins is encountered at a later time, they will be attacked instantly by the immune system. One advantage of DNA vaccines is that they are very easy to produce and store. As of 2011, DNA vaccination is still experimental.

T-cell receptor peptide vaccines are under development for several diseases using models of valley fever, stomatitis, and atopic dermatitis. These peptides have been shown to modulate cytokine production and improve cell mediated immunity.

Targeting of identified bacterial proteins that are involved in complement inhibition would neutralize the key bacterial virulence mechanism.

While most vaccines are created using inactivated or attenuated compounds from micro-organisms, synthetic vaccines are composed mainly or wholly of synthetic peptides, carbohydrates or antigens.

Other types of vaccines:

Conjugate vaccines:

Certain bacteria have polysaccharide outer coats that are poorly immunogenic. By linking these outer coats to proteins (e.g. toxins), the immune system can be led to recognize the polysaccharide as if it were a protein antigen. This approach is used in the *Haemophilus influenzae* type B vaccine.

Toxoid:

Toxoids are inactivated toxic compounds in cases where these (rather than the micro-organism itself) cause illness. Examples of toxoid-based vaccines include tetanus and diphtheria. Not all toxoids are for micro-organisms; for example, *Crotalus atrox* toxoid is used to vaccinate dogs against rattle snake bites.

Adjuvants

Adjuvants are substances like aluminium hydroxide, Freund's complete adjuvant and mineral oils. These substacnes when mixed with vaccines enhance immune response by slow release of antigen and its retention for a longer period and activation of mcrophages involved in the production of humoral and cell mediated immunity. Adjuvant vaccines need lesser antigens per dose and require fewer doses. Their immune response is for a longer duration (Ganguly *et al.*, 2012).

Valency:

Vaccines may be monovalent (also called univalent) or multivalent (also called polyvalent). A monovalent vaccine is designed to immunize against a single antigen or single microorganism. A multivalent or polyvalent vaccine is designed to immunize against two or more strains of the same microorganism, or against two or more microorganisms.

Mechanism of immunity development by vaccine:

The immune system recognizes vaccine agents as foreign,

destroys them and remembers them. When the virulent version of an agent comes along the body recognizes the protein coat on the virus, and thus is prepared to respond, by neutralizing the target agent before it can enter cells and by recognizing and destroying infected cells before that agent can multiply to vast numbers.

Conclusion:

Proper schedule of administration, route of administartion, effectiveness, maintenance of cold chain and cost efficiency are some of the primary governing factors for use of any vaccine (Dunn, 1996; Stern and Markel, 2005).

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