Chapter 07

Conventional and Advanced Approaches in Veterinary Vaccines

Nawal Amin[1], Marriam Munawar[1], Ayesha Ijaz[1], Aleeza Shaffaq[1], Raqeeb Ullah[2], Muhammad Anas[3], Hafsa Tahir[4], Ayesha Waris[3], and Saleha Tahir[5*]

[1]National Institute of Biotechnology and Genetic Engineering, Faisalabad, Pakistan
[2]Department of Zoology, Bacha Khan University Charsadda, Qurtaba University of Science and Information Technology, Pakistan
[3]Institute of Microbiology, Government College University Faisalabad, Pakistan
[4]Department of soil sciences and engineering, University of Agriculture Faisalabad, Pakistan
[5]Institute of Microbiology, University of Agriculture Faisalabad, Pakistan
*Corresponding author: salehatahir999@gmail.com

ABSTRACT

Veterinary vaccination is one of the main effective measures to reduce and eradicate impairment prompted by infectious diseases in animals and humans. Various vaccines are used as either, prophylactic vaccines that protect body prior to pathogenic exposure, or as therapeutic vaccines that are responsible for strengthening immunity post pathogenic infections. Several effective vaccines have been developed which have significantly reduced the impact of a number of diseases, playing a decisive role in the health, survival and well-being of livestock and companion animals. Thus, vaccination has a pivotal role in the prevention, management and eradication of lethal diseases as the use of antibiotics against these infections is developing antibiotic resistance in livestock as well as in humans due to the consumption of food derived from these animals. Conventional vaccinations, such as live or killed modified pathogen, have been used for centuries to regularly immunize animals to reduce the impact of disease. However, current developments in genetics, molecular biology, microbiology, and immunology have led to the development of numerous innovative, safer, and more effective approaches to vaccine development. This chapter sheds light on the conventional and advanced approaches in veterinary industry to combat the challenges in vaccine development against veterinary diseases.

KEYWORDS
One-Health, Veterinary, Vaccination, Immune Response, Advanced Approaches

Received: 20-May-2024
Revised: 12-Jul-2024
Accepted: 11-Aug-2024

A Publication of Unique Scientific Publishers

Cite this Article as: Amin N, Munawar M, Ijaz A, Shaffaq A, Ullah R, Anas M, Tahir H and Tahir S, 2024. Conventional and advanced approaches in veterinary vaccines. In: Alvi MA, Rashid M, Zafar MA, Mughal MAS and Toor SI (eds), Complementary and Alternative Medicine: Immunization/Vaccinology. Unique Scientific Publishers, Faisalabad, Pakistan, pp: 50-58. https://doi.org/10.47278/book.CAM/2024.130

INTRODUCTION

History of Veterinary Vaccines and Immunization

The vaccine inoculations have been started for about 500 years ago when Edward Jenner first inoculated a boy with the small pox lesions for immunization in 1796 (Barakat, 2021). After 80 years, Louis Pasteur developed the vaccine for viral disease rabies. With the advancements in the vaccine production, further research involving erysipelas and rabies investigated serial passage as a substitute method to lessen or eradicate virulence in animals or other animal-derived tissues. This immunization technique aided in the prevention of anthrax and rabies (Saleh et al., 2021). Another method of immunizing against veterinary diseases was developed by Salmon and Smith in 1886, which was based on attenuation and inactivation principles (Nooraei et al., 2023). To increase vaccine diversity, these vaccine types were expanded to include toxoid vaccinations developed by Gaston Ramen at the Pasture institute against tetanus (Conti, 2021). Thus, in early twentieth century, first toxoid vaccine was created in 1924 by chemically inactivating the toxin, which was then adjuvanted to increase its effectiveness (Gupta and Pellett, 2023).

Veterinary Vaccines and One-Health

The rise and dissemination of zoonotic infections such as COVID-19 emphasized on averting the emergence of novel and hazardous zoonoses that could have adverse effects on human health. This is especially significant as the pandemic aligns with the One Health theory, which takes into account the relationship that exists between people, animals, and the environment (Zinsstag et al., 2023). At least 75% of newly discovered diseases have a zoonotic origin, with a variety of

animal species serving as their main reservoir. Prominent instances of these zoonoses comprise pandemics and/or epidemics including the Ebola virus, H1N1, SARS, MERS, and Spanish flu (de Melo et al., 2020).

In veterinary medicine, vaccination decreases disease rate within animal populations and improves public health by targeting zoonoses. There are various diseases that are zoonotic and can be transmitted by direct interaction or contact with the diseased animals, fluids, tissues or by some vectors like arthropods, effecting both food security and public health (Udainiya et al., 2024). It is very important to secure animal and human life by preventing the transmission of diseases at animal-human interface. Hence, veterinary vaccination acts as a bridge in "One-Health" and as a barrier to pandemic and epizootics control (Entrican and Francis, 2022).

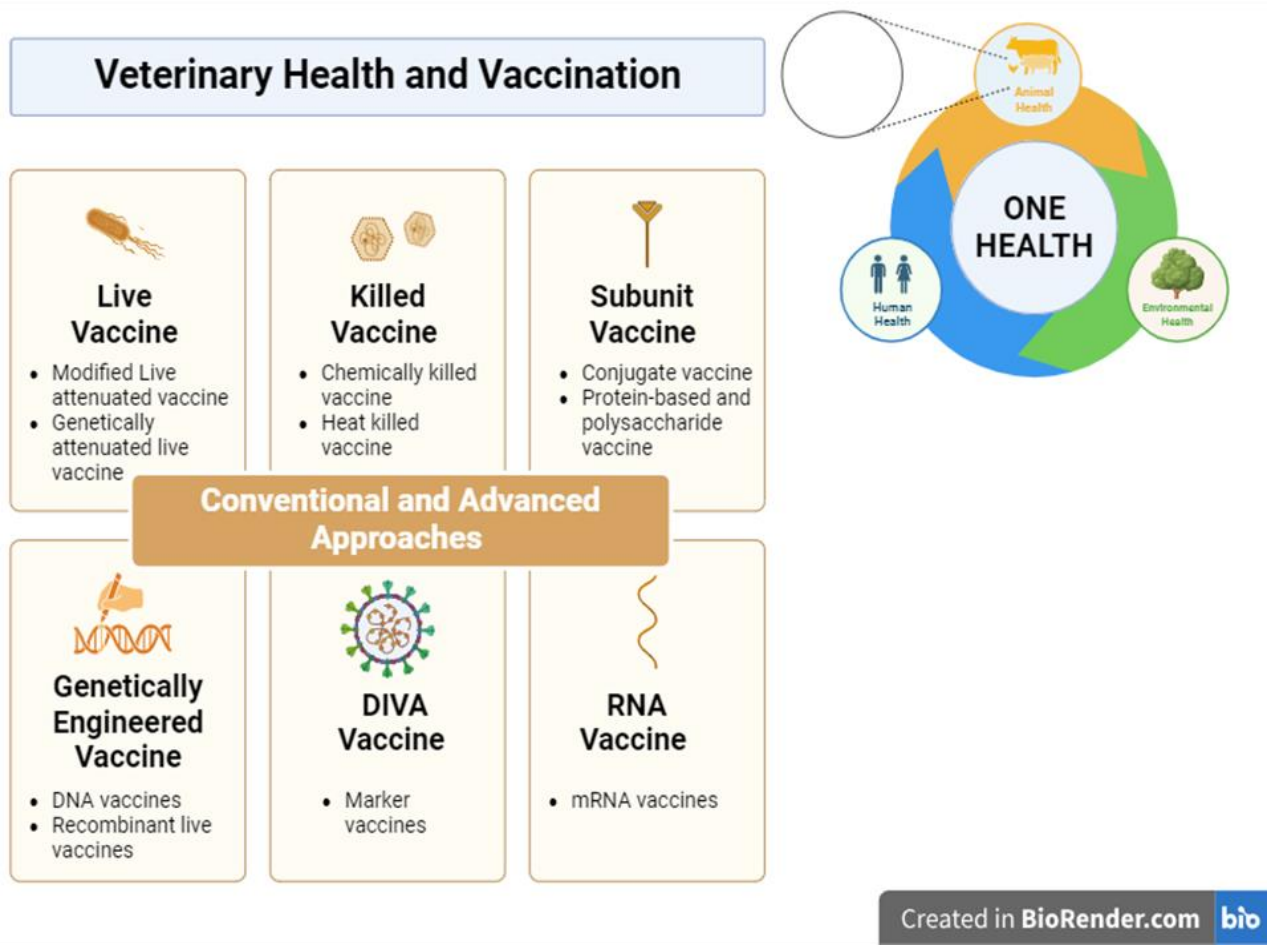

Fig. 1: Veterinary Vaccines – One Health Perspective

Development of Vaccine and Immune Responses

For many of the animal diseases, licensed vaccines produced by classical methodologies are being administered according to standard immunization schedule (Ghattas et al., 2021). Vaccines exploit two main principles, specificity and memory. Specificity is the crucial factor for the successful production of vaccines. This can be achieved by selection of whole antigen or some particular antigens that will induce the pool of memory lymphocytes as the primary response after vaccination (Brun, 2022). Ideally, the immunity would not only protect against morbidity and mortality but also prevent infection by blocking the infectious agent and its replication (Ali et al., 2023). There are several methods for developing vaccine against pathogenic microbes. These decisions are usually based on fundamental knowledge about the infectious agent, including how it infects the host cells, how the immune system responds to it, and the type of field strain in the particular region of the world (Yadav et al., 2020).

The developed vaccine should have the following properties

- It should provide long lasting immune responses including B-cell and T-cell responses
- It should be thermostable, should not be dependent on cold chains maintenance
- Easy administration of the vaccine, preferably through oral means
- It should provide protection against multiple diseases, hence be multivalent
- It should be cost effective and acceptable to country's authorities and policy (Gravagna et al., 2020).

Vaccine Design and Selection of Antigen

The vaccination methodology in past was designed empirically, but by optimizing the response of immune system,

synthesizing a rational vaccine can maximize their effectiveness. The logical design of vaccine is substantially influenced by the determination of the immunological connection with protection. This simplifies the choice of the appropriate antigens and adjuvants for vaccination to produce optimal adaptive and cell-meditated responses. Certain critical steps are involved in the potential design of modern vaccines (Schijns et al., 2021). These tactical decisions should ideally depend on targeting the immune response for designing successful vaccine, selection of the antigen, its presentation and delivery, effective immunomodulator and vaccine adjuvant.

The strategies behind successful capturing target-antigen are opting the target receptor, antigen to be administered, and antigen transporter. The APC target, adjuvant, and specific receptor work together to assemble the CD4+ T-cell response toward the Th1, Th2, and Th17 profiles in addition to selecting a specific target receptor. (Sulczewski et al., 2020). These features are mandatory for triggering immunity to combat future pathogen eradication. The mode of delivery has also a major impact on progress of the systemic or mucosal responses. The most commonly used immunization routes include intradermal, subcutaneous, intramuscular, and oral (Melgoza-González et al., 2023).

Types of Vaccines and Immune Response

There are several vaccines that helps body to cope with infectious diseases and boost the immunity. Currently, there are four types of vaccines that are available:

Type 1 Vaccines

Inactivated or killed vaccines have been used for decades and are generally being prepared by various chemicals or physical methods which results in disruption of pathogen replication ability. Chemical methods that are most widely used include formaldehyde and organic compounds based on cyclic esters (β-propiolactone) or binary ethylenimine (BEI). Some other cross-linking agents like glutaraldehyde can be used for this purpose. However, the limitation of using these cross-linking agents is their potential for disrupting the antigenic epitopes by aggregation leads to reduced immunogenicity (Jarvi and Balu-Iyer, 2021). Hence, other inactivation approaches can be opted such as hydrogen peroxide or some protonating compounds such as diethyl-pyrocarbonate (DEPC). The ability of hydrogen peroxide to inactivate both RNA and DNA viruses reduces the antigenic structural damage and minimize the effect on immunogenicity (Brun, 2022). However, such types of vaccines provide short duration of protection and induce ineffective immune response, as compared to live viral vaccines. This is why strong adjuvant is required when administering inactivated vaccinations, and it requires multiple booster doses to maintain long term and satisfactory immunity (Vashishtha and Kumar, 2024) .

Type 2 Vaccines

Live attenuated vaccines are one of the most successful kinds of vaccines with respect to providing booster immunity. The most highlighting feature of these vaccines is their ability to eliminate the virulence factors while maintaining the immunogenicity. The prominent benefit of attenuated vaccines is that it presents wider range of epitopes, leading to expression of more proteins as a result of viral replication into the infected host cell. The other possibility is its administration through natural routes of infection. Therefore, the induced immune responses are also similar to that of infections which triggers innate immune responses along with humoral and cellular responses (Torina et al., 2020) .

Type 3 Vaccines

This category of vaccine includes both subunit and nucleic acid vaccines. Subunit vaccines are superior to attenuated vaccines especially in production and safety factors. In subunit vaccines, another effective aspect is its possibility of generating virus like particles (VLPs) devoid of ribonucleoproteins by co-expressing the capsid proteins that are constituents of virions. Just like viral capsids, VPLs are also made of geometrically arranged patterns of proteins that forms the repetitive structures against which B-cell receptors or soluble antibodies can interact with high affinity. These VPL structures are good inducers of T-cell independent responses. In addition, these VPL structures can also be internalized and processed by antigen presenting cells (APCs) to trigger Th and CTL responses, showing the capacity to generate broader immune responses as compared to monomeric forms of protein subunit (Banerjee and Madhyastha, 2021).

On the other hand, genetic vaccines or nucleic acid vaccine were first discovered upon gene therapy experiments conducted by Wolff and Felgner when they were designed to transfer DNA into muscle cells using cationic lipid as carrier (Tiwari and Menghani, 2020). Generally, DNA vaccines are usually delivered by intradermal or intramuscular injections. But muscle cells can also be directly transfected and express the proteins. This can be achieved by using dendritic cells that are present in interstitial spaces, actively responsible for the uptake of soluble antigens, or can take up the cells killed by vaccines, or can be transfected directly. The advantages of these DNA vaccines are their easy design and production procedure, differentiation of vaccinated and infected animals (DIVA), natural processing of antigens, mimicking the immune response generated by virus replication as a result induce both humoral and cell-mediated immune responses. To date, the only DNA vaccine licensed have been against VHS in Salmonids and WNV in horses (Brun, 2022).

Type 4 Vaccines

Recombinant viral vectors, which make up the fourth category of vaccines, are an essential domain for the development of vaccines and for exploratory vaccination point of view. In this technique, non-pathogenic, infectious, virus

can be used to provide a system for recombinant incorporation and to express foreign genes. This technique has been used for different RNA viruses but among the DNA viruses, Poxvirus (from parapoxvirus and orthopoxvirus genus), Adenovirus, Herpesvirus and Baculovirus have been most widely used to deliver vaccine in experimental vaccine trials. The advantage of using DNA viruses over RNA viruses is the high stability of DNA genomes, containing more insertional sites and availability of BAC-DNA clones making it possible to engineer and rescue recombinant virus, a conventional laboratory task. Additional beneficial factors include, cytoplasmic expression and generation long term humoral and cell-mediated immune responses. These immune responses with immense emphasis on CD8-T-cell activation that is mediated by attenuated adenovirus and poxvirus infections (Dhakal et al., 2021).

Conventional Veterinary Vaccines against Bacterial Infections

Historically, vaccination with a range of raw antigen preparations was tried to control a number of bacterial veterinary infections. Live vaccinations are wild-type or naturally occurring variations of parental strains, whereas bacterin vaccines are prepared from complete dead cells or cell lysates (Rabie and Amin Girh, 2020). Due to the lack of knowledge about specific protective antigens and low cost of manufacturing, early vaccination followed bacterins or live cells for immunization. For sheep, cattle, and pigs, bacterin immunization showed that piliated bacteria were required for protection against foot rot, pinkeye, and scours respectively. For each of these infections, the early bacterin vaccines were unable to offer sufficient levels of host protection because of poorly piliated vaccine cultures containing only one or two potential serotypes. To overcome this problem, eight *B. nodosus* (Tizard, 2021) and twelve *E. coli* strains are currently present in the effective foot rot and scours bacterin vaccines respectively, which in each case represent all known serotypes.

The effectiveness of live-cell and bacterin vaccinations against cow mastitis has been studied. It was discovered that vaccinations against *Staphylococcus aureus* given into the mammary gland, generated protection against *Staphylococcus* infections to considerable extent, which are one of the main causes of mastitis (El-Diasty et al., 2021). Nevertheless, the large *S. aureus* bacterin doses necessary to promote protective immunity may cause lactation loss in the future. For commercial application, intramammary immunization is therefore not a viable choice. Differently from the case of killed vaccine, live *S. aureus* administered systemically to cows elicited protective immune responses because only live cells growing in vivo produce immunogenic level of capsular and toxin antigens. Which are critical for eliciting protective immunity. The cost of producing live vaccinations is higher than that of inactivated vaccines, which are also more resilient to environmental changes (Côté-Gravel et al., 2019). Since inactivated immunizations stop the spread of pathogens, they are not effective for long-term protection, even though their safety profiles are superior (Jorge and Dellagostin, 2017).

Salmonellosis and brucellosis in cattle are those infections in which the bacterial pathogen lacks both virulence elements associated with toxins and pili. Calves have been protected against oral *Salmonella* challenges by vaccination with live, virulent *Salmonella* and with a dead whole-cell bacterin; however, attenuated live bacteria are generally recommended as salmonellosis vaccine (Edrington et al., 2020).

Whereas, brucellosis caused by *Brucella* affects both humans and domestic animals including sheep, goats, cattle, and pig. Although live vaccinations including *B. suis* S2 and *B. melitensis* M5 have been widely utilized for preventing brucellosis infection in China (Li et al., 2023), the live attenuated *B. abortus* strain 19 is currently the recommended vaccine against bovine brucellosis (de Oliveira et al., 2022). The 45/20 strain of killed *B. abortus* vaccine has been used successfully in several nations with variable immunogenic properties. Originally isolated in the early 1920s, strain 19 is inexpensive and easy-to-use option for vaccination, but it has drawback of its lethal nature as a tiny portion of vaccinated animals shed the bacterium and experience chronic illnesses (Maruf et al., 2019).

Conventional Veterinary Vaccines against Viral infections

The most prevalent viral infections causing gastroenteritis in neonatal calves are rotavirus and coronavirus. In the gastrointestinal tract, local immunity is necessary to offer sufficient protection against infection. For calves, an oral vaccination has been designed to confer local immunity. Since nearly all cattle have antibodies to the coronavirus and rotavirus in their milk, the vaccine virus is swiftly neutralized by the antibodies in the milk, preventing the formation of immunity. Therefore, the vaccination needs to be given before nursing. The current vaccination contains only one serotype (serotype 6) contributing to the lack of potential action in the field. According to recent research, calves may carry multiple serotype infections, and vaccination against one serotype may not guarantee protection against heterologous serotype challenges (Geletu et al., 2021). The obstacle in the active immunization within calf is resolved by hyper immunizing the dam in mid-gestation and increasing antibody levels during the end of gestation. This methodology resulted in increased levels of milk and colostrum antibodies.

The foot-and-mouth disease (FMD) is a highly feared bovine viral infection in prevalent regions such as South America, Asia, and Africa, where immunization is the only measure of prevention. Inactivated and live-attenuated vaccines have been tested, which are mostly synthesized by inactivating viruses cultivated in tissue cultures (Kamel et al., 2019). Numerous serotypes of FMDV exist, including 0, A, C, SATl, SAT2, SAT3, and Asia 1. Apart from these seven serotypes, there is a significant level of antigenic diversity among these serotypes. Due to this antigenic diversity, it is crucial to make sure that control efforts through vaccination are being made against those specific serotypes circulating in the field. The antigenic structural analysis of the virus reveals VP1 protein as primary immunogenic location on FMDV. This localization led to the expression of FMDV VPl in *E. coli*, which was one of the first proteins to be evaluated as a vaccine in the early

1980s (Qadeer et al., 2021).

A member of the morbillivirus genus, rinderpest induces acute systemic infection that erodes the mucosal epithelium of the respiratory and digestive tracts in ruminants. Vaccination against rinderpest using inactivated viruses have been administered in regions where the disease is enzootic (Jia et al., 2020). The immune response associated with these vaccines was frequently transient, necessitating yearly booster shots providing enhanced degree and duration of immunity.

Table 1: Licensed Vaccines against Veterinary Bacterial and Viral Infections

Vaccines	Disease	Pathogen	Protected Host	Category of Vaccine	References
WEST NILE-INNOVATOR®	Encephalomyelitis	West Nile Virus	Horses	DNA vaccine	(Pereira et al., 2014)
Plowright Tissue Culture Vaccine	Rinderpest disease	Rinderpest Virus	Cattle, Buffalo	Live attenuated	(Sills and Robertshaw, 2010)
Human Diploid Cell Rabies Vaccine (HDCV), Purified Chicken Embryo Cell Vaccine (PCECV)	Rabies	Rabies lyssavirus	Rabid animals	Live attenuated	(Prevention, 2024)
Avinew	Newcastle Disease Virus	Newcastle Disease	Chickens	Live VG/GA virus strain	(Bwala et al., 2009)
AE-Poxine	Avipox virus, Avian encephalomyelitis virus	Fowl pox, Avian encephalomyelitis	Chicken	Combination modified live virus	(Islam et al., 2008)
Tetanus toxoid	*Clostridium tetani*	Tetanus	Equines	Subunit vaccine	(Manual, 2021)
Bovilis Vistal Once SQ	*Mannheimia haemolytica, Pasteurella multocida, BHV-1, BVDV, BPI3V, BRSV*	Bovine respiratory disease, IBR, Bovine viral diarrhea, Bovine parainfluenza 3, viral pneumonia,	Cattle	Modified live virus vaccine	(Purtle et al., 2016)
Nobivac Lepto	*Leptospira canicola, Leptospira iterohaemorrhagiae*	Leptospirosis	Dogs	Bivalent inactivated vaccine	(Health, 2023)

Advancements in Veterinary Vaccines

Despite accessibility of innovative classes of vaccines, the same fundamental technologies continue to be the backbone of vaccine manufacture in the contemporary era of vaccination use. The fundamentals of manufacturing, registration, and developmental research still adhere to the magnificent heritage methods. The majority of these vaccines were created in local research facilities. When Waldman and others employed large-scale, regulated procedures to create FMD antigens in Germany in the 1930s and 1940s, the processes started to become industrialized (Abbas et al., 2022). In the 1950s and 1960s, primary cell lines were developed, followed by clean cell lines (Szkodny and Lee, 2022). Moreover, significant developments in the field of vaccination have been made possible by advances in inactivation technologies, antigen concentration, purification, bulk antigen storage, enhanced aluminum gels, and oil suspension as adjuvants used in the preparation of polyvalent antigens (McVey and Shi, 2010).

The area of vaccine technology with the quickest rate of growth is DNA vaccination. DNA vaccinations cause the host to produce antigens through a plasmid containing a gene for a protein, found in mammals or for a virus, bacteria, or parasite that can be generated in mammals (Shafaati et al., 2021). Innate and adaptive immunity are both stimulated by DNA vaccination. The innate immune system can be triggered by identifying the dsDNA of the plasmid backbone, whereas the adaptive immune response comprises the processing of antigen and its presentation in class I and class II MHC molecules to CD8+ and CD4+ T cells, respectively (Gómez and Oñate, 2018).

Attenuated live vaccine Attenuation via extended tissue culture could be considered an early form of genetic engineering. While molecular genetics technique modifies an organism's genes to cause irreversible attenuation and helps pinpoint certain virulence genes (Antoine et al., 2021). This can be achieved by introducing many mutations or even eliminating the entire gene, depending on the pathogen. Using this methodology, it is possible to create a vaccination that is both safe and affordable instead of utilizing traditional techniques. To change the attenuation level, the appropriate gene or gene set(s) should be removed or modified (Dolan, 2020). The capacity to deliver live vaccines that have been genetically attenuated that resemble their actual infection pattern is the primary advantage of this technique. Therefore, they should elicit an immunological response same as induced by highly pathogenic field isolates of the pathogen (Gutiérrez-Álvarez et al., 2021).

Live recombinant vaccines are based on a genetically modified live virus or bacterial vector that expresses a variety of foreign antigens in the cytoplasm of target cells. As a vaccination, the recombinant organism itself may be used. The most frequent viruses utilized as a vector for the creation of live recombinant virus vaccines are adenoviruses, herpesviruses, and

poxviruses (Kamel and El-Sayed, 2019). Poxviruses with large, stable genomes that allow it relatively easy to insert a new gene, such as vaccinia, fowl pox, and canarypox, have been the most commonly used viruses in the design of live recombinant vaccines (Lee et al., 2012). The rinderpest vaccine is made up of a capri pox or vaccinia vector that has the rinderpest virus's fusion (F) or hemagglutinin (H) genes (Minhas et al., 2016; Teffera, 2021). Live recombinant vaccines can induce robust humoral and cell-mediated immune responses that can result in immunological memory. It can also encode for many antigens from different diseases. There is a chance that one vaccination could soon be available for several diseases. One of the drawbacks (Francis, 2018) of live recombinant vaccine is its live-attenuated nature (either bacteria or viruses), so there is potential for reversion to virulence form of the pathogen.

Short polypeptides can be chemically synthesized to create subunit vaccinations. While solid phase peptide synthesis is not a novel technology, advancements in the last ten years have reduced costs and raised process efficiency (Ferrazzano et al., 2022). The methodology involves precisely sequencing DNA to pinpoint protective antigenic determinants on antigens and availability of monoclonal antibodies to identify these epitopes. The FMDV was among pioneer viruses to be tested for determining the viability of exploiting synthetic peptides as a vaccine candidate. Unfortunately, antigenic variation can occur in many viruses, including FMDV. Therefore, prior to the development of a single broad coverage synthetic peptide vaccination, it is necessary to identify important conserved epitopes on the virus. Furthermore, to enhance the efficacy of these vaccines, genetic engineering methods are followed. For instance, all rotavirus serotypes share a proteolytic cleavage site in VP4, which is present in all rotaviruses (Hoxie and Dennehy, 2020). It has been demonstrated that a synthetic peptide vaccine targeting the VP4 cleavage site can produce protection against several other serotypes from different species. These molecular approaches have resulted in new strategies for creating novel vaccines against infectious, parasitic, or metabolic diseases in addition to improving knowledge of the genes causing virulence and making it easier to identify the factors influencing protective immune responses.

Subunit Vaccine comprise of one or more pure or semi-pure antigens from the target pathogen. These subunit vaccines are being produced in huge quantities using a variety of expression systems including, prokaryotic systems, and eukaryotic systems, such as yeasts, filamentous fungi, algae, mammalian and insect cells. To enhance the immunogenic response against multiple serotypes of the same pathogen, it is advantageous to immunize an animal with a vaccine comprising several defensive proteins from several serotypes. This can be accomplished by creating chimeric proteins, which are proteins that combine protective epitopes from several organisms into a single protein. (Karch and Burkhard, 2016). One example of subunit vaccine which makes use of recombinant DNA technology, incorporates the fusion and hemagglutinin-neuraminidase proteins of rinderpest into the vaccinia virus, resulting in the development of a strain that is resistant to heat (Cid and Bolívar, 2021) .

Marker vaccines enable serological distinction between vaccinated and infected persons. The basis for this distinction is lack of one or more microbial proteins within vaccine formulation that are found within wild type microbe. Consequently, an antibody response against those particular protein or proteins can be found after infection but not after immunization. Thus, it is possible to differentiate between vaccinated and infected patients using a protein-specific antibody test. Through conventional methods as well as recombinant DNA technologies, marker vaccines against infections caused by the pseudorabies virus (PRV) and the bovine herpesvirus 1 (BHV1) have been created (Zheng et al., 2022). It has been demonstrated that these vaccinations are effective in lowering clinical symptoms following infection, replication of the wild-type virus following infection, and transmission of the wild-type virus in both the laboratory and the field.

mRNA vaccines are becoming focus of research in recent years because of their high efficacy, speed of production, potential for low-cost manufacture, potential for safe delivery, and as a replacement for conventional vaccination methods. mRNA vaccines do not create or incorporate infectious particles into the host cells; therefore, their genome remains unaltered. They can express complex antigens without being limited by packing restrictions and can be used to transport antigens for in-situ expression without any requirement to breach the nuclear membrane barrier (Nitika et al., 2021). By utilizing the machinery of the host cell to convert mRNA into the proper antigen in vivo, the mRNA vaccine imitates a natural infection and elicits robust humoral and cellular immune responses (Zhang et al., 2019).

Conclusion

Vaccination in veterinary sector is the most economical method for preventing and controlling newly emerging and reemerging infectious diseases. Improving animal health acts as a tool in improving public health and welfare, and maintaining the balance of One-Health triangle. New and more potent vaccinations have been created as a consequence of recent developments in molecular biology and genetic engineering. Novel methodologies within vaccine development can revolutionize the fate of vaccine industry through low-cost, high production rate, safe delivery, and high efficacy.

REFERENCES

Abbas, R., Khan, A., Liu, P., and Saleemi, M. (2022). *Animal Health Perspectives (Volume 2)*.

Ali, A., Waris, A., Khan, M. A., Asim, M., Khan, A. U., Khan, S., and Zeb, J. (2023). Recent advancement, immune responses, and mechanism of action of various vaccines against intracellular bacterial infections. *Life Sciences*, *314*, 121332.

Antoine, L., Bahena-Ceron, R., Devi Bunwaree, H., Gobry, M., Loegler, V., Romby, P., and Marzi, S. (2021). RNA Modifications in Pathogenic Bacteria: Impact on Host Adaptation and Virulence. *Genes*, *12*(8), 1125. https://www.mdpi.com/2073-

4425/12/8/1125

Banerjee, K., and Madhyastha, H. (2021). Immunology and Nanotechnology: Effects and Affects. *Nanotechnology in Medicine*, 17-34.

Barakat, A. (2021). The history of vaccination.

Brun, A. (2022). An overview of veterinary viral diseases and vaccine technologies. *Vaccine Technologies for Veterinary Viral Diseases: Methods and Protocols*, 1-26.

Bwala, D. G., Abolnik, C., van Wyk, A., Cornelius, E., and Bisschop, S. P. (2009). Efficacy of a genotype 2 Newcastle disease vaccine (Avinew) against challenge with highly virulent genotypes 5d and 3d. *Journal South Africa Veterinary Associate*, *80*(3), 174-178. https://doi.org/10.4102/jsava.v80i3.197

Cid, R., and Bolívar, J. (2021). Platforms for production of protein-based vaccines: from classical to next-generation strategies. *Biomolecules*, *11*(8), 1072.

Conti, A. A. (2021). Vaccination through time: from the first smallpox vaccine to current vaccination campaigns against the COVID-19 pandemic. *Acta Biomed*, *92*(S6), e2021453. https://doi.org/10.23750/abm.v92iS6.12211

Côté-Gravel, J., Brouillette, E., and Malouin, F. (2019). Vaccination with a live-attenuated small-colony variant improves the humoral and cell-mediated responses against Staphylococcus aureus. *PLoS One*, *14*(12), e0227109.

de Melo, R. T., Rossi, D. A., Monteiro, G. P., and Fernandez, H. (2020). Veterinarians and One Health in the Fight Against Zoonoses Such as COVID-19 [Opinion]. *Frontiers in Veterinary Science*, *7*. https://doi.org/10.3389/fvets.2020.576262

de Oliveira, M. M., Pereira, C. R., de Oliveira, I. R. C., Godfroid, J., Lage, A. P., and Dorneles, E. M. S. (2022). Efficacy of Brucella abortus S19 and RB51 vaccine strains: A systematic review and meta-analysis. *Transboundary and Emerging Diseases*, *69*(4), e32-e51.

Dhakal, S., Loube, J., Misplon, J. A., Lo, C.-Y., Creisher, P. S., Mulka, K. R., and Epstein, S. L. (2021). Effect of an adenovirus-vectored universal influenza virus vaccine on pulmonary pathophysiology in a mouse model. *Journal of Virology*, *95*(9), 10.1128/jvi. 02359-02320.

Dolan, S. K. (2020). Current knowledge and future directions in developing strategies to combat Pseudomonas aeruginosa infection. *Journal of Molecular Biology*, *432*(20), 5509-5528.

Edrington, T. S., Arthur, T. M., Loneragan, G. H., Genovese, K. J., Hanson, D. L., Anderson, R. C., and Nisbet, D. J. (2020). Evaluation of two commercially-available Salmonella vaccines on Salmonella in the peripheral lymph nodes of experimentally-infected cattle. *Ther Adv Vaccines Immunother*, *8*, 2515135520957760. https://doi.org/10.1177/2515135520957760

El-Diasty, M., Ghobrial, R., Zayed, S., Elkady, M., Ebrahim, A., Eisa, M., and El-Beskawy, M. (2021). Field Evaluation of Staphylococcus aureus Bacterin Use in Dairy Farms. *Zagazig Veterinary Journal*, *49*(3), 358-373.

Entrican, G., and Francis, M. J. (2022). Applications of platform technologies in veterinary vaccinology and the benefits for one health. *Vaccine*, *40*(20), 2833-2840.

Ferrazzano, L., Catani, M., Cavazzini, A., Martelli, G., Corbisiero, D., Cantelmi, P., and Felletti, S. (2022). Sustainability in peptide chemistry: current synthesis and purification technologies and future challenges. *Green Chemistry*, *24*(3), 975-1020.

Francis, M. J. (2018). Recent advances in vaccine technologies. *Veterinary Clinics: Small Animal Practice*, *48*(2), 231-241.

Geletu, U. S., Usmael, M. A., and Bari, F. D. (2021). Rotavirus in Calves and Its Zoonotic Importance. *Veterinary Medicine International*, *2021*, 6639701. https://doi.org/10.1155/2021/6639701

Ghattas, M., Dwivedi, G., Lavertu, M., and Alameh, M.-G. (2021). Vaccine technologies and platforms for infectious diseases: Current progress, challenges, and opportunities. *Vaccines*, *9*(12), 1490.

Gómez, L. A., and Oñate, A. A. (2018). Plasmid-based DNA vaccines. *Plasmid*.

Gravagna, K., Becker, A., Valeris-Chacin, R., Mohammed, I., Tambe, S., Awan, F. A., and Basta, N. E. (2020). Global assessment of national mandatory vaccination policies and consequences of non-compliance. *Vaccine*, *38*(49), 7865-7873.

Gupta, S., and Pellett, S. (2023). Recent developments in vaccine design: From live vaccines to recombinant toxin vaccines. *Toxins*, *15*(9), 563.

Gutiérrez-Álvarez, J., Honrubia, J. M., Fernández-Delgado, R., Wang, L., Castaño-Rodríguez, C., Zúñiga, S., and Enjuanes, L. (2021). Genetically Engineered Live-Attenuated Middle East Respiratory Syndrome Coronavirus Viruses Confer Full Protection against Lethal Infection. *mBio*, *12*(2). https://doi.org/10.1128/mBio.00103-21

Health, M. A. (2023). *Nobivac LEPTO*. Retrieved 30 March from https://www.msd-animal-health-me.com/products/nobivac-lepto/#:~:text=Nobivac%20Lepto%20is%20a%20bivalent,lead%20to%20infection%20of%20people

Hoxie, I., and Dennehy, J. J. (2020). Intragenic recombination influences rotavirus diversity and evolution. *Virus Evolution*, *6*(1), vez059.

Islam, M. R., Khan, R., Islam, M., Kayesh, M. E. H., Karim, M., Gani, M., and Kabir, A. (2008). Comparative Efficacy of Imported Fowl Pox Virus Vaccine with Locally Produced One in Backyard Chicks.

Jarvi, N. L., and Balu-Iyer, S. V. (2021). Immunogenicity challenges associated with subcutaneous delivery of therapeutic proteins. *BioDrugs*, *35*(2), 125-146.

Jia, X.-X., Wang, H., Liu, Y., Meng, D.-M., and Fan, Z.-C. (2020). Development of vaccines for prevention of peste-des-petits-ruminants virus infection. *Microbial Pathogenesis*, *142*, 104045.

Jorge, S., and Dellagostin, O. A. (2017). The development of veterinary vaccines: a review of traditional methods and

modern biotechnology approaches. *Biotechnology Research and Innovation*, *1*(1), 6-13.

Kamel, M., and El-Sayed, A. (2019). Utilization of herpesviridae as recombinant viral vectors in vaccine development against animal pathogens. *Virus Research*, *270*, 197648.

Kamel, M., El-Sayed, A., and Castañeda Vazquez, H. (2019). Foot-and-mouth disease vaccines: recent updates and future perspectives. *Archives of Virology*, *164*, 1501-1513.

Karch, C. P., and Burkhard, P. (2016). Vaccine technologies: From whole organisms to rationally designed protein assemblies. *Biochemical Pharmacology*, *120*, 1-14.

Lee, N.-H., Lee, J.-A., Park, S.-Y., Song, C.-S., Choi, I.-S., and Lee, J.-B. (2012). A review of vaccine development and research for industry animals in Korea. *Clinical and Experimental Vaccine Research*, *1*(1), 18.

Li, P., Jiang, H., Feng, Y., Zhang, G., Banai, M., and Ding, J. (2023). The advances of the Chinese Brucella suis strain 2 vaccine. *Animal Research and One Health*, *1*(1), 115-126.

Manual, M. V. (2021). *Tetanus in Animals* Retrieved 30 March from https://www.msdvetmanual.com/generalized-conditions/clostridial-diseases/tetanus-in-animals#:~:text=Tetanus%20toxoid%20is%20given%20for,other%20domestic%20or%20laboratory%20mammal

Maruf, A., Yasmin, F., Yeasmin, F., Rahman, A., Hossain, M., Neubauer, H., and Rahman, M. (2019). Comparison of humoral immune responses between heat-inactivated Brucella abortus biovar 3 and strain RB51 vaccines in indigenous cattle of Bangladesh. *Journal of Veterinary Medical and One Health Research*, *1*, 247-259.

McVey, S., and Shi, J. (2010). Vaccines in veterinary medicine: a brief review of history and technology. *The Veterinary clinics of North America. Small Animal Practice*, *40*(3), 381.

Melgoza-González, E. A., Bustamante-Córdova, L., and Hernández, J. (2023). Recent advances in antigen targeting to antigen-presenting cells in veterinary medicine. *Frontiers in Immunology*, *14*, 1080238.

Minhas, S., Pandey, A., Ramakrishnan, M., Kamble, N., and Chaudhary, D. (2016). Capripoxviruses as vaccine vectors: a review. *Journal of Pure and Applied Microbiology*, *10*(3), 2055-2062.

Nitika, Wei, J., and Hui, A.-M. (2021). The development of mRNA vaccines for infectious diseases: recent updates. *Infection and Drug Resistance*, 5271-5285.

Nooraei, S., Sarkar Lotfabadi, A., Akbarzadehmoallemkolaei, M., and Rezaei, N. (2023). Immunogenicity of different types of adjuvants and nano-adjuvants in veterinary vaccines: a comprehensive review. *Vaccines*, *11*(2), 453.

Pereira, V., Zurita-Turk, M., Luerce-Saraiva, T., Castro, C., Souza, B., Agresti, P., and Miyoshi, A. (2014). DNA Vaccines Approach: From Concepts to Applications. *World Journal of Vaccines*, *04*, 50-71. https://doi.org/10.4236/wjv.2014.42008

Prevention, C. (2024). *Rabies Vaccine*. Retrieved 30 March from https://www.cdc.gov/rabies/medical_care/vaccine.html

Purtle, L., Mattick, D., Schneider, C., Smith, L., Xue, W., and Trigo, E. (2016). One year duration of immunity of the modified live bovine viral diarrhea virus type 1 and type 2 and bovine herpesvirus-1 fractions of Vista® Once SQ vaccine. *Vaccine*, *34*(13), 1582-1588. https://doi.org/10.1016/j.vaccine.2016.02.009

Qadeer, S., Khan, M. S., Joyia, F. A., and Zia, M. A. (2021). Immunogenic profiling and designing of a novel vaccine from capsid proteins of FMDV serotype Asia-1 through reverse vaccinology. *Infection, Genetics and Evolution*, *93*, 104925.

Rabie, N. S., and Amin Girh, Z. M. (2020). Bacterial vaccines in poultry. *Bulletin of the National Research Centre*, *44*, 1-7.

Saleh, A., Qamar, S., Tekin, A., Singh, R., and Kashyap, R. (2021). Vaccine Development Throughout History. *Cureus*, *13*(7), e16635. https://doi.org/10.7759/cureus.16635

Schijns, V., Majhen, D., Van Der Ley, P., Thakur, A., Summerfield, A., Berisio, R., and Gizurarson, S. (2021). Rational vaccine design in times of emerging diseases: The critical choices of immunological correlates of protection, vaccine antigen and immunomodulation. *Pharmaceutics*, *13*(4), 501.

Shafaati, M., Saidijam, M., Soleimani, M., Hazrati, F., Mirzaei, R., Amirheidari, B., and Ahmadyousefi, Y. (2021). A brief review on DNA vaccines in the era of COVID-19. *Future Virol*. https://doi.org/10.2217/fvl-2021-0170

Sills, J., and Robertshaw, D. (2010). Credit to Plowright for Rinderpest Eradication. *Science*, *330*(6010), 1477-1477. https://doi.org/doi:10.1126/science.330.6010.1477-a

Sulczewski, F. B., Martino, L. A., Almeida, B. d. S., Zaneti, A. B., Ferreira, N. S., Amorim, K. N. d. S., and Boscardin, S. B. (2020). Conventional type 1 dendritic cells induce TH1, TH1-like follicular helper T cells and regulatory T cells after antigen boost via DEC205 receptor. *European Journal of Immunology*, *50*(12), 1895-1911.

Szkodny, A. C., and Lee, K. H. (2022). Biopharmaceutical Manufacturing: Historical Perspectives and Future Directions. *Annual Review Chemistry Biomolecular Eng*, *13*, 141-165. https://doi.org/10.1146/annurev-chembioeng-092220-125832

Teffera, M. (2021). *Generation of Recombinant Capripoxvirus Vaccines: the Development of a Bivalent Peste des Petits Ruminants Vaccine and a Differentiating Infected from Vaccinated Animal Vaccine*

Tiwari, S., and Menghani, E. (2020). Mode of viral and non-viral gene transfer: an overview. *S. Tiwari and E. Menghani, Mode of Viral and Non-Viral Gene Transfer: An Overview, International Journal of Advanced Research in Engineering and Technology*, *11*(11).

Tizard, I. R. (2021). Sheep and goat vaccines. *Vaccines for Veterinarians*, 215.

Torina, A., Villari, S., Blanda, V., Vullo, S., La Manna, M. P., Shekarkar Azgomi, M., and Sireci, G. (2020). Innate immune response to tick-borne pathogens: Cellular and molecular mechanisms induced in the hosts. *International Journal of*

Molecular Sciences, *21*(15), 5437.

Udainiya, S., Tiwari, A., Mishra, A., and Dubey, A. (2024). Chapter 37 - Zoonotic diseases of dogs and cats. In T. Rana (Ed.), *Introduction to Diseases, Diagnosis, and Management of Dogs and Cats* (pp. 559-572). Academic Press. https://doi.org/https://doi.org/10.1016/B978-0-443-18548-9.00037-8

Vashishtha, V. M., and Kumar, P. (2024). The durability of vaccine-induced protection: an overview. *Expert Review of Vaccines*(just-accepted).

Yadav, D. K., Yadav, N., and Khurana, S. M. P. (2020). Vaccines: present status and applications. In *Animal Biotechnology* (pp. 523-542). Elsevier.

Zhang, C., Maruggi, G., Shan, H., and Li, J. (2019). Advances in mRNA vaccines for infectious diseases. *Frontiers in Immunology*, *10*, 429065.

Zheng, H.-H., Fu, P.-F., Chen, H.-Y., and Wang, Z.-Y. (2022). Pseudorabies virus: from pathogenesis to prevention strategies. *Viruses*, *14*(8), 1638.

Zinsstag, J., Kaiser-Grolimund, A., Heitz-Tokpa, K., Sreedharan, R., Lubroth, J., Caya, F., and Dobell, E. (2023). Advancing One human–animal–environment Health for global health security: what does the evidence say? *The Lancet*, *401*(10376), 591-604.