

Future of Veterinary Vaccines: Review

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ABSTRACT

The rate of emerging infectious diseases is increasing day by day not only in humans but also in animals and with that the need for new veterinary vaccines is becoming vital. The classical vaccines are not favourable and advantageous to such necessity as a result veterinary vaccines have taken a lead in developing new vaccinations to get around some of the drawbacks of conventional vaccines. Veterinary vaccinations have taken part in a significant capacity in preserving the health of animals and the public, minimizing animal suffering, and facilitating the efficient production of food for animals to feed the expanding human population. Due to these varied goals, several methods for creating veterinary vaccines have been used, ranging from simple yet efficient preparations (i.e. whole-pathogen to molecularly described subunit vaccines or genetically modified organisms). The current article gives detail about the importance and types of veterinary vaccines along with an overview of emerging vaccine technologies that are now being used in the control of diseases in companion animals, food animals, and wildlife that are commercially available.

Keywords: Vaccines; veterinary; conventional vaccines; whole-pathogens; chimaeras; commercially

INTRODUCTION

The use of vaccines to prevent and treat disease has a long and successful history. The main objective of vaccination is to produce humoral and/or cell-mediated immunity, which triggers the emergence of immunological memory and safeguarding in opposition to repeated natural infection. Neutralizing antibodies are one of the major goals of vaccination, but cell mediated (T cell) immune responses have also been required or essential against pathogens. All of the characteristics of an ideal vaccine cannot be found in a single vaccine. Assessing the dangers and calculating the benefits of vaccinations is the foundation for using vaccines to control the disease. Genetic vaccines are often made of RNA or DNA (as plasmids), which the cells of the animals receiving the vaccines take up and translate into proteins [1, 2]. Moreover, vaccines should be used in conjunction with thorough control methods that take into account the epidemiology of the disease in great detail, biosecurity, quarantine, surveillance, diagnostics, education, and management of the disease vector or reservoir species. Through vaccination, Rinderpest was eradicated as a result of this set of actions. Vaccines for animals can be incredibly successful. The introduction of safe, inexpensive rabies vaccinations suitable for several species has led to a major decrease in the impact of this horrific disease in various parts of the world as well as the eradication of Rinderpest. Furthermore, the veterinary vaccinations currently on the market are the result of years of creative research and

address many of the disease concerns currently faced by pets and farm animals in the world. The great majority of veterinary vaccines on the market today are toxoids, killed/inactivated microorganisms, cell membrane chemicals, or live attenuated microorganisms [3, 4].

IMPORTANCE OF VETERINARY VACCINES

Enhancing the health of poultry animals

Veterinary vaccines execute or improve the overall health and production rate of poultry and livestock animals. Due to the growing population maintaining high-quality animal production and protein is one of the major challenges. To address this need, vaccines that maintain animal health and increase productivity are crucial [5].

Control zoonotic diseases

The most prevalent domestic animals such as cats or dogs would not have been easily adopted as pets in a family if it had not been for the rabies vaccine. This was possible as veterinary vaccines can control zoonotic diseases. Another essential vaccine for the cattle and small ruminants was *Brucellosis* which was essential in the eradication of *Brucella abortus* that had severally impacted many countries [5, 6].

Control emerging pathogenic diseases

New emerging and exotic diseases for animals are now a threat to animals as well as humans and controlling these diseases are difficult to overcome without proper vaccination. Pathogens can easily be transferred between and across species as a result of rising human and animal populations, environmental deterioration, and global trade and travel. The accompanying diseases present significant concerns both today and in the future. These diseases are emerging at a faster rate and the development of new veterinary vaccines against such diseases could play a vital role in maintaining animal and public health [7].

TYPES OF VETERINARY VACCINES

Depending on the vaccine, either pure antigens from these species or living or dead organisms may be present. The best protective responses are generally produced by live attenuated vaccines. Since they can't flourish and disseminate within the host, purified/killed organisms used as antigens might be less immunogenic or effective than living ones. Some of the major types of vaccines [8-10] are-

Non-Living Vaccines

Subunit Vaccines

Toxic components such as endotoxins might be present in vaccines containing whole killed organisms which are economical to produce. Therefore, it may be useful to discover, isolate, and purify the essential protective antigens, depending on costs. Which can then be utilized independently in a vaccination. For example- the vaccine for tetanus.

Production of antigens using Gene Cloning

Physically purifying a particular protein or antigen might be too costly or expensive. In these circumstances, cloning the genes that code for the protective antigens into a vector like a bacterium, yeast, baculovirus, or plant may be more effective. It is possible to insert the DNA encoding the desired antigens into the vector, which then expresses the protective antigen. These antigens are

mainly produced by the inserted genes extracted, purified, and given as a vaccine after the recombinant vector has developed. One such vaccine is the one that targets the cloned portion of *E. coli* enterotoxin.

DNA plasmid vaccines

DNA encoding viral antigens may be injected into animals to immunize them. A bacterial plasmid, a circular segment of DNA that serves as a vector, is where this DNA gets introduced. The host cells take the genetically modified plasmid up after injection. The vaccine protein is subsequently created by the transcription of the DNA and the translation of mRNAs. Thus, the transfected host cells produce the vaccination protein alongside components from class I of the major histocompatibility complex. As a result, cytotoxic T cells and neutralizing antibodies are both produced. This type of vaccine has been used against West Nile Virus in horses [8-10].

Alphavirus Replicons

Additionally, RNA vaccines successfully stimulate the synthesis of endogenous antigens. They require to enter the cell cytoplasm rather than the nucleus, which makes them more effective and more stable than DNA plasmids. It is also possible to design RNA vaccines so that they can replicate on their own. These are typically produced from alphaviruses like the virus that causes Venezuelan equine encephalitis. They reproduce for a brief period within cells, producing high levels of endogenous antigen [8-10].

Modified live vaccines

Gene-deleted vaccines

It is now possible to alter an organism's genes using molecular genetic techniques in order to permanently reduce it. It is becoming more and more appealing to purposefully delete the genes that produce virulence-related proteins. For instance, the Aujeszky disease herpesvirus was the target of the first gene-deleted vaccinations in pigs. The virus in this instance had the thymidine kinase gene deleted. Thymidine kinase is necessary for the herpesvirus to emerge from dormancy. Viruses without this gene can still infect neurons, but they are unable to spread and cause disease.

Bacterial growth *in vivo* can be constrained through similar genetic manipulation. For instance, a modified live vaccine with *Pasteurella multocida* and *Mannheimia haemolytica* streptomycin-dependent is developed. Streptomycin is indispensable for the expansion of these mutants. Due to its scarcity of streptomycin in a vaccination which may be responsible for causing the germs to die, but not before it will have triggered a protective immune response.

It is also practicable to switch the expression of other antigens so that a vaccination will generate an antibody response that can be distinguished from the one brought on by wild strains. This allows for the distinction between infected and vaccine-protected animals [11].

Virus-vectored vaccine

The genes that encode protective antigens can also be inserted into an avirulent "vector" bacterium to create a very effective living vaccination. Genes from the vector are deleted and replaced with genes encoding pathogen antigens to produce these vaccines. When cells are infected by the vector virus, which is injected as the vaccine, the inserted genes cause the antigens to be expressed. The

vector may be limited to a particular host or attenuated so that it does not multiply within the tissues of the animal that has received the vaccination. Vaccines made from virus vectors are ideal for use against organisms that are risky or difficult to cultivate in a lab. Large DNA viruses including poxviruses (*fowl pox*, *canarypox*), vaccinia virus, adenoviruses, and various herpesviruses are among the most frequently utilised vaccine viral vectors. The vast genome of these viruses makes it easier to splice in new genes. Additionally, they produce a sizable amount of the recombinant antigen. Even when there are large amounts of maternal antibodies present, vectored vaccinations seem to be able to generate immunity in at least some instances. A comparable vaccinia vector containing the gene generating rabies glycoprotein is successful in protecting dogs and cats against the rabies virus [12].

Attenuated Vaccines

There are several benefits to using live organisms in vaccinations. For instance, they frequently induce cell-mediated immune responses more effectively than inactivated vaccines. However, using them can also be dangerous. For a living organism to be utilized for vaccination, its virulence must be lowered such that it can still reproduce but is no longer harmful. For vaccination to work, attenuation must be at a certain level. Under attenuation will lead to a return of virulence and disease, while excess attenuation will lead to an ineffective vaccination. Extensive reversion to virulence studies must be performed to demonstrate stability. It is not recommended to provide attenuated vaccines to species on whom they have not been evaluated or tested. Pathogens that are sufficiently or inadequately attenuated for one species may not be in others.

Historically, attenuation has entailed creatures being adapted to grow in unexpected environments. Viral virulence was attenuated by growth in species to which they are not normally adapted, whereas bacteria were attenuated by culture under unusual conditions. Growth of vaccine viruses in other media, such as tissue culture or eggs, may also attenuate them. Bluetongue, rabies, and canine distemper vaccines have all through this process. The most used attenuation technique for several years was prolonged tissue culture. An early version of genetic engineering is the prolonged tissue culture attenuation of viruses. Essentially, this led to the emergence of a virus strain that was incapable of spreading disease. The risk of returning to virulence made this often difficult to accomplish [11-13].

FUTURE DEVELOPMENTS IN VETERINARY VACCINATIONS

Through the diversification of antibody (IgG and its subtypes) responses induced or generated through vaccine antigen and it may totally differ from those induced during infection rate. Now a day, we can identify and isolate the defective genes from a pathogen which is responsible for causing disease. Several diseases and their corresponding diagnostic tests, such as those for infectious bovine rhinotracheitis (IBR), pseudorabies, and classical swine fever (CSF), are either available or under development. The development of differentiating infected from vaccinated animals and assays has received attention since IBR, which is brought on by a BHV-1 infection in livestock, and pseudorabies (Aujeszky's disease) in pig have been reported and identified as potential molecule for eradication from national herds [9-12].

Advances in Next Generation Sequencing, Bioinformatics, and Protein Modelling Enable New Methods in Vaccinology

Vaccines are potent tools, but developing safe and effective ones for some diseases has proven difficult. Using reverse vaccinology methods, recent advancements in nucleic acid sequencing, bioinformatics, and protein modelling are making it easier to find previously unidentified antigens. The identification of paratopes shared by many people and a complete evaluation of the immune repertoire are made possible by sequencing the complementarity-determining area of antibodies and T cell receptors, supporting the choice of antigens that may be broadly protective. Systems vaccinology techniques can identify previously unrecognised pathways and interactions associated to protective immunity by evaluating differentially expressed genes in blood, cellular, or tissue transcriptomes to assess the overall host immune response to vaccination. Although it's crucial to keep in mind that findings from systems and reverse vaccinology still need to be verified using conventional challenge models and clinical studies, these methods can offer fresh ideas that could help resolve enduring issues in veterinary vaccinology.

BOVINE MUCOSAL VACCINES: OPPORTUNITIES AND CHALLENGES

Since over 50 years ago, mucosal vaccinations have been administered to cattle, primarily by intranasal and oral methods. The use of mucosal vaccination in cattle is becoming more and more popular for a number of reasons. Intranasal immunizations for new-born calves offer a method to lessen maternal antibody interference with vaccines and improve disease protection when mother immunity declines. Mucosal vaccinations are also advantageous for managing clinical illness and lowering the spread of mucosal infections. Mucosal vaccines may provide chances to target both innate and adaptive mucosal effector cells and improve control of mucosal infections while keeping mucosal barrier integrity and essential mucosal functions. Further, a deeper comprehension of the interactions between the host and the microbiome may help vaccine designers control opportunistic infections that live in the commensal microbiome. When it comes to vaccination, specific features of the bovine mucosal immune system are taken into account, and the drawbacks and potential advantages of mucosal vaccines and vaccine delivery methods are explored. Finally, prospects to address contemporary infectious disease concerns in cattle are reviewed in the perspective of the potential for innovative vaccine delivery systems and vaccination techniques to enhance mucosa vaccine efficacy [13, 14].

Recombinant viral vector vaccines

Recombinant viral vector vaccines are novel veterinary medical innovations that utilise viruses as vaccinology instruments. These vaccines are created genetically by inserting DNA encoding important antigens into a viral vector [15]. Inactivated (killed) subunit vaccinations have a comparable safety profile and promote both humoral immune responses and cell-mediated immune responses, notably CD8+T cell responses. The first pox viral vectors were explored and developed in the 1980s, using different backbones to elicit reactions to different animal diseases, such as canarypox and fowlpox backbones. Adenovirus vectors have been investigated as vaccinations against tumor-associated antigens as well as systems of therapy for a variety of illnesses. Alphaviruses with positive sense RNA have also been employed as the basis of two other types of vector constructs: full-length infectious clones and replicon vectors. The other kind, which only contains the non-structural genomic region and the genes encoding the relevant antigen(s), is favourable because it lacks structural protein genes. In order to create self-replicating RNA

replicons, scrutinize the foreign genes can be substituted for the structural genes in alphavirus-replicons (RP). After inoculation, dendritic cells engulf the RP, which then controls the translation of a significant amount of protein in the cells and causes the antigen to be presented. They are essentially self-replicating RNA molecules as a result. The same ideas can then be applied to chimeric recombinant vector vaccines, which attempt to elicit a larger immune response. In these vaccines, the genes—and consequently the antigens—of interest are taken (i.e. pathogen) and inserted within the identical vector [11-15].

Veterinary Cancer Vaccines

As a result of the improved understanding of immunology that has been made possible over the past 4–5 decades by the tools of molecular biology, cancer immunotherapy has recently emerged as one of the most intriguing and quickly developing topics. Along with surgery, radiation, and chemotherapy, human cancer immunotherapy is increasingly acknowledged as one of the main treatment pillars. With a few commercially accessible medicines, including a xenogeneic DNA cancer vaccine, and a multitude of investigational cancer immunotherapies, the area of veterinary cancer immunotherapy has likewise advanced quickly in the past ten years and is expected to continue to do so [16].

In short, large-animal model based studies are required and convenient for the trial of non-identical delivery systems. New animal health vaccines (i.e. veterinary) are required and more probable to be therapeutic somewhat than prophylactic vaccines with fewer side effects.

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