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FACTORS INFLUENCING VACCINE EFFICACY - A GENERAL REVIEW

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ABSTRACT

Vaccines are essential tools for disease prevention and the control of disease spread. Their universal acceptance is based on the recognition of their high effectiveness and good safety record. Vaccines have significantly contributed to a steady decline in the mortality and morbidity that is caused by infectious diseases. Sometimes, vaccine failure to protect from disease is usually due to problems with either client education or compliance with good animal management practices. A number of factors involve in the vaccine efficacy. Some are beyond the control of either veterinarian or farmer. The present article aims to study the factors influencing the vaccine efficacy.

Keywords: Vaccines; Effectiveness; Veterinarian; Farmer

INTRODUCTION

Veterinary vaccines have produced dramatic benefits in term of animal health and efficacy of food production. Advances in research and accumulating experience with vaccines are leading to safe and more effective vaccines. In connection with the introduction of antibiotics and modern hygiene, vaccines have significantly contributed to a steady decline in the mortality and morbidity that is caused by infectious diseases. It has been shown that vaccination of a large proportion of a population can lead to the protection of the entire population due to a "herd effect" that slows down circulation of a pathogen in the immunized population. Vaccine failure to protect from disease is usually due to problems with either client education or compliance with good animal management practices. It is important for clients to understand the proper timing and method of vaccine administration, what to realistically expect for vaccine efficacy and the importance of minimizing immunosuppressive factors and exposure to high doses of infectious agents in vaccinated animals (James, 1999).

A safe vaccine is not simply one that has been manufactured, tested and found to be safe in clinical trials. Important as those aspects are, there are other possibilities for making immunization safer. These include safe transport to the point of administration, safe administration, safe disposable of the vial and injection equipment and post-marketing surveillance to detect any unexpected reactions as soon as possible (Clements *et al.*, 2004).

The present article narrates the factors influencing vaccine efficacy which are as follows;

1. Vaccine Factors

Veterinary vaccines whether attenuated or non-infectious from the different manufacturers can vary in their potency, efficacy and duration of immunity. Attenuated vaccines tend to induce stronger and long-lasting immunity than non-infectious vaccine. Non-infectious vaccines include killed, toxoid, subunit and DNA vaccines are safer and more stable than attenuated vaccines. However, due to risk of using live vaccines in pregnant or immunosuppressed animals as well as the risks of shedding vaccine virus, non-infectious is preferred for some diseases (James, 2007).

Vaccine, if used properly, induces protection from challenge in a high percentage of vaccinated animals. This is achieved by presenting the correct antigen in a safe manner to the host's immune system. However, wild type organisms change with time and place. Vaccines that were effective may become ineffective due to antigenic drift. Individual veterinary vaccines often incorporate different strains of organisms. For example, several strains of canine distemper virus may be found ineffective vaccines. Some vaccines with poor efficacy may not be recognized until for use. During a distemper outbreak in Finland, a disproportionate number of vaccinated dogs had been vaccinated with one popular vaccine, which was withdrawn from the market by the manufacturer once this was recognized (Ek-Kommonen *et al.*, 1997). Significant difference was demonstrated between this vaccine and three other distemper vaccines used in Finland. 54% of the dogs vaccinated with poorly efficacious vaccine had no detectable antibodies to this pathogen (Rikula *et al.*, 2000).

Vaccines only contain specific strains of the virus or bacteria that cause disease. This is true for

panleukopenia in feline, canine leptospirosis in dog and foot and mouth disease in cattle. Vaccines against canine leptospirosis only protect against two types of the bacteria. It would not protect an animal against the other types

Annual Revaccination: Vaccines manufacturers often recommend that booster doses of vaccine should be given following a primary course. In most cases, this advice is based on their own duration of immunity studies showing that animals given a primary course of vaccination are protected when challenged 12 or sometime 24 months later. From observation, on the persistent of antibody levels following vaccination, particularly of the canine virus, it has been suggested that dog do not require to be vaccinated annually, and a period of 3 years between vaccinations has been suggested (Ramsey and Bryn, 2001).

Adjuvants: All non-living vaccines require an adjuvant to provide an adequate immune response. A wide range of adjuvants are used in animal vaccine including aluminum salts and derivatives of the glycosides sapnin. The major theoretical advantage of non-living vaccine over living is that they are safer because they are incapable of replication. Their main disadvantages are that higher doses of the organism have to be given and they do not present such a wide range of potential immunogens to immune system. It has also been reported that the adjuvant contained in non-living vaccines may cause adverse reaction in the host (Ramsey and Bryn, 2001).

Degree of attenuation: Virulent living organisms can not normally be used in vaccines. However, their virulency can be reduced so that they can no longer cause disease. The most common methods of attenuation involve adapting organisms to growth in unusual condition. Virulent canine distemper virus preferentially attack lymphoid cells. Therefore, for vaccine purpose, this virus is cultured repeatedly in canine kidney cells, as a result of which its virulencey is lost (Tizard, 2000).

The cause of vaccine failures does not necessarily reflect on the quality of the vaccine. If stringent quality control tests have been carried out and proper methods of storage and handling under tropical conditions have been observed, the vaccine quality factor can eliminated (De Alwis, 1999).

2. Host Factors

All animal do not respond equally well to vaccination and some may not mount an effective immune response to a vaccine. The host factors most affecting vaccine efficacy are as follow;

Maternal Antibody: New born animals acquire immunoglobulins from their mother in the immediate perinatal period. Neonatal antibody titers are lower in larger litters or if suckling is impaired. The antibodies from the mother generally circulate in the newborn's blood for a number of weeks. There is a period of time from several days to several weeks in which the maternal antibodies are too high to provide protection against disease, but too low to allow a vaccine to work. This period is called the window of susceptibility. The length and timing of the window of susceptibility is different in every litter and between animals in the same litter. Maternal antibodies can interfere with the ability of vaccines to induce immunity. This is particularly true for live virus vaccines that contain relatively small amounts of infectious virus and may be readily neutralized by maternal antibody. For example canine distemper vaccines when given at conventional times left many puppies unprotected as their levels of maternal antibody were sufficient to neutralize the virus used in the vaccine (Ward, 2006).

Concurrent Disease: Infectious organisms require an incubation period before clinical signs of disease become apparent. This incubation period may be as short as a few hours or as long as a few years but in general, are a few days. If an animal is incubating infectious diseases at the time of vaccination then it may well develop clinical signs. Similarly, young animals from large multi-animal environments will be particularly likely to be incubating disease at the time of vaccination. Mixed infections are common in these environments. However, little is known about how concurrent infections affect the immunity to each other. A range of antagonist and synergistic interactions has been shown in hosts co infected helminth and protozoa which might have implications for successful vaccination (Helmby *et al.,* 1998 and Christensen *et al.,* 1987). It is also suspected that trypanosomiasis and theillerosis diminish the immune response to vaccination (Phan *et al.,* 1996).

Immune System Function: An animal must have an effective immune system if it is to respond appropriately to a vaccine. An animal's age may affect vaccine responses. Old age has also been suggested to suppress vaccine response, however, this is uncertain. In one study, older animals had lower titres after vaccination (Mansfield *et al.,* 2004). In other study, elderly pet dogs had higher prevaccination rabies titres than had younger dogs (HogenEsch *et al.,* 2004). In this study, young and old dogs had similar post-vaccination rabies, distemper and parvo titres despite decreased proliferative responses of lymphocytes and other changes in immune parameters in older dogs (HogenEsch *et al.,* 2004).

Similarly, animal that are sick or receiving drugs (particularly glucocorticoids and cytotoxic agents) may have a reduced ability to respond appropriately to vaccination. Moreover, hyperthermic puppies (>39.8 ^{o}C or 103.6 ^{o}F) are unable to mount an effective immune response to canine distemper virus vaccination and will

succumb to disease if subsequently challenged. Anesthetics have not been shown to influence vaccine efficacy on their own, but the stress of surgical procedures may affect the ability of the immune system to respond effectively. Management practices that expose animals to severe stress following vaccination may results in an inadequate immune, although Bock and De Vos (2001) could not find published evidence of this being significant under field condition.

Poor nutrition can suppress immune responses by decreasing nutrient availability for cell division and protein (e.g., antibody and cytokine) synthesis (James, 2007).

Breed variation: Some breeds of cats and dogs are more susceptible to certain diseases. Studies in dogs have shown that Doberman and Rottweiler tend to be more susceptible to canine parvovirus and may need a different vaccination schedule than other dogs, if there are to be protected through vaccination.

3. Human Factors

There are several factors within the control of the vaccinator or farmer that may affect vaccine efficacy. First, vaccines should be stored at the appropriate temperature recommended by the manufacturer. This is especially true for live vaccines which might be inactivated at higher temperatures. Each vaccine has an expiry date printed on the vial which should strickly adhere. Vaccines should be reconstituted with the diluents with which they are supplied. Once reconstituted, they should be used immediately. Similarly, vaccines are developed to be given by a certain route, either intranasally, subcutaneously or intramuscularly. If a vaccine is administrated by a route different from the route for which it was developed, it may not be effective and could cause considerable harm. For example, studies in dogs suggest that antibody titres remain elevated longer after intramuscular than subcutaneous administration of attenuated rabies vaccines (Sikes *et al.,* 1971).

Sometimes, needle inserted into the injection site to administer vaccines may pass close to the nerve. Irritant vaccines injected into or close to the nerve have been documented to the cause paralysis in some instances. For this reason, careful training is needed to ensure vaccine are injected the appropriate depth and appropriate site. Moreover, syringes and needles are widely re-used in developing countries because of scarcity and re-sale value. More than 30% of immunization injection may be unsafe, primarily due to re-use (Farghaly and Barakat, 1993).

There are also several factors within the control of the owner that may affect vaccine efficacy. It is important that owners adhere to the vaccination schedule advised by their veterinarian. Excessive or decreased delays between the first and second doses reduce the secondary antibody response and therefore both the length and quality of the immunity produced. A particular owner may achieve a high coverage among his animals. However, if these animals mingle with large numbers of un-vaccinated animals in common pastures. They are at risk, particularly the few unvaccinated animals in his herd.

Incorrect handling or storage of the vaccine: Incorrect handling or storage of the vaccine, resulting in an in-effective vaccine being administered that will not provide protection e.g., the toxicity of dimethyl sulf oxide (DMSO) for Babesia parasites at temperature above freezing is a serious constraint on the infectivity of the vaccine. After thawing the vaccine at between 37 and 40 ^{o}C, it must be injected immediately. It has been shown that if the vaccine is thawed slowly in melting ice and kept in melting ice, it is still infective for upto 8 hours without showing significant changes in the prepatent period (De Waal, 1996). However, to ensure on margin of safety, it is recommended that the vaccine be used within 4 hours of thawing.

Vaccines must be maintained at the correct cool or cold temperature during transport and storage as well as after reconstitution and during use, their shelf life must not be exceeded.

Insufficient time between vaccination and exposure: A vaccine does not immediately provide protection. It takes from days to a week or more for an animal's body to respond to the vaccine. For some vaccines, an adequate level of immunity usually does not occur until 2-3 weeks after the second vaccination in the series. A young animal is susceptible to a disease if it is exposed to the disease before a vaccination has had time to stimulate the body's immunity.

4. Environmental Factors

Although vaccination programme may be adequate to control infectious disease under normal condition of exposure, it should be recomembered that they may not protect under severe condition of challenge. This situation has been observed in kittens infected with feline parvovirus (FPV). In many cases, FPV was not suspected initially as a cause of death because vaccination was performed in the households in which diseases occurred. Disease was thought to develop as a result of accumulation of virus in an environment that either overcame vaccinal immunity in the affected kittens or infected the kittens in the period between the weaning of maternal antibodies and the administration of the vaccination.

Conclusions: Proper following the instructions stick to vaccine label, safe transport and administration, screening the animals for concurrent infection as well as reporting

systems from farmer to veterinarian and from veterinarian to vaccine manufacturer can improve the vaccine efficacy.

REFERENCES

Bock R. E. and A. J. De Vos (2001) Immunity following use of Australian tick fever vaccine; a review of the evidence. Aust. Vet. J. 79: 832-839.

Christensen N. O., P. Nansen, B. O. Fagbemi and J. Monrad (1987). Heterologous antagonistic and synergistic interactions between helminths and between helminths and protozoans in concurrent experimental infection of mammalian host. Parasitol. Res. 73: 387-410.

Clements, C. J., L. Gordon and J. Lins (2004) Technologies that makes administration of vaccines safer. Vaccine. 22: 2054-2058.

De Waal, D. T. (1996) Vaccination against babesiosis. Acta. Parasitol. Turcica. 20: 487-499.

De Alwis, M. C. L. (1999) Haemorrhagic Septicaemia. Monograph No.57 ACIAR. Canberra, Australia.75.

Ek-Konmmonen, C., L. Sihvonen, K. Pekkanen and U. Rikula (1997). Outbreak of canine distemper in vaccinated dogs in Finland. Vet. Rec. 141: 380-383.

Farghaly, A. G. and R. M. Barakat (1993) Prevalence, impact and risk factors of hepatitis C infection. J. Egypt. Public Health Associ. 68: 63-79.

James, A R. (1999) Mechanistic bases for adverse vaccine reactions and vaccine failures. Advances in Vet. Medicine 41, 681-700.

James A R. (2007) Factors influencing vaccine duration of immunity. In: Proceedings of North America Veterinary conference.

HogenEsch M., S. Thompson, A. Dunham, M. Ceddia and M. Hayek (2004). Effect of age on immune parameters and the immune response of dogs to vaccines: a cross-sectional study. Vet .Immuno. Immunopathol. 97: 77-85.

Helmby, H., M. Kullberg and M. Troye-Blomberg (1998) Altered immune response in mice with concomitant schistosoma mansoni and plasmodium chabaudi infections. Infect Immunol 66: 5167-5174.

Mansfield, K. L., P. D.Bur, D. R Snodgrass, R. Sayers and A. R. Fook (2004). Factors affecting the serological response of dogs and cats to rabies vaccination. Vet. Rec. 157: 423-426.

Phan, T. P., M. Nguyen, R. Hamers and N. Wuyts (1996) The effect of trypanosomiasis on immune response of buffaloes to vaccination against pasteurellosis. Khoa. Hoc. Ky. Thuat .Y. 3: 15-20(Vietnamese).

Ramsey, I. and T. Bryn (2001) Manual of canine and feline infectious diseases. BSAVA, 46-48.

Rikula, U., L. Nuotio and L. Sihvonen (2000). Canine distemper virus neutralizing antibodies in vaccinated dogs. Vet. Rec.147: 598-603.

Sikes, R. K., G. V. Peacock, P. Acha, R. J. Arko and R. Dierks (1971). Rabies vaccines: duration of immunity study in dog. J. Am. Vet. Med. Assoc. 159: 1491-1499.

Tizard, I. R. (2000) Veterinary Immunology, An Introduction. 6th Ed. W.B. Saunders Company. Philadelphia. 239.

Ward, E. Jr (2006) Three-year vaccines: What, How and Whey to tell your clients. In: Proceedings of North America Veterinary Conferences.