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Analysis of types of common veterinary vaccines and influencing factors of immunogenicity

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Abstract. This article provides an in-depth analysis of the types and immunogenicity factors affecting common veterinary vaccines. First, we introduced the common types of veterinary vaccines, including nucleic acid vaccine, attenuated vaccine and conjugated vaccine, and described their immunogenicity characteristics. Then, factors affecting the immunogenicity of veterinary vaccines were explored, including vaccine dose, vaccination route, and vaccination time. Finally, the current research progress on the factors affecting the immunogenicity of veterinary vaccines is summarized, and future research directions are discussed. This study provides important reference for further optimizing the design and immune effect of veterinary vaccines.

Keywords: Veterinary Vaccines, Immunogenicity, Animal Breeding.

1. Introduction

Veterinary vaccines are a type of biological product that can prevent and control the spread of various infectious diseases. They are affected by many factors during the production, transportation, and use of vaccines. Especially in the transportation and use of vaccines, any improper behavior at any stage can affect the activity and expected immune effect of the vaccine, and in severe cases, it can also endanger the quality and safety of the entire aquaculture industry and animal products. In recent years, with the continuous development of China's animal husbandry industry towards intensification and scale, vaccination is the most effective and economical means to prevent the spread of various diseases. To ensure the effectiveness of vaccine immunization, it is necessary to effectively manage the preservation and use of vaccines.

Animal vaccines have experienced four significant transformations throughout history. In 1796, Jenner conducted the pioneering human experiment that successfully prevented smallpox, resulting in the creation of the world's first vaccine. The late 19th century marked the beginning of a golden age in microbiology, led by Pasteur, who developed attenuated vaccines for anthrax, cholera, and rabies. This breakthrough marked the advent of the initial vaccine revolution. Subsequently, in the mid-20th century, vaccines were produced through the isolation and extraction of immunogenic protein components from pathogens. Notable examples include diphtheria toxoid and tetanus toxoid vaccines. Additionally, the chemical extraction and purification of bacterial surface membrane polysaccharides resulted in the production of polysaccharide-protein conjugate vaccines. Notable examples employing this method

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include the group A meningococcal vaccine, the 23-valent polysaccharide vaccine for pneumonia, and the Hib vaccine. Since the 1970s, advancements in molecular biology have enabled the manipulation of microorganism genes at the molecular level. This breakthrough led to the invention of recombinant vaccine technology, which yielded vaccines such as those for hepatitis B and influenza. In the 21st century, with the progression of genomics, humans embraced genome-based vaccine development strategies, referred to as reverse vaccinology. The utilization of this approach resulted in the development of vaccines such as the 5-valent rotavirus vaccine and live influenza vaccine, marking the fourth vaccine revolution.

2. Types of common veterinary vaccines

2.1. Nucleic acid vaccine

Nucleic acid vaccine, also known as DNA vaccine and Genetic Vaccine. It refers to the application of genetic engineering technology to recombine the exogenous gene encoding a certain antigen protein with the eukaryotic expression vector and directly introduce it into the body [1], and use the antigen protein expressed by the immunogen gene in the host to cause the immune response of the body, so as to achieve the purpose of preventing and treating diseases.

DNA vaccines possess several advantages. Firstly, there is no risk of infection associated with DNA vaccines. Additionally, both MHC class I and class II molecules are involved in presenting antigens, ensuring a more comprehensive immune response. Unlike traditional vaccines, DNA vaccines do not require peptide synthesis, expression, and purification of recombinant proteins, or the use of toxic adjuvants [2]. Moreover, the in vivo expression of DNA vaccines ensures that the protein closely resembles the normal eukaryotic structure and undergoes post-translational modifications.

Despite these advantages, DNA vaccines have not yet gained widespread application and safety remains a major concern. Several issues are associated with DNA vaccines. Firstly, it is uncertain whether exogenous DNA integrates into the host genome after administration, potentially activating cancer genes or deactivating tumor suppressor genes [3]. Secondly, long-term expression of vaccine DNA may lead to immune tolerance in the body, resulting in a decline in overall immune function. Furthermore, it is unclear if vaccine DNA triggers the production of anti-DNA antibodies as a foreign substance. Lastly, there is a question of whether the cytotoxic T lymphocyte (CTL) response induced by DNA vaccines might have detrimental effects on other cells.

2.2. Attenuated vaccine

An attenuated vaccine, also known as a live attenuated vaccine or LAV, is produced by reducing the virulence of pathogens while maintaining their vitality. This process involves modifying infectious agents to render them harmless or less toxic [4]. In contrast to inactivated vaccines, which are produced by killing viruses, attenuated vaccines are capable of eliciting strong and long-lasting immune responses.

Attenuated vaccines prompt the body to produce antibodies and memory immune cells that specifically target the pathogens addressed by the vaccines. They have been effective in generating robust and durable immune responses at a faster rate compared to inactivated vaccines. Examples of live attenuated vaccines include those for measles, mumps, rubella, and certain strains of influenza.

The process of vaccine action mainly involves stimulating immune system-related cells and antibodies, and the biochemical reactions generated by attenuated vaccines increase vaccine effectiveness [5].

An attenuated vaccine is essentially a "weakened" version of a pathogen, be it a virus or bacterium. It is modified to ensure that it does not cause harm or illness, yet still activates the immune system. This type of vaccine operates by triggering both the cellular and humoral immune responses of the adaptive immune system [6].

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2.3. Conjugated vaccine

Conjugate vaccines, a type of subunit vaccine, combine a weak antigen with a potent carrier antigen to enhance the immune system's response to the weak antigen. Traditional vaccines elicit an immune response by targeting antigens, leading to the production of T cells and antibodies. B memory cells retain information about encountered antigens, allowing for antibody production upon subsequent exposure. For bacteria coated with polysaccharides, B-cell responses can occur independently of T-cell stimulation. By conjugating polysaccharides with protein carriers, it becomes possible to induce T-cell responses.

Polysaccharides alone cannot be presented on the major histocompatibility complex (MHC) of antigen-presenting cells (APC) due to the MHC's exclusive binding ability with peptides. However, when carrier peptides linked to polysaccharide target antigens are presented on MHC molecules, T cells can be activated. This innovation improves the effectiveness of vaccines as T cells stimulate more robust immune responses and facilitate faster and longer-lasting immune memory. Furthermore, combining polysaccharide target antigens with carrier proteins enhances vaccine efficiency, as non-conjugated vaccines targeting polysaccharide antigens are ineffective in children. The immune systems of children struggle to recognize antigens because the polysaccharide coating camouflages them. By merging bacterial polysaccharides with another antigen, the immune system can generate a response.

The goal of vaccines is to prevent diseases by stimulating immune responses against specific antigens—molecules from bacteria or viruses that trigger recognition by the immune system. This recognition is typically achieved through the use of attenuated or inactivated versions of pathogenic microorganisms in vaccines, enabling the immune system to identify the antigens later in life.

While most vaccines contain antigens that the human body can recognize, some pathogens have antigens that do not provoke a strong immune response. Vaccinating against these weak antigens may not provide adequate protection in the future. In such cases, conjugate vaccines are employed to enhance the immune system's response to these weak antigens. Conjugate vaccines involve chemically binding weak antigens to strong antigens, thereby inducing a more robust immune response to the weak antigen. The most common example of a weak antigen is a polysaccharide attached to a potent protein antigen. Additionally, peptide/protein and protein/protein conjugates have also been developed.

3. Interfering factors

3.1. Undemanding Immunization Procedure Specification

In the process of animal immunization, it is generally required that neonatal animals must have to do a supplementary immunization in 30 days after the initial immunization. But in many cases, animals are often immunized only once. The immunization procedure is not standardized to reinforcing the immunization, which will directly affect the immune effect.

3.2. Inadequate Vaccinating Dose

Foot-and-mouth disease (FMDA) is a highly contagious and acute febrile disease prevalent in the breeding industry. It primarily affects domestic animals, including pigs, cattle, and sheep, as well as various other domestic and wild cloven-hoofed animals. The disease has the potential to impact over 70 different species of susceptible animals. The clinical feature is that blister-like rash occurs in the oral mucosa, hoof and breast skin. The vaccine for preventing FMDA is produced by inactivating the virus grown in the kidney cells of young hamsters. The current problem with this vaccine is its lack of stability [7]. The disease is more common in pigs, and pigs with mild disease show fever, loss of appetite, and even death in severe cases. Therefore, in the epidemic prevention work, the epidemic prevention personnel are afraid that the pigs will have adverse immune reactions, leading to economic disputes with the farms, so they often take reduced injections in violation of regulations.

According to the standard injection dose for FMDA vaccine for domestic animals, it is generally injected with 1 ml for a 25-50 kg weight and 2 ml for a 50kg or more. However, according to the survey, in actual vaccination, the average injection dose for small pigs is 0.7-0.8 ml, and for large pigs is 1.5 ml.

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Sometimes even the amount of injections can be reduced by half, which results in inadequate immunity and antibody production for pigs.

3.3. Unreasonable Mixed-use of Multiple Vaccines

The vaccine produced by most veterinary biological products factories only conducted separate safety and efficacy tests on healthy animals to determine the immune effect. When multiple vaccines, especially live attenuated vaccines, are administered together, the immune response of the body may be affected, thereby reducing the effectiveness of the vaccine [8]. Additionally, the majority of viral live vaccines contain certain antibacterial agents, which will decrease the immune efficacy of the bacterial vaccine if administered simultaneously with the viral live vaccine.

3.4. The influence of Vaccine

The vaccine itself may have the following problems. First, the vaccine strains used for vaccine production have poor immunogenicity. Secondly, the vaccine may contain insufficient antigen or contain excessive heterologous proteins and endotoxins. Third, the inactivated vaccine seed bacteria are not thorough; The fourth is demulsification, delamination, discoloration, and mildew of oil adjuvant vaccines; Fifth, the freeze-dried vaccine did not form a vacuum state; The sixth is live avian vaccines contaminated by exogenous pathogenic microorganisms (especially mycoplasma) or produced from non-SPF chicken embryos [9].

Instability in vaccine quality is one of the main factors that cause unsatisfactory immune effects in animals. First of all, whether the vaccine manufacturer has national qualifications and whether the vaccine products produced by it have the national official batch number directly affect the product quality of the vaccine itself. Secondly, vaccines are generally sensitive to light and heat. If there is no special cold chain transportation vehicle during the transportation of vaccines, it is likely that the vaccine's actual shelf life will be shortened or even deteriorated due to substandard transportation and storage conditions, thus affecting the final immune effect. Finally, during the storage process of vaccines, if there is no suitable low temperature, light-proof and dry environment, the vaccine may also fail.

3.5. Impacts on breeding management

First of all, extreme temperatures, poor ventilation, high breeding density, sudden changes in diet, transportation or transfer of animals may cause stress reactions in animals, which may reduce their immune response ability and lead to unsatisfactory vaccination results [10]. Secondly, if animals have been given certain antibiotics or antiviral veterinary drugs before or after immunization, it may also lead to a decrease in the animal's immune system and affect the immune response. Finally, when animals live in a dirty, messy and poor environment for a long time, it can also lead to a decline in animal performance and affect the actual vaccination effect of the vaccine.

Breeders should do a good job in the epidemic prevention and health management of the farm, provide high-quality and full price feed for animals, and ensure the comfort of the temperature, humidity and air of the animal living environment. Scientific immunization procedures should be formulated according to the epidemic characteristics of animal epidemics in the area under their jurisdiction.

4. Summary

The advantages of animal vaccine compared with other treatments are as follows. First of all, vaccination can improve the ability of animals to resist diseases and avoid animal infection, which can also prevent zoonosis and protect human health. Second, the cost of vaccination is lower than the cost of re treatment after animal infection.

However, animal vaccines also have some disadvantages. First, a small number of animals will have allergic reactions after injection. In rare cases, some animals will suffer from sequelae, such as paralysis and excessive excitement.

To address concerns regarding potential allergies and adverse effects associated with animal vaccines, sponsors (which may include companies, research institutions, and other organizations responsible for

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drug development) are required to conduct comprehensive preclinical testing in laboratory animals. This testing encompasses a range of tests, procedures, medication administration, dosage determination, study duration, study objectives, and other critical details. All these aspects must be thoroughly studied and evaluated before the vaccines can be introduced into the market.

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