Vaccines, vaccination and immunity – an overview

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Different infectious agents, such as viruses, bacteria, mycoplasmas, and parasites cause infectious diseases. These diseases remain a major health problem for poultry flocks in today's intensive poultry sector. Veterinary practitioners in poultry medicine and poultry growers around the world are certainly more interested in the prevention rather than in the control of infectious diseases. Vaccination is an important component of any integrated programme to prevent infectious diseases in poultry flocks.

Although the dramatic improvements in biosecurity and management practices in the poultry industry play a key role in reducing exposure to infectious agents, the decline in the infectious diseases was greatly accelerated by vaccination and by continuous improvement in vaccine quality, vaccination programme, and methods of administering vaccines. Vaccination represents the most successful attempt yet to protect poultry from infectious diseases, and, in fact, it is the only practical approach to preventing some diseases (for example Marek's disease) in commercial poultry flocks.

Vaccines and how they work

A vaccine is an attenuated (naturally or artificially) or killed micro-organism that induces an immunologically mediated resistance to infection and/or disease.

'Active immunisation' is the process of administering a vaccine to a live host with the purpose of inducing an immune response. The terms vaccination and immunisation are now partly interchangeable. The micro-organism (antigen) in a vaccine stimulates an immune response that protects birds from contracting infection and/or disease as a result of subsequent exposure to the virulent variant of the same infectious agent in the vaccine.

Depending on the infectious agent, immunologic resistance is mediated by humoral (circulating) and local antibodies or by cellular immunity. A vaccine should promote resistance to the disease, but not necessarily to the infection. Depending on infectious agent, the vaccine may stimulate an immune response that prevents an infectious agent from infecting a bird, or the infectious agent may infect the vaccinated bird but produces no or only minor disease. Most vaccines operate by limiting infections, not necessarily by preventing them. It is the host immune system that mediates control and ultimate clearance of the infectious agent.

Following the first vaccination, the immune system is stimulated and starts to produce antibodies against the infectious agent in the vaccine. Antibodies continue to be produced until the antigen (the micro-organism) in the vaccine is completely eliminated from the body. The result of this immunologic stimulation is the production of a reserve pool of antibodies that are capable of overcoming the virulent variant of the same disease agent in the vaccine, if exposure occurs in the near future. However, antibodies naturally decline with time, and therefore, it is necessary to restimulate (boost) the immune system with a subsequent (booster) vaccination. The first vaccination produces a 'primary immune response', which usually develops slowly and is weak (low antibody levels) and of short duration.

The first vaccination also induces 'immunologic memory' (memory cells) that allows the immune system to respond rapidly and efficiently upon second contact with the same infectious agent. Therefore, the subsequent vaccination results in a 'secondary immune response' in which the antibody concentration rises sooner, the peak concentrations of antibody are higher, and high levels of antibody persist for a longer period of time.

The immunoglobulin class of antibody that appears in the primary immune response is IgM, whereas IgG is the predominant antibody in a secondary immune response. In general, antibodies produced during a secondary immune response have increasing cross reactivity and are more efficient in attracting and binding to antigens. IgG usually peaks at three to four weeks after booster vaccination and then slowly decreases. IgG is the major type of antibody found in the yolk, and consequently, it is the major type of maternally derived antibody in the progeny.

Second line of defence

It is extremely important to realise that vaccine induced immunity is the second line of defence against infectious diseases. The first line of defence is biosecurity measures. Vaccines do not prevent the introduction of disease agents into a flock. Moreover, for some infectious diseases even the best vaccine and vaccination programme may not confer good protection against severe field disease challenge. In essence, biosecurity and immunity are a complement to each other. Biosecurity may reduce the dosage of field disease challenge, thus helping the immunity to resist the challenge.

The concept of flock immunity

When a vaccine is used to control a disease in a poultry flock, the concept of 'flock immunity' should be considered. Flock immunity is the resistance of an entire flock to a disease. In any vaccinated flock, a certain percentage of birds in the flock may not mount a protective immune response and thus remain susceptible to infection and/or disease. If very few birds in a flock are susceptible, then the virus shed from an infected bird is unlikely to find another susceptible bird to infect, and eventually the spread of the disease is slowed or terminated. Therefore, the more birds in a flock that are immune, the less likely it is that the field disease challenge will result in a severe disease in the flock. The efficacy of a vaccine or the success of vaccination for a disease is relative rather than absolute; in other words, a vaccine may not induce 100% protection but it greatly reduces the severity of field challenge. Therefore, a vaccination (a vaccine) should be primarily assessed in the sense of how much it reduces the severity of field challenge and the impact of the challenge on the flock. Immunity depends upon a large number of complex variables, including not only the resistance of the host but also the virulence of the infectious agent, dose, and route of infection.

Vaccination checklist

The following factors are to be considered in deciding against which diseases a chicken or turkey flock should be vaccinated:

- Prevalence of a disease agent in or around the area of operation. There is no point vaccinating a poultry flock against a disease that is not present in or around the area of operation. Moreover, care should be taken to avoid introducing a live vaccine to areas where a particular disease problem is not known to occur.
- Virulence of the field disease agent. One can establish a balance between the expected deleterious effect of field disease challenge on performance, livability, and/or productivity of the flock and the cost associated with the purchase and administering of the vaccine. As a general rule, the benefits from vaccination must outweigh the cost.
- Density of poultry population around the farm (commercial and backyard flocks).
- Levels of biosecurity measures and risk of exposure.

Designing a programme

Once it is decided to vaccinate a poultry flock against certain diseases, the next step is to decide on the elements of vaccination for each disease (vaccination programme). These are shown in Table 1. The objectives in designing a vaccination programme are shown in Table 2.

An infectious disease can be regarded as a race between the replication and spread of the infectious agent on the one hand, and the ability of the immune system to overcome it on the other

Continued on page 12

- Frequency (number) of vaccination. If a protective level of immunity has to be maintained for a long period of time, a series of vaccinations is commonly given.
- Age of first vaccination and interval between the initial and second vaccination or between subsequent vaccinations.
- Method of administering the vaccine or route of vaccination (drinking water, spray, aerosol, eye drops, wing web stab, injection).
- Type of vaccine (live or killed; what strain, subtype, or serotype).

Table 1. The elements of vaccination for each disease programme.

Continued from page 11

hand. The level of vaccinal immunity at the time of infection and the speed with which the immune system responds to the pathogenic infectious agent will determine the outcome of the infection. A powerful immune response that is mounted a day or two earlier may often have a determining effect on the course of the infection, favouring earlier recovery and less severe disease.

There is no single vaccination programme that suits all chicken or turkey flocks in different parts of the world. The factors in Table 3 are to be considered when designing a vaccination programme.

- To stimulate and maintain protective levels of immunity throughout the period during which the birds are susceptible (or most susceptible) to the disease.
- To elicit immunologic memory so that a subsequent exposure to the pathogenic agent will stimulate a faster and higher immune response with successful elimination of the pathogenic disease agent.
- To protect progeny through maternal antibody transfer.

Table 2. The objectives in designing a vaccination programme

Types of poultry vaccines

Viral, bacterial, and mycoplasma vaccines for poultry are of two types, either live or killed.

Examples of live vaccines are shown in Table 4.

For many diseases, there are different types of commercially available live vaccines that vary in virulence. For example, live fowl cholera vaccines may contain CU strain, M-9 strain, or PM-1 strain. CU strain is the most virulent while M-9 is the least virulent. The different vaccines (which contain different serotypes, subtypes, or strains) of a particular disease (for example infectious bursal disease, infectious bronchitis, Newcastle disease) vary in virulence and immunogenicity. As a general rule, the more virulent and invasive the infectious agent in the vaccine, the more it is immunogenic (elicits an immune response).

Killed (inactivated) vaccines are produced by destroying the infectivity of infectious agents (virus, bacteria, mycoplasma) by heat or chemical means while retaining the antigenicity. Killed bacterial and mycoplasma vaccines (also called bacterins) for poultry are based on whole inactivated bacterial or mycoplasma cells. They are administered by intramuscular or subcutaneous injection of individual birds. Because a killed infectious agent does not multiply, it is eliminated at a high rate from the body, and for this reason induces an immune response that is usually weak and of short duration. In order to enhance the immune response and to prolong the duration of immunity and immunologic memory, killed vaccines for poultry are usually mixed with water-in-oil-emulsion adjuvant. The oil in the adjuvant induces a local, chronic, inflammatory response, and as a result, a granuloma is formed around the site of injection and the antigen is slowly released over a long period of time from the aqueous phase of the emulsion. The slow release of the antigen from the site of injection gives rise to a long lasting antibody response. Inactivated vaccines with adjuvant are used to vaccinate layers and breeders to confer protective immunity during the laying cycle.

It should be noted that killed viral vaccines normally require prior vaccination (priming) with live vaccine for the disease for which you are vaccinating against. Killed bacterial vaccines require two injections. A four to six week interval between the last live vaccine and the killed vaccine or between the two injections of a killed bacterial vaccine is required for a good immune response. The last inactivated vaccines are usually given no later than four weeks before the start of egg production to allow time for a full immune response. In the case of infectious agents with multiple serotypes that are antigenically related (for example. infectious bronchitis virus and pasteurella multocida), killed vaccines do not provide as good cross protection as do the live vaccines. Also, killed vaccines induce predominantly humoral antibody response; they are less effective in inducing cell mediated immunity and in eliciting an IgA response (local immunity).

Failures in vaccinations

Vaccine failure (vaccine break) occurs in a poultry flock when the vaccine fails to protect a large number of the birds in the flock from infection and/or clinical disease.

Vaccine failure can be caused by factors associated with the vaccine or the birds (see Table 5).

Successful vaccinations

There are three critical requirements for successful vaccinations (immunisation) of a chicken flock:

- A good quality vaccine which contains the right strain, serotype, or subtype of the disease agent.
- A well designed vaccination programme.
- An appropriate route (method) and correct technique of administering the vaccine.

The following points should be considered to ensure a successful immunisation of chicken flocks:

- Use only approved quality vaccines.
- Transport and store vaccines properly.
- Follow exactly label directions for vaccines, and consult a professional if you have question.
- A correct vaccination technique is crucial for a successful immunisation. Errors in the vaccination technique are probably the most common cause of vaccine failures. The key points in any vaccination method are:

- Maintaining the potency of the vaccine.
- Administering the recommended dose.
- Assuring a uniform distribution or accurate injection of the vaccine.

In any vaccination method, many things could go wrong during preparing (mixing) and administering the vaccine, and minor errors that seem insignificant may greatly reduce the dose of the vaccine that the birds receive and may result in uneven distribution of the vaccine or in missing the vaccination of many birds in the flock. The vaccination of a poultry flock should be carried out by a well trained crew. It is a very good idea that the farm manager assigns a qualified person for monitoring each step of preparing and administering a vaccine.

- In case of subcutaneous injection (under the skin) of a vaccine such as Marek's disease vaccine, a food grade dye can be added to the vaccine (to the diluent in case of Marek's disease). The accuracy

Table 3. Factors to consider when designing a vaccination programme.

- Virulence and serotype, subtype, or strain of the field disease agents. What level of field disease challenge (virulence and dosage of the disease agent) is expected? Severe field challenge requires a high level of immunity. It is also imperative that the vaccinal immune response is specific to the pathogenic field disease agent and, therefore, the disease agent in the vaccine and in the field must be of the same serotype or closely antigenically related.
- The age at which the birds are susceptible (or most susceptible) to each disease agent.
- Risk of exposure. For example, in an area of higher mosquito population it might be necessary to vaccinate birds at one day of age; another example is the vaccination of broiler chickens against infectious laryngotracheitis in high risk areas.
- The life span of the birds. For example, in layers and breeders there is a need to maintain protective levels of immunity during the long growing and production periods of the flock. Layers and breeders must be protected from diseases that cause drop in egg production, deterioration of egg quality, or reduction in hatchability.
- For early vaccination against certain diseases (for example infectious bursal disease), it is important to consider the levels and uniformity of maternal antibodies.
- The possibility of post vaccination reactions, which may have potential adverse effect on liveability and productivity of the flock. The benefits of vaccination should outweigh the adverse effect of post vaccination reaction.
- In breeders, the need to prevent vertical transmission of some disease agents (for example avian encephalomyelitis) to the progeny.
- In breeders, the need to provide the progeny with protective levels of maternal antibodies to protect them from early infection with certain disease agents present in the area where they will be raised.

of subcutaneous injection (for example under the skin of the neck) can be checked by monitoring the dye colour under the skin immediately after vaccination.

- The correct timing of vaccinations, the number of vaccinations, and the intervals between vaccinations are extremely important. Successful immunisation of young chicks against some diseases (for example infectious bursal disease) is effective only after passive immunity has waned. The first vaccination, however, should not be delayed and must be carried out before maternal antibodies decline to low levels, in order not to take the risk of field disease challenge.

For some diseases (for example avian encephalomyelitis), a single vaccination may produce a protective, long lasting immunity. For other diseases (for example infectious bronchitis and Newcastle disease), subsequent (booster) vaccinations are necessary to achieve and maintain protective levels of immunity.

Due to the longer duration of immunity produced by secondary immune response, the intervals between booster vaccinations (for example between the second and third vaccination) are usually longer than the interval between the initial and booster (second) vaccination. The intervals between vaccinations are very important; if the intervals are too short the immune system will respond poorly to the next vaccination, while if they are too long, the immunity (level of antibodies) may decline to a point that the birds become susceptible to natural infection.

- If possible, avoid vaccinating stressed birds. Avoid unnecessary additional stress on the birds during vaccination. Optimise the flock management practice during the few days after vaccination to avoid any stress, which could affect the mounting of an adequate immune response.
- Use a vaccine that contains the right serotype of the disease agent. The more virulent vaccine strains of an infectious agent produce a better immune response, but live vaccines that contain such strains may have an unacceptable adverse effect on the flock (severe vaccination reactions or complications).

With most live vaccines, there is more than one method of administering a vaccine, and one method may induce a better immune response and give a better protection than the other method(s). If the field disease challenge is expected to be severe one may consider administering the vaccine by a route that induces a better immune response.

For live vaccines, the vaccine type and/or the route of vaccination must be safe for the birds, with minimal acceptable vaccination reaction or complication. Unfortunately, for some diseases, the most immunogenic vaccines and the best route of vaccination usually produce the strongest reaction or complications. Sometimes a choice has to be made between inducing protection and producing a strong vaccination reaction, and in some instances this is not an easy choice. As a rule of thumb, a vaccine and/or route of vaccination should be safer than exposure to the disease, assuming that the risk of exposure is significantly high.

- For some vaccines such as pox and fowl cholera vaccines, check for 'takes' to assure that vaccination has been carried out properly.

- Vaccines prepared from naturally occurring apathogenic or mildly pathogenic strains of the causative agent. For example, vaccines made from La Sota strain of Newcastle disease virus, from TS-11 strain of Mycoplasma gallisepticum or from CU strain of Pasteurella multocida.
- Attenuated (modified live) virus vaccines that are developed by laboratory cultivation and serial passage of virulent field virus in either embryonated chicken eggs (virus vaccines of chicken embryo origin – CEO) or in tissue culture (virus vaccines of tissue culture origin – TCO). Examples of attenuated live virus vaccines are SB-1 and CVI-988 vaccine strains of Marek's disease virus. For some diseases (for example fowl pox and infectious laryngotracheitis), there are vaccines of both CEO and TCO. Generally, viral vaccines of CEO are more virulent and more immunogenic than viral vaccines of TCO.
- Bacteria may also be made avirulent by gene manipulation (selective deletion of genes that are necessary for virulence) to produce a virulent mutant strain that can be used as a vaccine.

Table 4. Examples of live vaccines.

Immune response and levels

The immune response to vaccinations and the levels of immunity can be monitored by quantitative estimation of humoral antibodies after vaccination. Serum samples can be collected from randomly selected birds three weeks after vaccination. The number of samples needed to make a reasonable estimate of the true distribution of flock antibody levels depends on the flock size, but generally 10 to 20 samples per flock in a house are enough to get a meaningful values of antibody levels that allow conclusions to be drawn about the immunity status of the flock.

The lag (time) between administering the vaccine and the detection or peaking of antibodies varies; part of this variation depends on the sensitivity of antibody detection method, but it is also a reflection of the potency of the immunogen. The serologic test enzyme linked immunosorbent assay (ELISA) is commonly used for quantitative estimation of antibody levels, especially viruses. The ELISA antibody titre (level) needed for protection varied from one disease to another, and even for a particular disease, it may depend on the degree of virulence of the field disease agent, dosage of field challenge, and genetic susceptibility of the host. Unfortunately, there is not always a correlation between antibody levels and protection and, in many instances, ELISA titres do not correlate well with resistance to challenge.

ELISA measures IgG immune response (humoral immune response) only, but for some diseases IgA (secretory antibodies on the mucosal surfaces of the body) or cell mediated immune responses are considered to be the primary protective immune mechanisms against some diseases. Challenge studies (the effectiveness of the vaccine in protecting experimentally challenged birds) is a much more better criterion than antibody levels to assess the efficiency of a vaccine. However, it is obvious that challenge study is not a practical way to measure immunity under field conditions. ■

Table 5. Reasons for vaccination failure.

- Failure to administer the recommended dose of the vaccine. In order to induce a protective immune response a certain number of micro-organisms must enter the body. Administering a suboptimal dose of a vaccine could be caused by:
  - Poor vaccine quality (rare).
  - Improper handling of the vaccine during transport and storage that reduces the potency of the vaccine (occasionally occurs).
  - Errors in the vaccination technique that could also result in failure to vaccinate all birds in the flock (common). For example, subcutaneous neck injection is very difficult to perform accurately, and the vaccination crew may miss vaccinating many birds in the flock.
- Severe immunosuppression of the birds at the time of vaccination or field infection will lead to inadequate immune response.
  Some common causes of immunosuppression are:
  - Infection with viruses that are able to compromise immunity by causing severe depression of the host immune response; the best examples of these viruses are infectious bursal diseases virus, chicken infectious anemia virus, and Marek's disease virus.
  - Stress caused by adverse house environmental conditions, inadequate nutrition, or illness. Birds that are vaccinated or naturally infected during periods of stress may not mount an adequate immune response to resist infection and clear the infectious agent from the body. Remember, it is the host immune system that mediates control and ultimate clearance of the infectious agent.
  - High levels of mycotoxins in the feed. Many mycotoxins have been proven to cause immunosuppression.
- High levels of maternal antibodies, which neutralise the antigen (infectious agent) in the vaccine and thus interfere with mounting an adequate immune response.
- Exposure to large numbers of the disease agent (strong field challenge) that might overwhelm the immunity of the host.
- Infection by a serotype or antigenic variant of the causative agent that is not contained in the vaccine (for example failure of infectious bronchitis and fowl cholera vaccines).
- Birds may already be incubating the disease at the time of vaccination, and so the vaccine may be given too late to affect the course of the disease. The birds might have been infected before the development of vaccinal immunity. Because the immune response is a complex chain of events, there are several days between vaccination and development of vaccinal immunity. The poultry producer should not assume that his/her flock becomes fully protected from field challenge on the second or third day after vaccination. Approximately 10 to14 days is required following vaccination before minimal protective immunity is produced.
- Field disease challenge occurs after waning of vaccinal immunity.