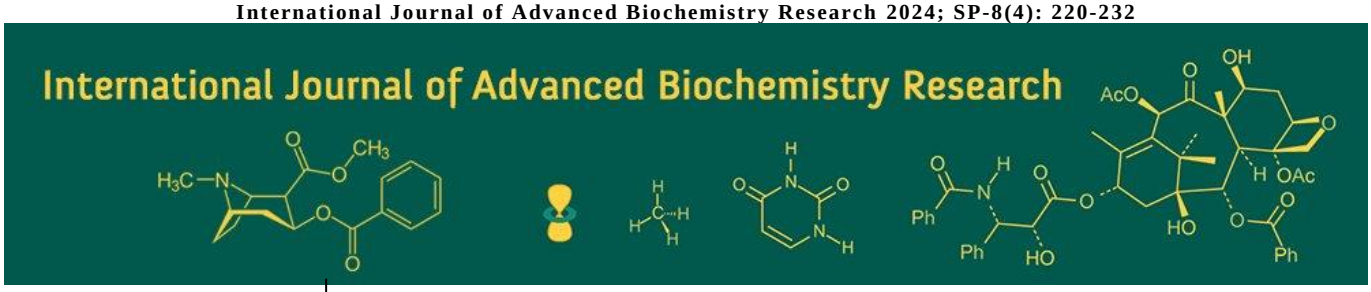

ISSN Print: 2617-4693
ISSN Online: 2617-4707
IJABR 2024; SP-8(4): 220-232
www.biochemjournal.com
Received: 16-02-2024
Accepted: 20-03-2024

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Recent advances in veterinary vaccines

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DOI: https://doi.org/10.33545/26174693.2024.v8.i4Sc.981

Abstract
A vaccine is a suspension of killed or weakened microbes, toxins, or biological preparations to prevent illness. It can confer active immunity by stimulating the immune system to attack the harmful agent, while passive immunity may be provided by providing antibodies or lymphocytes from an animal or human donor. There are several types of vaccines, including inactivated vaccines, live-attenuated vaccines, DNA vaccines, mRNA vaccines, subunit, recombinant and viral vector vaccines. Conventional inactivated and modified-live vaccines have provided advantages to people and animals alike against harmful bacteria. Inactivated vaccines are generally safe and inexpensive to create, mostly delivering antigens via the MHC-II route. DNA vaccines, on the other hand, transfect a specific antigen-coding DNA sequence into an organism's cells to induce an immune response. They work by injecting genetically engineered plasmid containing the antigen(s) against which an immune response is sought, causing cells to directly produce the antigen, causing a protective immunological response. Recombinant DNA vaccines are being explored as a potential strategy against bovine Foot and mouth disease virus (FMDV). Current vaccines, including synthetic proteins, offer short-term immunity but face challenges like lack of cross-protection against multiple strains, cold storage, and reinfection risk. A multi-epitope DNA-based vaccine is designed as a cost-effective and non-pathogenic alternative for FMD protection. RNA vaccines involve introducing an mRNA sequence coding for a disease-specific antigen, which the immune system recognizes and prepares to fight the infection. Recombinant viral vector vaccines are novel veterinary medicine technologies that use viruses for vaccinology. Novel vaccines, including DNA, RNA, and recombinant viral-vector vaccines, are economically manufactured, safe, and differentiate infected animals.

Keywords: DNA, foot and mouth disease virus (FMDV), mRNA, vaccine, veterinary

Introduction
A vaccine is essentially a suspension of toxins or weak, dead, or fragmented microorganisms, or it might be another biological preparation like lymphocytes, messenger RNA (mRNA), or antibodies. By encouraging the immune system to combat a particular dangerous element, a vaccine can provide active protection against it. The antibody-producing cells, known as B cells (or B lymphocytes), stay sensitized and prepared to react to the chemical should it ever enter the body after being triggered by a vaccination.
By transferring antibodies or lymphocytes that have previously been created by an animal or human donor, vaccination can also confer passive immunity. Usually, vaccinations are administered by injection (parenteral administration). Nonetheless, some are injected orally, or even nasally (like the flu shot). Immune system stimulation appears to occur when vaccinations are applied to mucosal surfaces, such as the nose or stomach. Therefore, the most effective delivery technique might be one that elicits a higher antibody response.

History of vaccinology
English physician Edward Jenner made progress toward this discovery in May 1796 when he used material from a cowpox sore on a milkmaid's hand to inoculate 8-year-old James Phipps (Fig. 1). Phipps felt sick for many days and received a local response, but he recovered fully. To test Phipps's resistance, Jenner injected material from a human smallpox sore two months later, in July 1796. Phipps continues to be well and receives the first smallpox vaccination.
French biologist Louis Pasteur demonstrated anthrax immunization in 1881 by injecting a combination comprising weakened strains of the bacillus that cause the disease into sheep. He obtained a rabies-protective suspension four years later. The Latin word for cow, "Vacca," is where he came up with the phrase "vaccine." Patient Joseph Meister started a

series of 13 injections in 1885, each time administering a larger dose of the rabies virus. Meister stays put and later looks after Pasteur's monument in Paris.

Types of Vaccine

Vaccines can be of many various types, but they always work in the same manner. This is done to train the immune system to identify a pathogen—an organism that causes disease—or a portion of a pathogen. The immune system has been taught to identify this, so if the body is subsequently exposed to the virus, it will be removed from the body. Specifically, the immune system finds external "antigens," or pathogen elements that are present on the pathogen's surface or within the pathogen (Fig. 1 & 2).

The Whole Pathogen Vaccines: Using the full disease-causing virus in a vaccine to induce an immune response similar to what is seen during natural infection is the most conventional and well-known type of vaccination.

1. Live attenuated vaccines: These vaccinations include whole bacteria or viruses that have been "weakened" (attenuated) to trigger a defence mechanism in healthy persons without posing a threat to their health.
2. Inactivated vaccinations: Inactivated vaccinations include whole bacteria or viruses that have been altered or destroyed to stop them from replicating.

Component vaccines: Immunizations free of any whole bacteria or viruses. Rather, one or more specific pathogen-surface antigens are frequently included in these vaccinations. Component vaccines come in a variety of forms, including vaccinations based on protein subunits, particles that resemble viruses, DNA, RNA, and viral vectors.

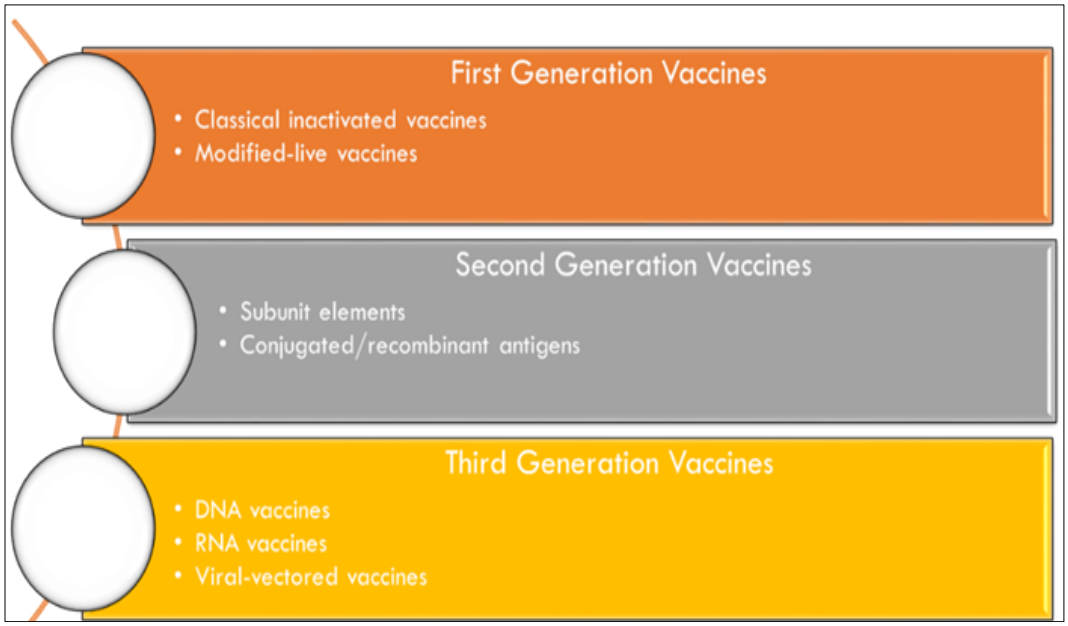

Fig 1: Types of vaccine (1)

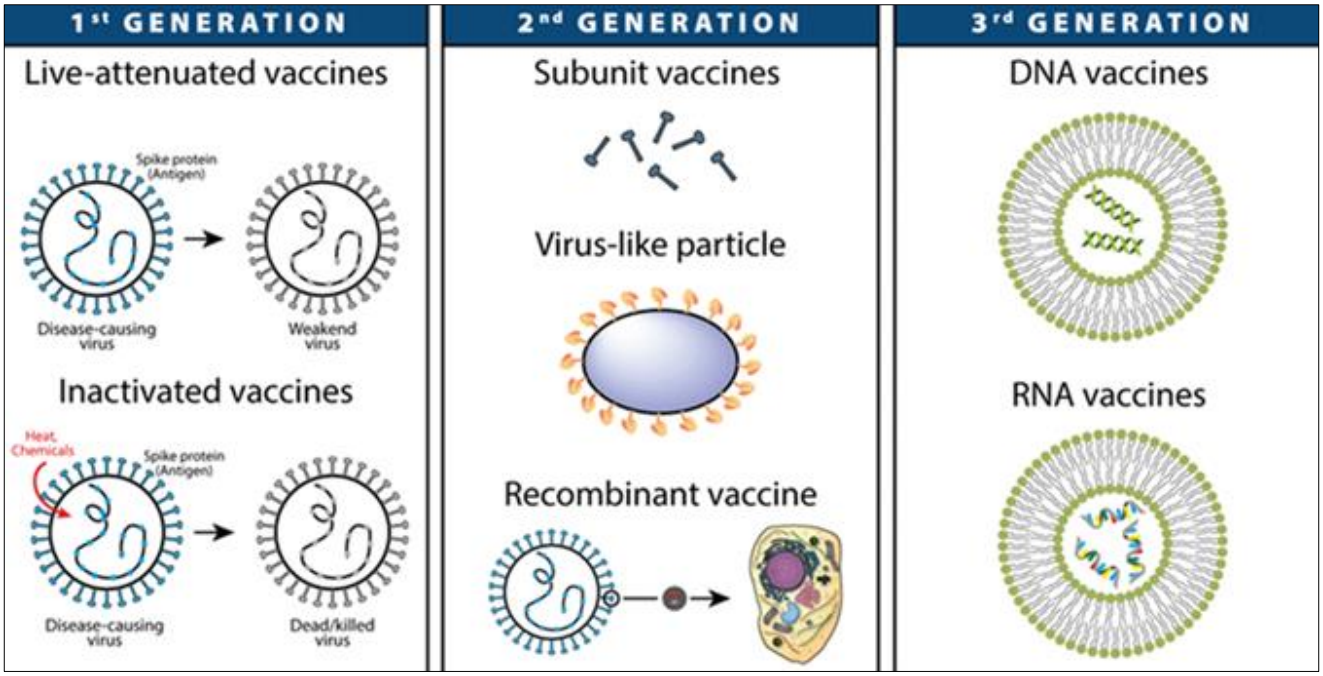

Fig 2: Types of vaccine (2)

Vaccines of the First Generation

Conventional inactivated and modified-live (MLV) vaccines, sometimes referred to as first-generation immunizations, offer benefits to both humans and animals in terms of protection against pathogenic germs. IVs are typically used to induce humoral immune responses, are safe and affordable to produce, and mostly transport antigens via the MHC-II pathway. This drawback might allow illnesses that require a strong cell-mediated response to elude the pressures of vaccination (1).

Because MLVs may multiply within the host and elicit protective immunity against their specific pathogens, they can sidestep this issue. By mimicking a typical infection, these viruses trigger the MHC-I and MHC-II pathways. On the other hand, MLVs pose little harm to animals since, very infrequently, attenuated strains regain their virulence and spread illness. Moreover, MLVs should not be administered to those with severely impaired health because of the risk of infection.

Vaccines of the Second Generation

Subunit elements and conjugated/recombinant antigens are examples of second-generation vaccinations. Recombinant subunit vaccines, as opposed to live or inactivated viruses, generate antigens by the overexpression and purification of the antibody. Subunit vaccines typically lack the pathogen-associated molecular patterns (PAMPs) that the immune system utilizes to identify infections via pattern recognition receptors (PRR) (Fig. 3). As a result, for subunit vaccinations to boost the extent and quality of the immune response, adjuvants with co-stimulatory action are necessary (1).

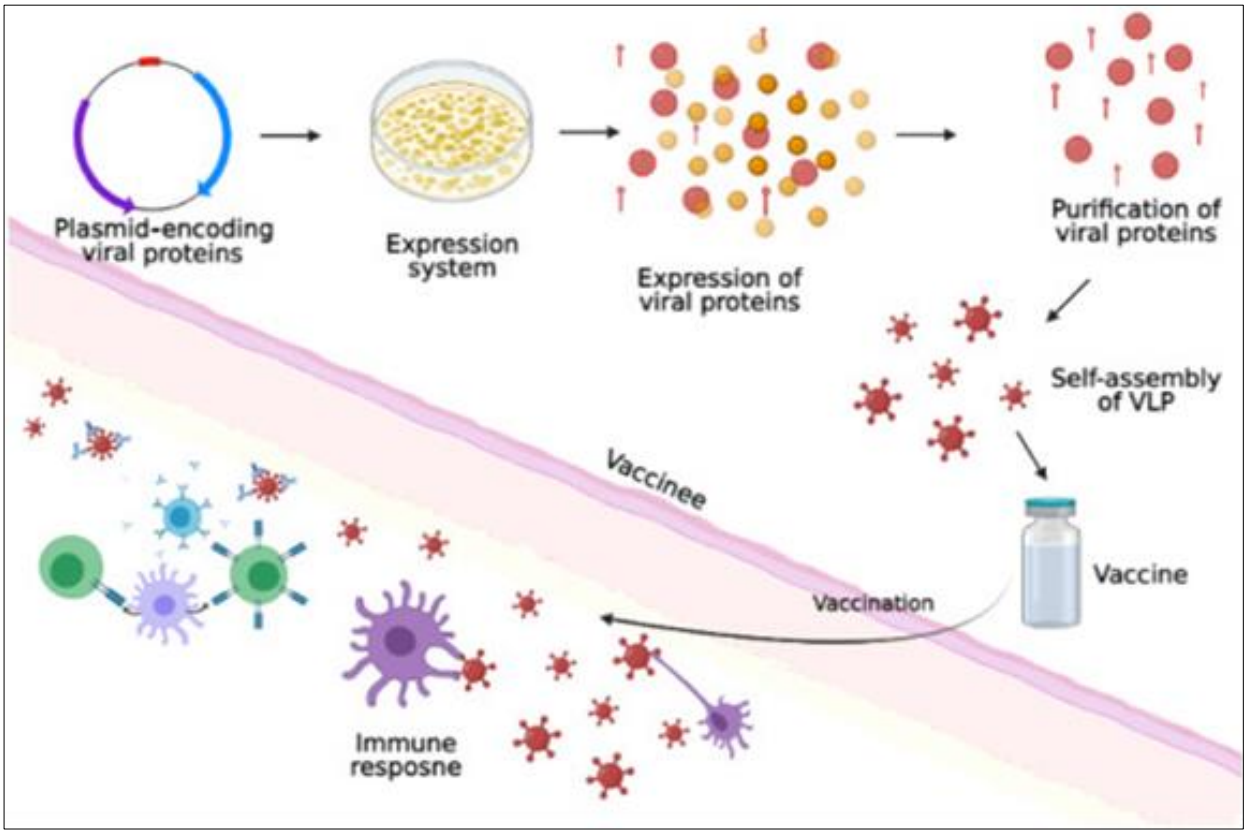

Fig 3: Mechanism of immune response by second-generation vaccine (1)

Vaccines of the Third Generation

Third-generation immunizations include live or inactivated chimeric vaccines, viral-vector platforms, and gene-based (DNA and RNA) vaccines. DNA and RNA-based vaccines are now in development. Injectable plasmid DNA is a radically novel approach to vaccination. Thanks to developments in molecular biology, we may now manipulate these polynucleotides to our advantage and replace conventional vaccination strategies.

DNA Vaccine

A DNA vaccination works by transfecting an organism's cells with a particular antigen-coding DNA sequence to trigger an immune response. DNA vaccines function by infusing genetically modified plasmids that carry the DNA sequences encoding the antigen(s) that the immune system is trying to defend against. This causes the cells to generate the antigen themselves, which triggers a defensive immune response. According to theory, DNA vaccines are superior to regular vaccinations in that they may "induce a wider range of types of immune response."

The DNA vaccine's background

To create recombinant DNA vaccines, Enzo Paoletti and Dennis Panicali of the New York Department of Health used genetic engineering in 1983 to transform standard smallpox vaccinations into vaccines that could prevent other illnesses. They added a gene from another virus (the herpes simplex virus, hepatitis B, and influenza) to the cowpox virus, changing its DNA. Jeffrey Ulmer and associates at Merck Research Laboratories discovered in 1993 that injecting mice directly with plasmid DNA encoding a flu antigen protected the animals from a subsequent influenza virus trial. In 2016, the National Institutes of Health started working on a human Zika virus DNA vaccine.

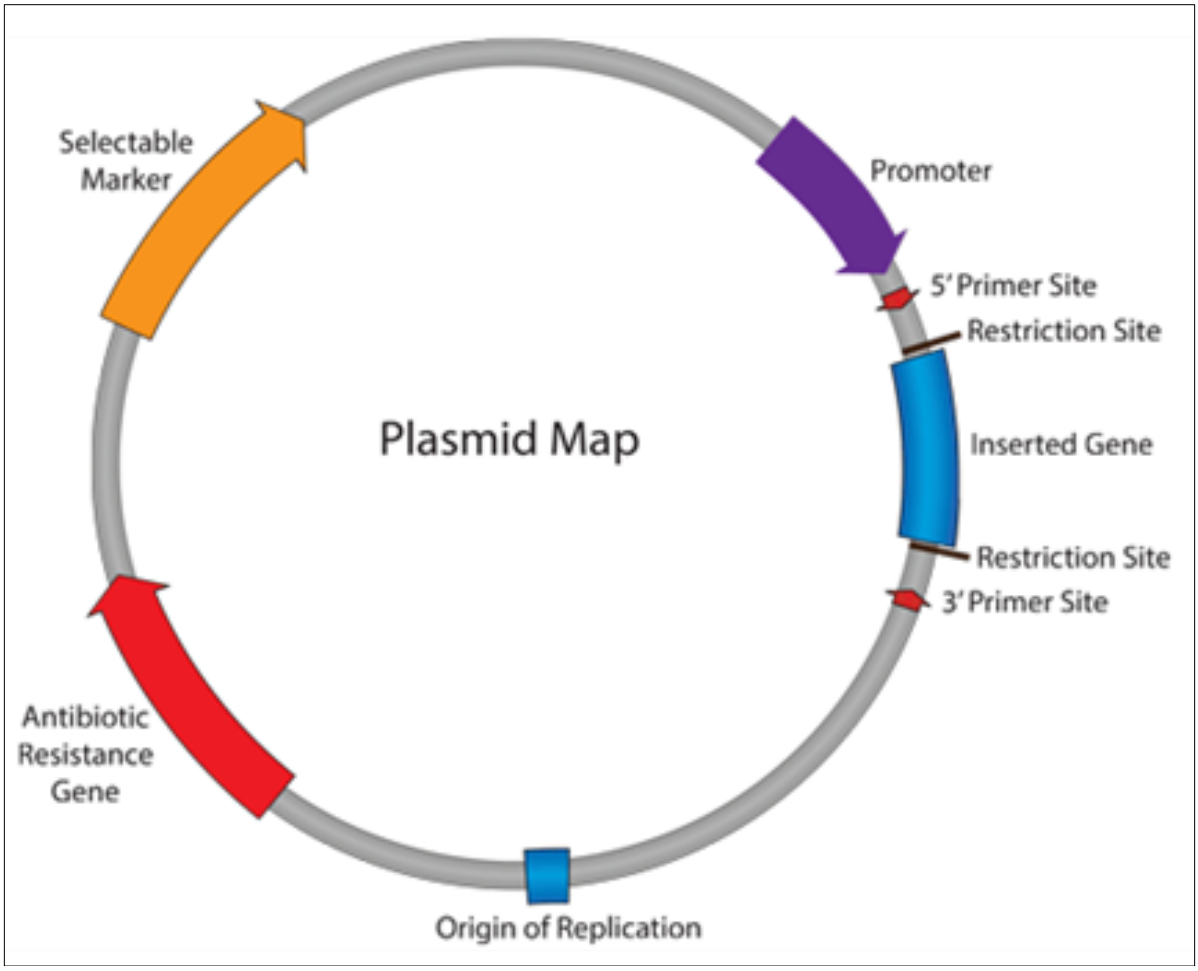

Fig 4: Plasmid vector used (3)

DNA Vaccine Plasmid Vectors

Circular deoxyribonucleic acid (DNA) vectors called plasmids can be utilized as vaccinations to stop a variety of illnesses. These plasmids are DNA platforms that are often made up of a gene coding for antibiotic resistance, a gene originating from the bacterial replication origin, a multiple cloning site (MCS) for a transgenic area, and a gene or several antigenic interest genes. To maximize the expression and development of a protective immune response, antigenic gene design is essential. To prevent the translation process inhibition of antigenic proteins, this design often includes codon optimization to decrease the occurrence of unusual codons and to reduce the creation of secondary structures in the mRNA sequences. Additionally, by including a Kozak consensus sequence that eukaryotic ribosomes use to recognize mRNA, the production of antigens in transfected eukaryotic cells may be maximized (Fig. 4).

Mechanism of plasmid

The plasmid codes for a foreign antigen peptide string after it has entered the transfected cell nucleus. The cell presents the foreign antigen with both class I and class II molecules of the major histocompatibility complex (MHC) on its surface. The immune response is then triggered when the antigen-presenting cell goes to the lymph nodes and provides the antigen peptide and costimulatory molecule signalling to the T-cell (4).

Mechanism of action of DNA vaccines

Professional APCs like macrophages and dendritic cells are either directly transfected or receive secreted antigens from transfected somatic cells. Major Histocompatibility Complex (MHC) Class II molecules are used by them to digest and transport antigenic peptides to helper T cells. These molecules then trigger the release of several cytokines that promote immune system activation. Degraded antigenic peptides combined with MHC Class I molecules stimulate cytotoxic T lymphocytes. The cellular immune responses are developed by these two routes. Antigens that are extracellularly present or produced as antigens in humoral or antibody responses are recognized and reacted to by B cells (Fig. 5).

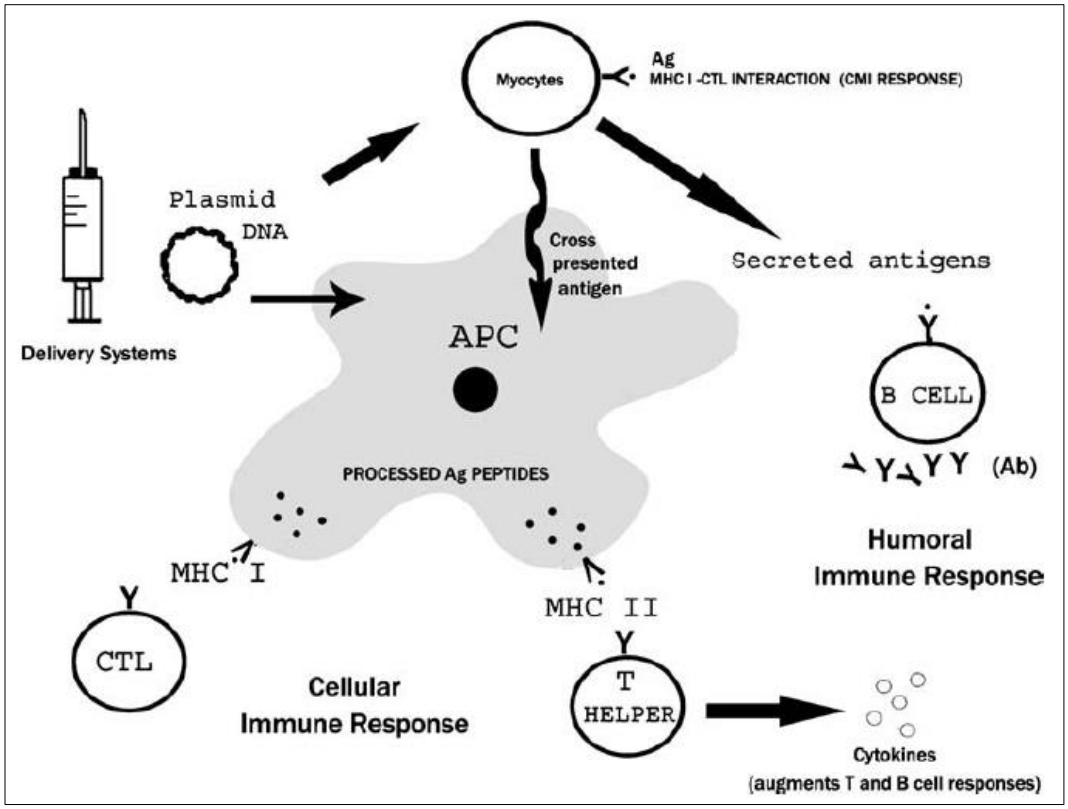

Fig 5: Mechanism of action of DNA vaccines (5)

Delivery System

Recombinant plasmids are inserted into bacteria once they have been created and developed. Numerous techniques have been used to deliver DNA vaccines into animal tissues. The two most widely used methods were either employing a gene gun delivery system or injecting DNA in saline using a regular hypodermic needle (Table 1).

Amphiphilic lipid vectors called Cationic Cholesteryl Cytofectins (CCCs) are presently being developed for gene transfer purposes. The majority of the time, CCCs are combined with a neutral co-lipid to create unilamellar cationic liposomes. These liposomes then form electrostatic complexes with DNA and RNA via charge-charge interactions between the anionic phosphodiester backbone of the nucleic acids and the cationic head groups of the CCCs (Fig. 6).

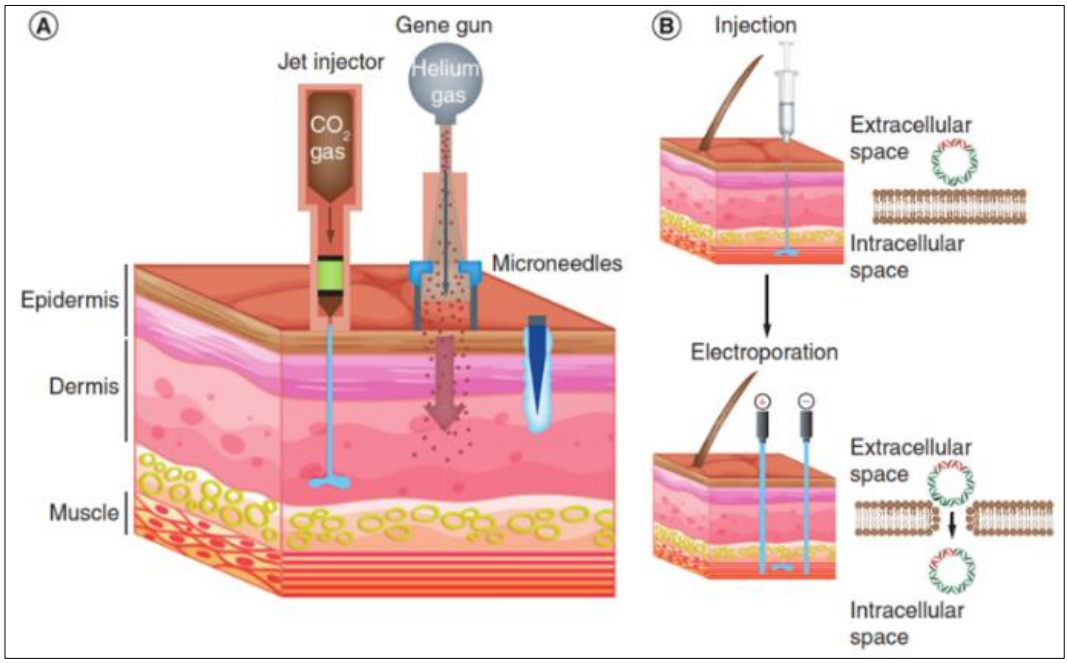

Fig 6: (A): Using a gene gun, jet injector, and microneedles, DNA vaccines are delivered into skin compartments. Because these physical approaches are safer and more effective than traditional needle procedures, DNA vaccines can be delivered into the dermis, epidermis, and subcutaneous compartments. (B): The cellular absorption of injected DNA across the cell membrane is improved by the use of *in vivo* electroporation. (6)

Table 1: Different Delivery Systems for DNA Vaccines

Method of delivery		Formulation of DNA	Target tissue	Amount of DNA
Parenteral	Injection (hypodermic needle)	Aqueous solution in saline	IM (skeletal); ID; (IV, subcutaneous and intraperitoneal with variable success)	Large amounts (approximately 100-200 μg)
	Gene gun	DNA-coated gold beads	ED (abdominal skin); vaginal mucosa; surgically exposed muscle and other organs	Small amounts (as little as 16 ng)
	Pneumatic (jet) injection	Aqueous solution	ED	Very high (as much as 300 μg)
Topical application	Aqueous solution	Ocular; intravaginal	Small amounts (up to 100 μg)	Topical application
Cytofectin-mediated	Liposomes (cationic); microspheres; recombinant adenovirus vectors; attenuated Shigella vector; aerosolised cationic lipid formulations	IM; IV (to transfect tissues systemically); intraperitoneal; oral immunization to the intestinal mucosa; nasal/lung mucosal membranes	Variable	Cytofectin-mediated

Recombinant DNA vaccine design as a potential strategy against bovine foot and mouth disease virus (FMDV)

The Foot and Mouth Disease Virus (FMDV), a species of the genus Aphthovirus of the family Picornaviridae, is the cause of Foot and Mouth Disease (FMD). Positive-sense, non-enveloped, single-stranded ribonucleic acid ((+) ssRNA) is what picornaviruses are. The formation of a promoter (60 copies) and the arrangement of the capsomere (pentamer) structure (12 copies) that will make up the procapsid surrounding the naked genomic RNA are the first steps in the formation of the FMDV procapsid. These four protein monomers are VP1, VP2, VP3, and VP4 facing internally (Fig. 7). The current FMD vaccine consists of synthetic, dead, or inactivated proteins that only provide temporary immunity and need to be repeated along with adjuvants and booster shots. A lack of cross-protection against various strains, the requirement for cold storage, and the possibility of reinfection in cattle that had previously received protection owing to short-term immunity are some of the other issues with this vaccination platform. A possible multi-epitope DNA-based vaccination is being developed as a non-pathogenic, affordable substitute for FMD protection to address these issues (7).

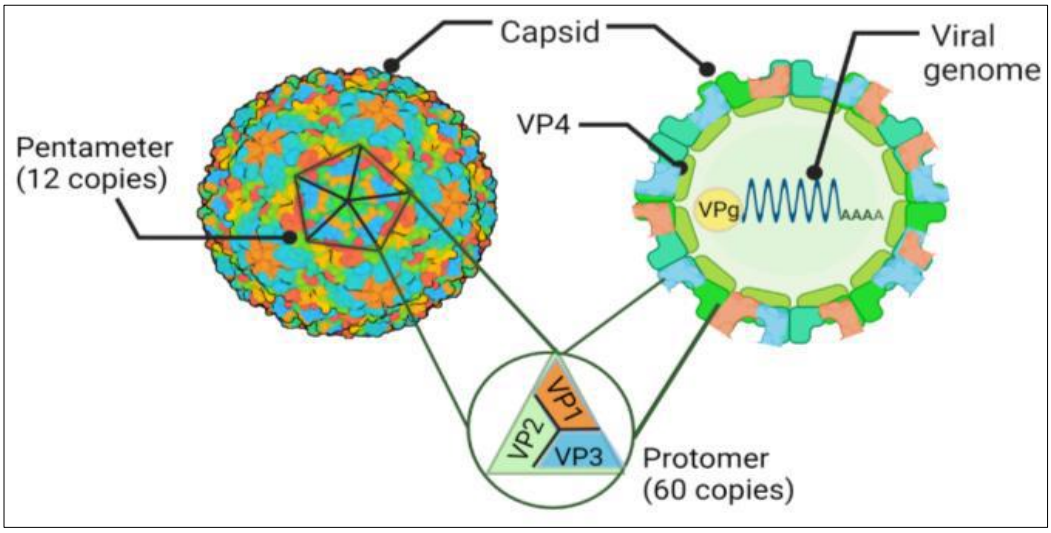

Fig 7: Schematic representation for the biological assembly of wild type of FMDV-O (7)

West Nile Virus

Major concerns about the health of people and animals were raised in 1999 when the West Nile (WN) virus was introduced to the US. A flavivirus illness known as WN fever is largely spread to vertebrates by different types of Culex mosquitoes. WNV is a positive-stranded RNA virus that is enclosed.

The WN virus remains alive by a natural cycle involving birds and arthropod vectors. In 1937, the virus was initially discovered in a feverish person in Uganda's West Nile province. The single open reading frame of the RNA makes up its estimated 11 kbp size. It has noncoding sections, commonly referred to as untranslated regions (UTRs), at the 3' and 5' ends that help with transcription, translation, packaging, and replication instead of a polyadenylated tail in the 3' end.

pCBWN was created by inserting the WN virus cDNA, which encoded the sequence between the prM and E genes, into the pCBJESS vector. This stable transformed cell line also generated recombinant antigens in the form of EPs, which induced strong anti-JE virus Nt antibody responses. The WN virus's prM and E genes were measured by transfecting COS-1 cells with the plasmid PCB. A fibroblast-like cell known as COS-1 was identified from an African green monkey's kidney (Fig.8).

The transcription unit is home to the bovine growth hormone poly(A) signal (BGH), WN virus prM and E gene area, JE virus signal sequence, and human cytomegalovirus early gene promoter (CMV).

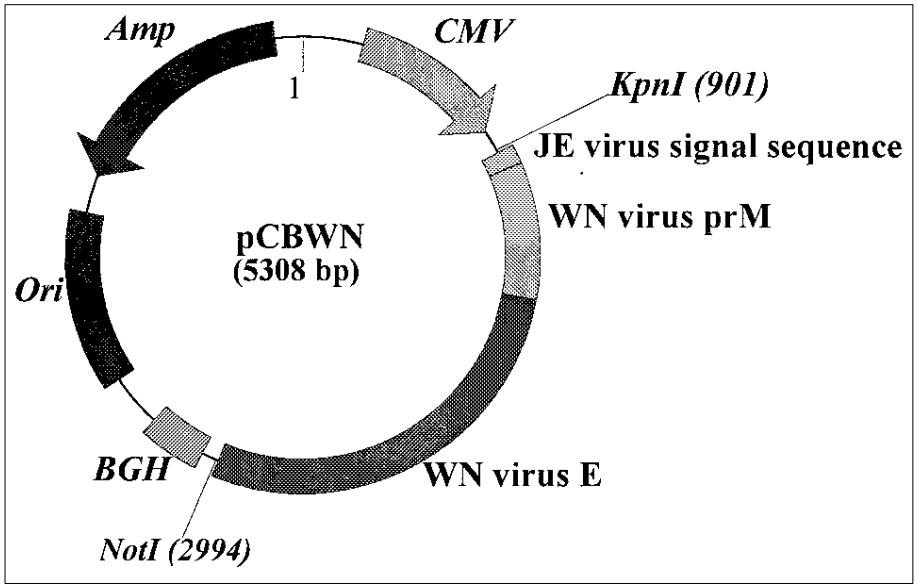

Fig 8: Map of the recombinant WN virus plasmid pCBWN (8)

Commercially available dna vaccines

Table 2: Commercially Available DNA Vaccines

Animal host	Disease	Etiological agent	Protective Ag gene	References
Cattle	Brucellosis	*B. abortus*	L7/L12; SOD	(9); (10)
	Tuberculosis	*M. bovis*	MPB83; Ag85B	(11,12)
	Mastitis	*S. aureus*	FnBP; ClfA	(13)
	Bovine leukemia	Retrovirus	gp51; gp30	(14)
	Infectious bovine rhinotracheitis	Bovine herpes virus	gC; gD	(15); (16)
	Bovine viral diarrhoea	Pestivirus	E2	(17)
	Foot and mouth disease	Foot and mouth Disease virus (Picornavirus)	VP1	(5)
Poultry	Colibacillosis	*E. coli*	K88	(18)
	Chlamydiosis	*C. psittaci*	MOMP	(19)
	Avian influenza	Influenza virus	HA	(20)
	Newcastle disease	Avian paramyxovirus	HN; F	(21)
	Infectious bronchitis	Coronavirus	N; S1	(22)
	Infectious bursal disease	Avibirnavirus	VP2	(23)
	Chicken infectious anemia	Gyrovirus	VP1 and VP2	(24)
	Coccidiosis	*E. tenella*, *E. acervulina*	3-1E; EtMIC2	(25)
Caprines	Johne's Disease	*M. avium paratuberculosis*	HSP-65	(26)
	Brucellosis	*B. melitensis*	OMP-31	(5)
	Cryptosporidiosis	*C. parvum*	15 kDa	(27)
	Schistosomiasis	*S. japonicum*	Sj28GST; Sj23	(28)
Equine	Broncho-pneumonia	*Rhodococcus equi*	VapA	(29)
	Equine influenza	Influenza virus	HA	(30)
	Equine herpes infection	Herpes virus	gB; gC; gD	(31)
	West Nile fever	West Nile virus	PrM; E	(32)
Ovines	Anthrax	*B. anthracis*	PA83	(14)
Canines	Leptospirosis	*L. canicola*	flaB2	(33)
	Parvoviral infections	Parvovirus	VP1; VP2	(34,35)
	Rabies	Rhabdovirus	gp gene	(36)
	Canine distemper	Morbilivirus	HA; F	(30)
	Babesiosis	*B. gibsoni*	p50	(37)
	Anaplasmosis	A. marginale	MSP1b	(38)
	Bovine respiratory syncytial disease	Bovine respiratory syncytial virus	BRSV F; N	(39)

[Major outer membrane protein (MOMP), haemagglutinin (HN) gene, Mycobacterium bovis protein MPB-83; clumping factor A (ClfA) or fibronectin-binding protein (FnBP) genes; major surface protein, MSP1b, (Protective antigen (PA83); heat shock protein antigen (HSP-65); outer membrane proteins (OMP); 15 kDa sporozoite surface protein; Schistosoma japonicum genes (Sj28GST and Sj23); virulence-associated protein (VapA)]

DNA Vaccines against Johne's Disease:

- Vector: Four rAgs (85A, 85B, 85C and superoxide dismutase) with two adjuvants (monophosphoryl lipid A and bovine IL-12)

- Dosage: 100 µg of each antigen and 100 µg of IL-12 IM.
- Vaccination age: 5-10 days
- Immunity: Antibodies within 3 weeks; significant IFN-gamma production within 11 weeks CD8+ T cells against all four rAgs; rAg-specific expression of IL-2, IL-12 and TNF-α. (40)

DNA vaccine for the treatment of Canine Oral melanoma

- Dosage: Administered after surgical excision of tumour Four 0.4 ml doses administered transdermally biweekly.
- Booster dose every 6 months thereafter.

Attractiveness of DNA-Based Vaccines

One desirable feature of any vaccine is the ability to protect individuals against a variety of disease agents following a single administration of a vaccine. Combining the four serotypes resulted in higher antibody levels against dengue-4 than if animals were immunized with a monovalent dengue-4 plasmid-based vaccine. Additionally, by combining plasmids encoding various genes of interest, it is also possible to introduce two distinct genes encoding various proteins from either the same or various pathogens in a single plasmid, further lowering the cost of production since one vaccine would protect against various agents.

Neonatal Immunization

Neonatal vaccinations are typically less effective than adult vaccinations. This is due to a variety of factors. When it comes to live vaccines, the level of replication is typically constrained by maternally derived antibodies, which leads to poor immune responses due to the fact there is less antigenic material created *in vivo*. It has been demonstrated that immunity can be produced using DNA vaccines both in utero and in neonates, proving that immunity may even be induced during pregnancy. So, lambs that received their third-trimester in-utero vaccinations were born with complete immunity. Furthermore, the animals acquired long-term memory.

RNA Vaccines

RNA vaccines work by introducing an mRNA sequence (the molecule that instructs cells what to create) that codes for a disease-specific antigen. Once the antigen is formed in the body, the immune system recognizes the antigen, preparing it to fight the actual infection.

Recombinant viral vectored vaccines

For infectious diseases, vaccination and establishment of herd immunity are of primary importance. Among all vaccine technologies, recombinant viral vectors represent promising vaccine platforms due to their ability to express heterologous antigens and induction of cellular immune responses and humoral immune responses without exogenous adjuvants. Viral vector vaccines consist of viral particles whose genomes have been modified to contain one or more foreign genes encoding the targeted antigens. The rationale for using viruses to deliver the 'vaccine gene' is in several folds. Viral vector vaccines are safe and induce both arms of innate and adaptive immune responses without the involvement of the completely hazardous pathogen (41).

Additionally, due to the production of several pathogen-associated molecular patterns (PAMPs) and the activation of innate immunity, viral vectors have inherent adjuvant capabilities. Furthermore, antigens can be delivered to certain cells or tissues using viral vectors that have been designed. To improve their safety and lessen reactogenicity, they might be made replication-competent or replication-deficient. Notably, the viral vector vaccine may mimic the pathogen's actual infection process to transport the vaccine to the mucosa and induce local, mucosal, and systemic immunity. This results in classical acute inflammation and immunological detection through the creation of PAMPs in the body naturally (42).

Recombinant viral vector vaccines are novel technologies in veterinary medicine that utilize viruses as tools for vaccinology. These vaccines are created genetically by inserting DNA encoding important antigens into a viral vector. The safety profile is comparable to that of inactivated (killed) subunit vaccinations, which also 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 responses to different animal diseases, such as canary pox and fowl pox backbones. Adenovirus vectors have been studied as vaccinations against tumour-associated antigens and as systems of therapy for a variety of illnesses.

Oncolytic viruses (OVs) are suitable in the field of malignancies since they may induce cellular immunity and can be armed, shielded and target tumour cells. The release of tumour-associated proteins TAAs has the potential to activate and control anti-tumor immunity. The immune system reacts. Several OV preparations have been approved for marketing, which shows promising immunotherapy directions for tumours (Table 2).

The viral vectored vaccines are of two types:

a) Non-replicated viral Vector: Contains viral genetic material packaged inside another harmless virus that cannot copy itself.
b) Replicating Viral Vector: Contains viral genetic material packaged inside another harmless virus that can copy itself Whole Virus Vaccines.

Mechanism of viral vector vaccines

To deliver target genes without causing illness, viral vectors are changed by deleting the virulence gene while keeping the ability to enter cells. This mechanism resembles the spread of viral infections. Many viruses, including the adenovirus, influenza virus, measles virus, and cowpox virus, have been created as vectors. These viral vectors lack disease-causing genes, and some of them have even had the genes necessary for replication deleted. For instance, in the ChAdOx1 nCoV-19 vaccination, the modified chimpanzee adenovirus ChAdOx1 transports the SARS-CoV-2 spike protein gene into the nucleus, where DNA polymerase transcribes it into mRNA. After that, mRNA exits the nucleus and moves into the cell plasma where it attaches to ribosomes to form the antigen proteins that are subsequently released. This is followed by the presentation of the antigen, which prompts the body to launch an immune response (43) (Fig. 9).

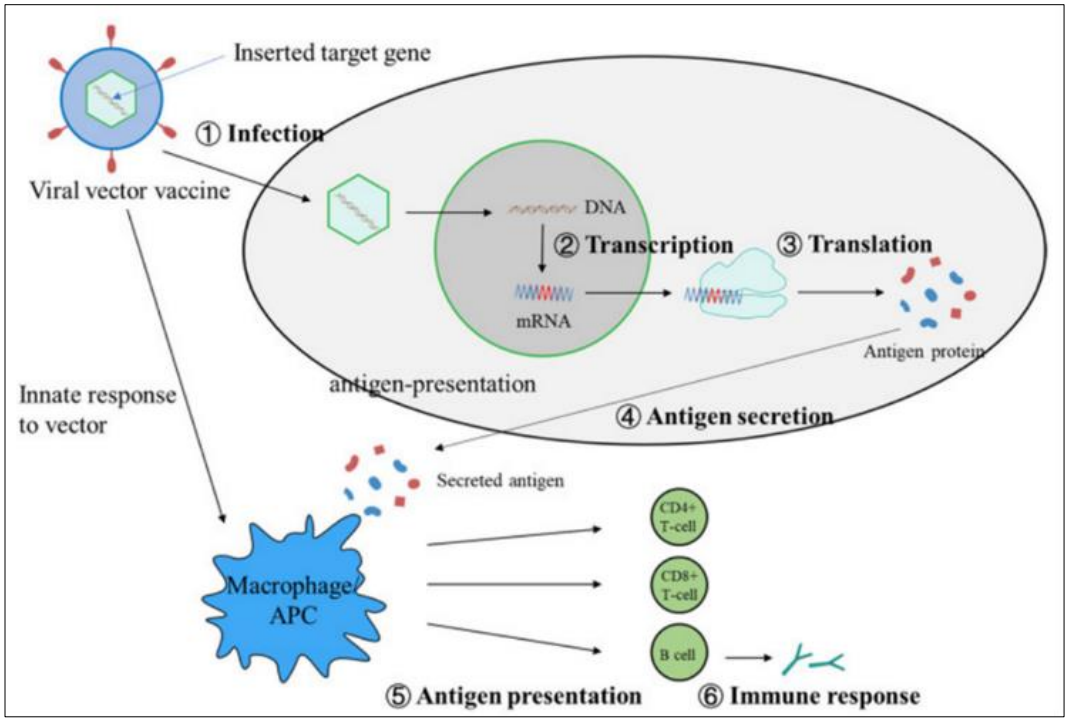

Fig 9: Mechanism of viral vector vaccines (43)

Table 3: Properties of Virus used as Vector (44)

Vector	Genome size (kb)	Genome type	Cargo capacity (kb)	Admini. route	Strengths	Weaknesses
Vesicular stomatitis virus	~11	Single-stranded, negative-sense, non-segmented	~6	IM. IN, or OR	small and easily manipulated genome; rapid replication	Safety concerns
Rabies virus	~12	Single-stranded, negative-sense, non-segmented	~6.5	IM or OR	Small and easily manipulated genome; designed as inactivated bivalent vaccines	A potential risk for reversion to virulence
Parainfluenza virus	~15	Single-stranded negative-sense, non-segmented	~4	IM, IN, or OR	Ideal for paediatric and respiratory diseases	Anti-vector immunity; Safety concerns
Measles virus	~16	Single-stranded negative-sense, nonsegmented	~6	IM IP or SC	effective and safe: lack of genomic integration in the host;	Limited challenge models: low viral titers
Newcastle disease virus	~15	Single-stranded negative-sense, nonsegmented	~4	IM, IN	High growth titers; lack of genomic integration in the host; host restriction; no pre-existing antibody to NDV in the human	Less immunogenic
Lentivirus	~9.2	Single-stranded positive-sense, nonsegmented	~4	IM, IN	Low anti-vector immunity; less integration into the host genome;	Safety concerns; potential batch-to-batch variation in manufacturing
Influenza virus	~13.5	Single-stranded negative-sense, segmented	<1.5	IM, IN	A broad host range; easily manipulated genome; highly attenuated	Limited transgene ability; genetic reassortment safety concerns
Adeno virus	26-45	Double-stranded nonsegmented	~7.5	IM, IN, or OR	Well-established; high titer of production	Anti-vector immunity
Poxvirus	130-300	Double-stranded non-segmented	~25	IM	Packing flexibility of the genome; without genomic integration in the host; expressing VLPs	Existence of the viral immunomodulatory genes
Influenza virus	~13.5	Single-stranded negative-sense, segmented	<1.5	IM, IN	A broad host range; easily manipulated genome	Limited transgene ability; genetic reassortment safety concerns

Table 4: Commercially Available Recombinant Viral Vector Vaccines(44)

Species	Vaccine	Manufacturer	Pathogen	Technology (viral vector)
Avian	Trovac® -AIV H5	Boehringer Ingelheim	Avian Influenza	Viral-vector (fowlpox)
	Vectormune® AI	CEVA Biomune	Avian Influenza	Chimeric Viral-vector (HVT/MD)
	Vectormune® ND		Newcastle Disease	Chimeric Viral-vector (HVT/MD)
	Vectormune® FP LT		Infectious Laryngotracheitis virus	Chimeric Viral-vector (fowlpox)
	Vectormune® FP MG		Mycoplasma Gallisepticum	Chimeric Viral-vector (fowlpox)
	Vectormune® FP-N		Newcastle Disease	Chimeric Viral-vector (fowlpox)
	Innovax® -ND	Merck Animal Health	Newcastle Disease	Chimeric Viral-vector (HVT/MD)
	Innovax® -ND-IBD		Newcastle disease and Infectious bursal disease	Chimeric Viral-vector (HVT/MD)
	Innovax® -ND-ILT		Newcastle disease and infectious laryngotracheitis	Chimeric Viral-vector (HVT/MD)
Wildlife	ORNAB®	Artemis Technologies	Rabies	Viral vector (human adenovirus type 5)
	Raboral V-RG®	Boehringer Ingelheim	Rabies	Viral-vector (vaccinia virus)
Canine	Recombitek® CDV	Boehringer Ingelheim	Canine Distemper Virus	Viral-Vector (canarypox)
Feline	PureVAX® Recombinant FeLV		Feline Leukemia Virus	Viral-Vector (canarypox)
	PureVAX® Feline Rabies		Rabies	Viral-Vector (canarypox)
Equine	ProteqFlu		Equine Influenza	Viral-Vector (canarypox)
Swine	ALVAC® -WNV FosteraTM PCV	Zoetis	West Nile Virus Porcine Circovirus Type 2	Viral-Vector (canarypox) Chimeric Viral-vector (PCV-1)
	Suvaxyn® CSF Marker		Classical Swine Fever virus	Chimeric viral vector (BVDV)
	iPED+	Merck Animal Health	Porcine Endemic Diarrhea virus	RNA Replicon (VEEV)
	Sequivity®		Swine influenza A virus	RNA Replicon (VEEV)
Rabbits	Novibac® Myxo-RHD		Rabbit Hemorrhagic Disease	Chimeric Viral-vector (myxoma virus)
Bovine	Adt.A24 FMD	GenVec	Foot and Mouth Disease	Viral vector (adenovirus)
Caprine	*Poxvirus* vectored vaccines	–	Peste des petits ruminants	Viral-vector(Poxvirus)
	Adenovirus vectored vaccine			Viral vector (adenovirus)

Conclusions

Inactivated and live-attenuated vaccines have improved livestock productivity, and food security, and reduced disease morbidity. However, inactivated vaccines may be suboptimal for specific pathogens, and safety concerns arise with live-attenuated vaccines. As infectious diseases increase, new vaccines are needed to combat these issues.

Veterinarian medicine has developed novel vaccines, including DNA, RNA, and recombinant viral-vector vaccines, which induce humoral and cellular immune responses, are economically manufactured, safe, and differentiate infected animals.

Viral vector vaccines have made significant progress in clinical trials, of COVID-19 vaccines. Advances in viral vector vaccines require an improved understanding of viral biology and understanding the reciprocal interactions between viruses and the host immune system. Interdisciplinary cooperation, structural biology, artificial intelligence, and gene editing can provide additional support.

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