Assessing Vaccine Efficacy and Data

Victor Cortese, *DVM, PhD*
Dip ABVP; Director, Cattle Technical Services, Pfizer Animal Health, Exton, PA 19341

Introduction

To scientifically choose a vaccine or design a vaccination program it is necessary to consider many variables.[7] Some of these include: 1.) presence and degree of challenge of the particular diseases on the farm or ranch; 2.) management practices on the facility that lend themselves to or hinder vaccination programs; 3.) at what times or ages are the disease problems occurring, and are they associated with any stresses; 4.) what immune system components are necessary to afford protection against the various disease; 5.) some basic immunology concepts; 6.) the information that is available on products being considered, and the source and quality of the information.

Challenge

The level of disease challenge and degree of protection fluctuate continuously. Due to biological variability, the level of protection is different in every vaccinated animal. The same is true with the amount of exposure to a pathogen—overwhelming challenge can override the immunity and lead to disease, even in well-vaccinated animals.[18]

Timing of Disease

Many farms have consistent times when certain diseases occur, and the timing may give some insight into stresses that are occurring in management of cattle. Correcting these stresses can have a positive impact on vaccination and lessen disease susceptibility. Furthermore, this history is helpful to determine the timing of vaccinations. This is a concept that is often under-utilized in veterinary medicine. Knowing when a problem has historically occurred will allow vaccinations to be scheduled when they will give maximum immune responses in preparation for anticipated challenges.

Assessing Vaccine Efficacy

Vaccine efficacy can be extremely difficult for the practitioner to assess. Serologic data showing pre- and post-vaccination titers traditionally has been equated to protection but for many diseases, there is a poor correlation between an antibody being measured and the protection generated by the vaccine in the animal.[9]

Cell-mediated immune function tests recently have been added to show a more complete stimulation of the immune response after vaccination.[1] Although this gives more information on the vaccine, it still does not answer the basic question of how well a vaccine really protects. This can only be answered by well-designed challenge studies.

There are many examples of well-designed studies with both viral[3,4] and bacterial[2,8] agents. To assess a challenge study, the following information is needed:

1. Trial design, including animal characteristics
2. Statistical analysis of the results
3. Route of administration of the challenge
4. Characteristics of the challenge organism
5. Method for clinical score assignment
6. Publication of the results in a peer-reviewed article.

For many diseases, the challenge model unfortunately is not well established, or it may be established for only one syndrome associated with a particular pathogen and not other associated syndromes. The syndrome for which efficacy was proven, then, might not be the one for which a vaccine is being used. This makes it extremely difficult to determine the true efficacy of a vaccine or to select one in which the desired protection can be determined. This can be further complicated by lack of vaccine studies performed in younger animals in which maternal antibody may be present. It is well established that maternal antibody is not as all-inclusive blocking of vaccination as once thought.[5,6,10,13,14,16,17] Thus, studies in young calves with pre-existing maternal antibody against a particular disease may be important to look for when designing young calf vaccination programs.

Field trials are even harder to assess but are valuable at answering the effectiveness (i.e. the efficacy in a particular situation) and efficiency of vaccines (cost effectiveness).[12] Several good references on field trial analysis are available.[11,15] As more of these studies become available, it will be essential to perform a good review of the study design and analysis, due to the difficulty of designing appropriate field trials.

Conclusion

Our knowledge of immune function in cattle, and its application to the design of efficacy trials, is developing very rapidly. With herd size increasing in the United States and the disappearance of the closed herd, it becomes incumbent that we critically assess vaccines as we design our vaccination program. Asking these important questions will give new insight into how well these vaccines work. However, since all vaccines have a point in which the protection can be overwhelmed, they are only one component of the biosecurity that must be in place to protect the health of the herd against a major outbreak.

References

1. Abbas AK, Lichtman AH, Pober JS: Antigen presentation and T-cell recognition and molecular basis of T cell antigen recognition and activation. in: Cellular and Molecular Immunology, WB Saunders Co, Philadelphia, Ch 6-7, 115-168, 1991.
2. Bolin CA, Thiermann AB, Handsaker AL, Foley JW: Effect of vaccination with a pentavalent leptospiral vaccine on *Leptospira interrogans* serovar *hardjo* type hardjo-bovis infection of pregnant cattle. Am J Vet Res 50(1):161-165, 1989.
3. Cortese VS, West KH, Hassard LE, Carmen SA, Ellis JA: Clinical and immunologic responses of vaccinated and unvaccinated calves to infection with a virulent type-II isolate of bovine viral diarrhea virus. JAVMA 213(9):1312-1319, 1998.
4. Cravens RL, Bechtol D: Clinical responses of feeder calves under a direct IBR and BVD challenge: a comparison of two vaccines and a negative control. The Bov Pract 26:154-158, 1991.
5. Ellis JA, Hassard LE, Cortese VS, Morley PS: Effects of perinatal vaccination on humoral and cellular immune responses in cows and young calves. J Am Vet Med Assoc 208:393-399, 1996.
6. Forsthuber T, Hualin, CY, Lewhmann V: Induction of T_H1 and T_H2 Immunity in neonatal mice. Science 271:1728-1730, 1996.
7. Hjerpe CA: Bovine vaccines and herd vaccination programs in: Large Animal Internal Medicine, Smith BP, CV Mosby Co., St. Louis, Ch 44, 1486-1500, 1990.
8. Hogan JS, Weiss WP, Todhunter DA, Smith KL, Schoenberger PS: Efficacy of an *Escherichia Coli* J5 mastitis vaccine in an experimental challenge trial. J Dairy Sci 75:415-422, 1992.
9. Kaeberle M: The Elements of Immunity. Large Animal Veterinarian. July/August 1991.
10. Kimman TG, Westenbrink F, Straver PJ: Priming for local and systematic antibody memory responses to bovine respiratory syncytial Virus: Effect of Amount of Virus, Viral Replication, Route of administration and maternal antibodies. Veterinary Immun and Immunopath, 22:145-160, 1989.
11. Meinert CL: Clinical trials; design, conduct and analysis. Oxford University Press, New York, 3-18, 1986.
12. Naggan L: Principles of Epidemiology. Class notes, Johns Hopkins School of Public Health and Hygiene, Summer Graduate Program in Epidemiology, 1994.
13. Parker WL, Galyean ML, Winder JA, Cravens RL: Effects of vaccination at branding on serum antibody titers to viral agents of bovine respiratory disease (BRD) in newly weaned New Mexico calves. Proceedings, Western Section, ASAS 44, 1993.
14. Pitcher PM: Influence of passively transferred maternal antibody on response of pigs to pseudorabies vaccines, Proceedings, AASP 1996.
15. Ribble C: Assessing vaccine efficacy. Can Vet J, Vol 31, 1990.
16. Ridge JP, Fuchs EJ, Matzinger P: Neonatal tolerance revisited: Turning on newborn T cells with dendritic cells. Science 271:1723-1726, 1996.
17. Sarzotti M, Robbins DS, Hoffman FM: Induction of protective CTL responses in newborn mice by a murine retrovirus. Science 271:1726-1728, 1996.
18. Tizard, I: General principles of vaccination and vaccines. in: Veterinary Immunology, An Introduction. 4th ed, WB Saunders Co. Philadelphia. Ch 22. 261-264, 1992.