NEW ERA AGRICULTURE MAGAZINE

VACCINATION FAILURE IN POULTRY PRODUCTION

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Introduction:

Eggs and meat from poultry provide a variety of animal proteins. The rising demand for high-quality meat and eggs has led to an increase in the demand for chicken meat over time. Poultry birds are susceptible to a variety of diseases, which cause significant financial losses to poultry producers, particularly in developing nations like India. Poultry disease continues to be the greatest threat to the producers who suffer enormous financial losses as a result. Prior to disease entry, chickens must be immunized because of the high prevalence of poultry diseases, which impose significant constraints on the expansion of the poultry industry. At the international, national, and farm levels, various strategies can be used to effectively prevent and control the entry and spread of poultry diseases.

Vaccinations are frequently included in poultry disease control programs. Chickens are currently the farm animal that receives the most vaccinations, according to various research findings. During their production cycles, a broiler chicken may receive an average of eight different vaccines, whereas a layer chicken may receive approximately twelve different vaccines. Despite the widespread use of vaccines in poultry farms, vaccination cannot completely eliminate infectious poultry diseases.

A vaccination failure arises when birds fail to develop adequate antibody titer levels and/or are at a risk of field disease outbreak. According to various research outputs, insufficient antibody titer levels following vaccination that predispose the chickens to an outbreak of a field disease are the causes of vaccination failure. Other causes include,

1. Improper vaccine schedule (timing)
2. Improper handling of vaccine
3. Poor vaccine quality
4. Vaccine strain/serotype

In addition, management practices, immune suppression, maternal antibodies, stress, and vaccination failure in poultry flocks were previously recognized. Worldwide, vaccines play a significant role in disease

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control and prevention. This, in turn, has a significant impact on the reduction of outbreaks at the farm level and the expansion of poultry production. The effectiveness of various vaccines and vaccination schedules depends on a number of factors, including the method of production, biosecurity level, disease pattern, maternal immunity, vaccine availability, costs, and potential losses.

Inadequate vaccine transportation, handling, storage, and administration are the most common causes of high vaccination failure rates in poultry flocks in developing nations. As a result, the purpose of this paper is to shed light on vaccine failure in poultry and control measures.

Predisposing Factors for Vaccine Failure

Good vaccines and proper application are necessary for the successful application of vaccines and vaccination programs. In vaccinated poultry, there are a number of factors that can lead to immunization failure and each of these factors should be given equal weight. In fact, disregarding any of the following will compromise the vaccination's overall quality. Poor vaccine quality, antigenic differences between the current vaccine and circulating strains in the field, instability in the cold chain, inappropriate application, and a lack of skilled veterinary technicians to administer the vaccine are among these factors.

PROBLEMS RELATED TO THE VACCINE

Inactivation of vaccine:

The vaccine's efficacy is contingent on the virus and bacterial agents' viability as well as their ability to replicate in birds. As a result, improper administration of vaccines and improper handling of vaccines, which may result in a failure of the immune response in birds that appear to be healthy, can lead to vaccine failure. Vaccines keep their effectiveness for a certain amount of time. However, even if it is stored at the appropriate temperature, its viability may be compromised by being past its expiration date. Additionally, if the vaccine is combined with a variety of residual disinfectants on the needles and syringes, it may become inactive.

Antigenic Differences between Existing Vaccine and Field Strains:

Antigenic variation between the vaccine and field strains, such as antigenic drift and antigenic shift, is typically a problem with killed vaccines rather than modified live vaccines and results in a lack of vaccine efficacy. As a result, effective antibody-mediated immunity is established when antibodies precisely bind to the particular antigenic strain on the surface of a bacterium or virus. Cell-mediated immunity lacks strain-specific immunization, unlike antibody-mediated immunity. As a result, the circulating

field strain must be isolated and compared to the existing vaccine strain.

Inadequate Level of Protection:

The antigenicity of the viral strain determines whether or not the vaccine strain should elicit an adequate immune response. In poultry, eggs are the source of maternal antibodies or passive immunity, which last for two weeks. The majority of poultry vaccines have a peak response that typically lasts between two and six weeks. After that, the level of protection or immunity begins to gradually decrease.

Due to neutralization, the vaccine may not be able to elicit an immune response in birds vaccinated against virulent infectious agents during these periods of high maternal antibody protection. Despite the fact that birds are frequently immunized, they may become susceptible to a variety of poultry diseases before developing their own active immune responses. To increase protection, it is recommended to administer booster doses according to the schedule.

FACTORS ASSOCIATED WITH BIRDS

The host needs a few days to develop an effective immune response after a proper vaccination. If an infectious agent infects the birds before and during vaccination, the vaccine may not produce enough antibodies, leading to an apparent failure of vaccination.

Stress Factors:

Stress is a non-specific response to environmental change that overtaxes birds' capacity for physiological and behavioral adaptation. Birds typically lack the resources necessary to protect themselves from environmental changes and diseases. Pheasant birds experience stress as a result of various risk factors. This includes stress caused by inadequate ventilation, cold, heat, and humidity, transportation, a high stocking density (overcrowding), inadequate spacing, poor sanitation, an excessive amount of litter, under and malnourishment (nutritional deficiency), parasitism, fever, and other similar conditions.

Due to their extreme sensitivity to extreme weather, health-related issues, and other management issues, poultry birds experience a diminished immune response. As a result, chickens become generally unresponsive to vaccinations and are more likely to become infected during outbreaks of disease. In addition, if live vaccines are given to immunocompromised chickens, they may result in large outbreaks. Therefore, stress causes chickens to have lower levels of immunity, vaccines to fail, and economic losses as a result of low production.

Interference with Maternal Antibodies/ Immunity:

On the basis of their prevalence, poultry is routinely immunized against various infectious diseases, and newly hatched chicks are passively immunized thanks to maternal antibodies in their blood. During the first week of life, chickens may be protected from Newcastle disease virus and Gumboro (IBD) disease by maternal immunity, according to some research findings. However, it is possible for these maternal antibodies to react with the vaccine antigens to produce neutralizing antigens. As a result, live vaccines, which reduce the number of antibodies in newly hatched chickens during their first weeks of life, have an effect on the development of immunity production.

Immunosuppressive and Coexisting Diseases:

A bird flock's increased risk of infectious diseases like mycotoxicosis, infectious bursal diseases (Gumboro), infectious anemia, Marek's disease, and others are caused by immunosuppression, which results from a compromised immune response. An impaired immune response as a result of all of these stressors may also result in vaccine failure and compromise effective vaccination. This could lead to a lack of immunity to vaccination and an excessive reaction to the vaccine, which could cause illness and death. The immune system is anticipated to be vigorously stimulated by vaccines.

As a result, vaccine efficacy may be reduced when mild local and systemic diseases are present simultaneously. Because the vaccine antigens react with naturally occurring antibodies that are produced against infectious pathogens, vaccinating infected or stressed birds for the same disease will also reduce the vaccine's effectiveness. This causes birds to react to the vaccine, which can worsen the disease and increase mortality and morbidity rates. Consequently, it is essential and highly recommended to check the health of birds prior to vaccination.

Genetic Factor:

The response to the vaccine varies depending on the bird species. The structure of the major histocompatibility complex (MHC) is what determines how birds respond to bacterial and viral antigens, which in turn helps to determine individual variation. Due to the absence of some structure in MHC, which helps to recognize one of the antigens, birds may be more susceptible to pathogens.

FACTORS ASSOCIATED WITH THE ADMINISTRATION OF VACCINES

Lack of proper Storage and Vaccine Instability in Cold Chain:

Vaccines should be stored, transported, and administered in accordance with the manufacturer's instructions. Lack of storage equipment, inappropriate storage temperature, a lack of functional and effective refrigerators,

mixing vaccines with other food items, and vaccine interactions with disinfecting agents are the most common issues during vaccine storage that result in inactivation in developing nations. If you try to transport or store the vaccine without following the cold chain, proper handling, and preservation, it will result in a denatured antigen and a failed vaccine.

When the vaccine is exposed to direct sunlight, the antigens die, reducing the vaccine's antigen concentration and effectiveness. For improved effectiveness, the vaccine ought to be placed appropriately and kept out of direct sunlight. During clinical development and commercial distribution, vaccine instability presents the greatest challenge.

The development of physicochemical and biological assays to evaluate vaccine integrity and potency, stabilization strategies to protect vaccine antigens and adjuvants, as well as their interactions during storage and the complex and delicate nature of antigen structures (viruses, proteins, carbohydrates, protein-carbohydrate conjugates), are among the various sources and mechanisms of vaccine instability.

Inappropriate Route of administration:

Poultry vaccines can be administered through oral, subcutaneous, intramuscular, wing web, drinking water, eye dropping, and spray. A vaccine may not provide sufficient protection to poultry flocks if it is not administered via the recommended route of administration or the appropriate vaccination site. In addition, the instability of vaccines frequently occurs and is the primary obstacle during clinical development and commercial distribution.

Mass vaccination through drinking water and aerosol lacks uniformity in dosage between individual birds during administration, which results in a lack of effective immunity. The development of physicochemical and biological assays to evaluate vaccine integrity and potency, stabilization strategies to protect vaccine antigens and adjuvants, as well as their interactions during storage and the complex and delicate nature of antigen structures (viruses, proteins, carbohydrates, protein-carbohydrate conjugates), are among the various sources and mechanisms of vaccine instability.

Improper dosing:

Vaccine failure and reaction can occur when vaccines are administered incorrectly, such as under or overdose. The incorrect dosage of a vaccine can be caused by a number of factors. The use of water with antimicrobial components, miscalculation of vaccine dosage, and high chlorine level in the water during vaccine preparation are among these. Additionally, applying vaccines to large flocks

of birds at a dose that is higher than the manufacturer's recommended dosage will result in inadequate dosage, which will result in low vaccine titers and vaccine inactivation.

Inappropriate Vaccine Formulation and Diluents:

According to the manufacturer's instructions, poultry vaccines should be prepared and properly formulated with a specific diluent (saline water). Some diluents, such as diluents for lyophilized vaccines, are made just for one vaccine and contain preservatives that can destroy the other vaccine's activity. Inadequate dilution and a lack of a standard procedure for vaccine formulation in which the diluent is used in a single syringe may also reduce vaccine potency. As a result, when making multiple vaccines in a single syringe, the potential effects of interactions should be thoroughly investigated.

MANAGEMENT, TECHNICAL & PRACTICAL ERRORS

Hygienic Practices:

The vaccine may increase the animal's resistance to disease, but if proper management practices are not followed, this resistance may be overwhelming. The effectiveness of poultry vaccines was diminished by factors like stress, overcrowding, concurrent infections, and poor sanitation. If successive flocks are not cleaned out and disinfected, the challenge dose may be too high or infection may occur too quickly.

Failure due to Concurrent Administration of Multiple Vaccines:

For a variety of infections, poultry vaccines are frequently given to birds simultaneously. However, there are only a few pieces of literature that talk about how safe and effective it is to administer multiple vaccines at once. Different studies have shown that when two or more vaccines are given together, there may be a reduced antibody response to the vaccine and an increased risk of morbidity and mortality.

Improper Vaccination Schedule:

Vaccinating poultry during the colder hours of the day, particularly early in the morning and late in the day or evening, is typically recommended to get a better response from the vaccination. However, if the birds are vaccinated during the hottest parts of the day (heat stress), the outcome of the vaccine may be less favorable for flocks that have received the vaccine. It is essential to take the bird's age into account during vaccination.

Some antigenic receptors develop from day one (when a chick hatches) to old age, making them age-specific. Birds begin to develop the receptors for Newcastle disease, infectious bronchitis, and infectious bursal disease (IBD) at an early age, whereas birds begin to develop the receptors for fowl pox

and infectious bursa disease as they get older. As a result, it is best to immunize birds once their bodies have developed these receptors because if the host does not have these receptors, the vaccine will not work.

Using Local Antigens/ Stereotypes:

Salmonellosis and Gumboro (IBD), two infectious poultry diseases, have distinct serotypes. In addition, the prevalence of the serotypes varies from region to region. The most crucial step in the production of vaccines is the identification of infectious agents that are locally prevalent in various regions. As a result, these locally isolated antigens (immunogens) are utilized in vaccine manufacturing. If these local antigens are not used during production, disease outbreaks may occur in the region. The majority of imported vaccines may contain serotypes that are distinct from the circulating local or field strain, making them ineffective against a variety of high-virulent strains.

Lack of booster dosage:

After a single dose of the vaccine, an additional dose of the vaccine known as a booster dose is administered to ensure continued protection. Consequently, the administration of multiple doses over a predetermined period of time, depending on the vaccine should be ensured. In addition, earlier vaccination is required for the introduction of the vaccine's antigen into the birds' bodies and booster doses are required to maintain maximum antigen protection. However, the absence of a booster dose results in low antibody titers, which in turn causes the vaccine to fail.

Lack of Biosecurity Measures:

In order to safeguard poultry farms from biological threats, both intentional and unintentional, biosecurity is a mandatory comprehensive practice. As a result, various outbreaks of poultry diseases are more likely to occur due to the absence of inclusive biosecurity strategies. As a result, the vaccine strain becomes pathogenic, weakening the immune system of the chicken and contributing to vaccine failure.

Alleviation Strategies for Vaccination Failure

Vaccines for poultry are frequently utilized in a variety of production systems. Before implementing the control, and options and taking into account a variety of circumstances, a cost-benefit analysis should be carried out to determine the most appropriate strategy. In developing nations, where compensation measures are limited, the application of stamping-out measures to control major poultry diseases has a significant impact on the long-term sustainability of farm production and the livelihoods of smallholder farmers.

Therefore, the following factors should be taken into account when conducting a cost-benefit analysis: the species of birds involved, the production system, the densities of birds, the antigenicity or virulence of the viral strain in question, the availability of veterinary facilities, and the effect on trade. The most effective methods for controlling the most common infectious and contagious poultry diseases are the following:

Proper Formulation of Vaccines:

Due to the fact that vaccine preparation and formulation vary, it is always recommended to follow the manufacturer's instructions. If, for instance, the chemicals (sanitizers) used to clean the drinkers are mixed with the vaccine, the vaccine's viable components may be destroyed during preparation. The timing, duration of efficacy, and kind of diluent should also be taken into consideration when making vaccines.

Additionally, any vaccine remnants should be carefully disposed of in the appropriate location following preparation. The duration of efficacy must be taken into consideration because vaccines against diseases like IBD and chicken pox lose 50% and 100% of their effectiveness after one hour of reconstitution, respectively.

Importance of Maternal Immunity:

Depending on the various outbreaks and prevalent infectious diseases of birds, fowl, particularly parent stocks, are vaccinated frequently in the majority of poultry farms. As a result, by default, newly hatched day-old chickens have developed passive immunity in their blood to their parent stock through the transfer of antibodies in the eggs. However, the vaccine will be neutralized when administered during the first two weeks, when these maternal antibodies are at their highest.

A vaccine should be administered to newly hatched chickens based on their antibody titration level against the proposed vaccines, according to various poultry manuals and research findings, in order to maximize vaccine immunity. For instance, for Gumboro disease (IBD), the chicken should be vaccinated at least 11 days after hatching, whereas for Newcastle disease, the chicken should be 7 days old at the time of vaccination.

Proper Storage & Maintenance of Cold Chain:

Due to temperature variation having a direct effect on the vaccine's efficacy, poultry vaccines should be properly stored and transported at the optimal temperature specified by the manufacturer. In addition, the vaccine must be stored separately from food, chemicals, and pathological samples during storage. Because of this, improper handling and storage can easily cause certain live vaccines, like Marek's disease vaccine, to become inactive.

To preserve the vaccine's viability, the appropriate temperature in the cold chain must be maintained. However, the cold chain temperature is influenced by a number of factors, including a lack of electric sources, cooling systems (refrigerators), over-chilling, and vaccine transporting equipment (icebox). As a result of the crystallization of the vaccine's adjuvants (aluminum salts), additional chilling of oil-based vaccines reduces their potency.

While freeze-dried vaccines should be transported using ice blocks or a cooling system to maintain the recommended temperatures, thermo-responsive vaccines are manufactured to withstand temperature fluctuations, such as those caused by cold or hot environments. The use of thermostable vaccines may be an alternative strategy for overcoming issues with storage temperature and the cold chain.

Use of Adjuvants & Stabilizers:

An adjuvant is a substance that is added to the vaccine to make it more bioavailable and to make the immune system react better to the target antigen. In turn, this helps to reduce the amount of antigenic required to produce effective immunity and increases the immunogenicity of vaccines, which in turn helps to provide long-term protection. Adjuvants may induce a mucosal immune response that contributes to the vaccine's increased safety.

For instance, oral vaccines face significant difficulties because of the gastrointestinal tract's microbial barriers. To overcome this obstacle, the antigen must be protected with adjuvants that help to activate the immune system. A combination adjuvant platform is promising and advantageous for vaccines that are not optimal and it is especially advantageous for vaccines that are effective against particular flocks of poultry populations that are more susceptible.

In contrast, a number of immune cell types, including dendritic cells, macrophages, lymphocytes, and others, are stimulated and activated simultaneously by single adjuvants and combined adjuvants.

During the manufacturing and administration of a different vaccine, a substance known as a stabilizer is added to the vaccine in order to stabilize the vaccine and extend its shelf life.

Stress Control:

Predictable stress, which is associated with problem management and handling, and unpredictable stress, which is associated with temperature fluctuations and variations in the incidence of disease outbreaks, are two types of stress that can be managed. To prevent vaccine failure due to unanticipated stress, it is necessary to develop a method for assessing

and identifying stress. To improve the quality of life and expand the immune response sources, first and foremost, the feeding, housing, microbial flora, and breeding system should be adjusted to the appropriate standard.

Secondly, administering various therapies to reduce the degree of immunosuppression in the birds caused by unknown or nonspecific factors. However, these treatments should not be regarded as the only means of avoiding stress and its effects. In addition, after determining the cause of the stress, corrective measures such as lowering the bird density, increasing the number of feeders and drinkers, and improving the ventilation should be taken.

Use of Antimicrobials:

Antimicrobials can be used in poultry production before and after vaccinations to reduce and prevent the development of a high risk of secondary bacterial infections caused by opportunistic microorganisms during stressful times. When choosing antimicrobials, consider their compatibility with the immune system's defenses, their range of activity, and their potential to combat pathogenic opportunistic microbes.

By stimulating the secretion of interleukins by leukocytes, antimicrobials like Erythromycin, for instance, have a special immunomodulating capacity that aids in the birds' strong immunity being maintained. However, antimicrobials and vaccines should not be combined. Therefore, the antimicrobials should be given for a sufficient amount of time and they should be given before and after the vaccination for at least two days.

Vitamin & Mineral Supplementation:

Vitamins and minerals that support the immune response by acting on the immune cell and rapidly enhancing antibody production should be given to immunocompromised birds. As a result, the birds develop greater immunity more quickly. Vitamins (vitamins A, E, C, and B) are added to poultry feed to alleviate some of the negative effects of stress and support the immune system. In addition, taking vitamins prior to a predictable stressor is crucial and should continue until the stressor is over.

Vitamins are used up directly during the synthesis of glucocorticosteroids (Vitamin C) or indirectly by increasing the number in the majority of intermediate metabolic reactions (Vitamin B), both of which should be administered 24 hours prior to vaccination. Vitamins are involved in all kinds of stress reactions. Studies indicate that routine poultry feed may not be sufficient to meet the demand for normal immunity, so additional vitamins and minerals must be supplemented to maximize disease resistance.

The most efficient strategy for dealing with vaccines is the combination of vitamins (water-soluble vitamins A, D_3, E, and B-group

vitamins), minerals (selenium), and amino acids. These substances play a significant role in modulating the immune system and stimulating humoral and cellular immunity.

Proper Vaccination Schedule & Biosecurity Measures:

Depending on the disease prevalence in the region, poultry flocks should be enrolled in a proper vaccination program to prevent disease outbreaks and financial losses. In order to develop the required amount of antibody titration, it is preferable to immunize them prior to the onset of the disease. Infectious bronchitis and avian influenza, for instance, should be immunized against prior to the winter season due to the prevalence of disease outbreaks in birds during the winter.

In addition, biosecurity, which should be maintained at a high level in addition to the use of vaccines, is the most important and crucial component of any poultry outbreak prevention and control strategy. In addition, strict stamping-out (all in all out) guidelines should be followed to prevent cross-contamination between flocks.

Follow the Manufacturer's Guidelines:

When administering vaccines, consideration should be given to the vaccine's type (inactivated, live attenuated, DNA, and recombinant vaccines) and use in accordance with the manufacturer's instructions regarding preparation, use, storage, and administration method. Therefore, vaccination should always be administered by a trained or qualified veterinarian to minimize vaccine-related adverse reactions like vaccine reactions (live attenuated vaccines) and local tissue reactions (activated or killed vaccines).

In addition, the majority of manufacturers advised testing for the appropriate titration level of antibodies prior to the application of poultry vaccines to avoid stressful conditions like transportation, overcrowding, and hot weather. For instance, the best times to get vaccinated are in the early morning or late afternoon, especially in the summer.

Preparation of Flock for Vaccination:

Depending on the route of administration, the age of the birds, the method of vaccination, and the type of vaccine, flocks of birds need to be properly prepared for vaccination. In addition, strict adherence to pre-vaccination precautions, such as withholding food and water for two to three hours, is required to improve vaccine efficacy. For instance, spray vaccination is currently given to day-old chicks shortly after hatching in cabinets for widespread aerosol vaccination.

Day-old chicks are given eye drops on individual chickens on eye drop day. The most prevalent method of vaccine administration is oral vaccination. The flock should be vaccinated after a brief period of fasting,

allowing the vaccine to be administered in a short amount of time (up to two hours) and the vaccines should be prepared and administered using clean equipment (drinkers). In order to accomplish this, a sufficient number of drinkers must be available, and regular bird movement and proper monitoring will ensure that all birds consume an adequate amount of the vaccine.

Conclusion

The poultry industry and poultry producers face significant financial losses as a result of infectious poultry diseases. Vaccines for poultry have been used for a long time and have a significant impact not only on production but also on poultry health and welfare. One of the most important and cost-effective tools for preventing disease in poultry is vaccination, which also reduces the need for antibiotics in poultry products and prevents significant loss. However, there are issues with poultry vaccines that contribute to vaccine failure. These issues include the vaccine's instability, improper handling, transportation, and administration, as well as the need for novel vaccine development solutions.

As a result, addressing these issues necessitates adhering to the instructions provided by the vaccine manufacturer, which are crucial to preventing failure. In addition, when administering vaccines, the level of maternally derived titers and flock health ought to be taken into consideration. As a result, the storage, timing, and administration instructions provided by the vaccine manufacturers should be adhered to by veterinarians working in various field clinics. Before administering the vaccine, poultry farmers and managers should also consult with veterinarians and monitor the health of the chickens. The farmer must take all necessary measures to control the vaccination practices as well as external factors and the vaccination goal must be clearly defined. Vaccination is an effective tool for disease control in poultry and ought to be used in conjunction with other strategies.

Key Words

Poultry – Vaccine – Failure – Biosecurity – Booster – Flock – Stress – Adjuvants – Immunity – Coldchain – Maternal antibody.