Vaccinating Dry Cows and Calves: With What, When, and Is It Effective at Protecting the Calf?

Amelia R. Woolums

Department of Large Animal Medicine, College of Veterinary Medicine, University of Georgia, Athens, GA 30602
Email: awoolums@uga.edu

Take Home Messages

- While the neonatal calf has an immune system capable of responding to infection or vaccination, it is naïve and immature compared to the adult immune system. Intake of adequate amounts of colostrum at birth is essential to protect calves from infection while their immune response is maturing and developing the capacity to respond to infection.
- While veterinarians and producers have traditionally understood that calves cannot be vaccinated effectively while they have circulating levels of maternal antibodies from colostrum, recent research indicates that calves vaccinated in the face of maternal antibody can sometimes mount T cell responses to vaccination, and may have improved protection against disease when maternal antibodies have disappeared. This is true even when calves do not seroconvert following vaccination in the face of maternal antibodies.
- Vaccinating cows late in gestation (dry cows) can increase their serum antibody titers and increase the antibody titers in their colostrum, which can lead to increased antibody titers in calves. This should help calves resist disease, although there is little research from properly designed studies proving that vaccination of dry cows decreases disease in calves to an important degree.
- When developing plans to vaccinate calves with circulating maternal antibody, keep in mind the following:
    a. calves are more likely than adults to require booster vaccinations, which should be given at least 2 to 4 weeks after the initial vaccination;
    b. intranasal vaccines may be more effective than injected vaccines in calves with moderate to high concentrations of maternal antibodies;

however, immunity from intranasal vaccines may not last more than a few months;

c. repeated doses of intranasal vaccines may not boost as effectively as repeated doses of injected vaccines;
d. calves with very high concentrations of maternal antibody, such as those found in the first month of life in calves with good passive transfer, may not respond as well to vaccination as calves with moderate to low concentrations of antibody;
e. vaccines should be administered so that the final dose is given no later than 1-2 weeks before the expected exposure of the group to infectious agents.

■ Impacts On Preweaning Calf Immunity

Peripartum Cortisol Surge

Serum cortisol concentration is increased in calves from approximately 10 days before parturition to 10 days after parturition, and serum concentrations on the day of birth are 10 to 20 times higher than those in normal cattle. Because cortisol can impair immune responsiveness, it is likely that this peripartum cortisol surge suppresses immune responsiveness. However, little research has assessed this, and the available research results do not distinguish the effect of the peripartum cortisol surge from the effect of early age, which also causes a degree of diminished immune responsiveness. The responses of blood lymphocytes of calves to stimulation over the first 7 days of life are relatively decreased from day 1 through 4, relative to the day of birth and days 5 through 7 (data from Kehrli, in Cortese 2009). However, calves in the first day or two of life have been shown to be capable of mounting a useful immune response. Calves vaccinated against tuberculosis at 8 hours of age were protected against disease due to experimental challenge when they were 15 weeks old (Buddle et al., 2003). Also, colostrum-deprived calves exposed to coronavirus at 1 day of age developed immunity that protected them from disease when they were exposed again at 3 weeks of life (Heckert et al., 1991). Therefore, while the peripartum cortisol surge likely has some relatively negative impact on immune responsiveness for at least a short time, it is clear that calves in the first day or two of life can mount useful immune responses to at least some stimuli. The presence of passively acquired immunity can impact this response, as will be discussed below. Thus, vaccination in the first week of life is more likely to be effective in calves with partial or total failure of passive antibody transfer. However, there is not enough evidence to demonstrate which day in that first week of life is the best day for vaccination when it is indicated; more research is needed to answer this question.

Calf Age

Numerous studies have shown that various immune responses in calves are decreased or weaker when compared to the same response in adult cattle. Responses that have been shown to be decreased or weaker include neutrophil and macrophage phagocytosis, T cell responses to stimulation, antigen presenting cell activity, and serum complement concentration. In general immune responses become comparable to adult responses when calves are 5 to 8 months of age. There are some responses in young calves that are superior to those in older cattle; for example, natural killer (NK) cells of 3- to 8 day-old calves were more cytotoxic and produced more interferon gamma in response to stimulation than NK cells from 4- to 10-month-old calves (Elhmouzi-Younes et al., 2009). Similar differences in NK cell function in human neonates as compared to older humans have been observed, and it has been speculated that these innate immune cells have improved activity in order to protect the neonate while acquired immune responses are sub-optimally protective. Repeated exposure to infectious agents early in life stimulates maturation of immune function; this is in part why booster vaccinations are particularly important for young animals.

Nutrition

Adequate nutrition is well known to be necessary for adequate immune responses to occur in cattle. In general, supplementing diets that are deficient in protein, energy, vitamins, or minerals has been shown to improve immune responses to vaccination and other stimulation. However, treatment of cattle with vitamins and minerals in excess of required levels has not reliably led to important improvements in immune response (reviewed in Galyean et al., 1999). With specific reference to neonatal calves, newborn Holstein calves fed at 50% of maintenance requirements for protein and energy for the first month of life had decreased lymphocyte responses and decreased ability to produce antibody following vaccination, as compared to calves fed at maintenance requirements (Griebel et al., 1987). Because these investigators fed calves 50% of their requirement of milk replacer but did not correct for deficiencies of vitamins and minerals that may have occurred in underfed calves, vitamin and mineral deficiency may have also impacted immune responses in the calves in this study. Another study showed that calves fed over the first 8 weeks of life at a rate intended to support no growth, low growth, or high growth had no impact on immune responses during that period (Foote et al., 2007). This study showed that a high plane of nutrition inducing a high rate of growth did not improve immune responses. In other research, lymphocytes from calves fed an intensified milk replacer (30% crude protein and 20% fat, fed at 2.5% of body weight on a dry matter basis per day) produced less interferon gamma and more nitric oxide following stimulation, as compared to calves fed a standard milk replacer diet (20% crude protein and 20% fat fed at 1.4% body weight of dry matter per day) (Nonnecke et al., 2003). As calves aged, lymphocytes from calves fed an intensified milk replacer diet did not respond to stimulation to the same degree as calves fed a standard milk replacer (Foote et al., 2005). The importance in these differences is not yet clear, but the research does indicate that diet can have effects on immune response of calves that are sometimes different than might be predicted.

Passive Antibody Transfer from Colostrum

Adequate transfer of passively acquired antibody from colostrum is arguably the most important factor influencing preweaning calf immunity. Many studies have shown that calves with failure of passively acquired antibody transfer are more likely to become ill or die before weaning, and to fail to reach productivity equivalent to their peers with adequate passive antibody transfer. In addition to antibody, other soluble factors such as lactoferrin and cytokines, and maternal cells, likely have an important impact on immune development, although less is known about the importance of these substances as compared to antibody. Research evaluating serum antibody concentrations in beef calves in the first week of life have indicated that the percent of calves with failure of passive transfer in conventionally managed herds ranges from 6% to 23% (Perino et al., 1995; Filteau et al., 2003; Dewell et al., 2006; Waldner and Rosengren, 2009). In these studies calves were 2 to 6 times more likely to be treated for disease before weaning, and 5 times more likely to die before weaning, as compared to herdmates with adequate or partial passive transfer. Calves at particular risk of having low levels of passive antibody transfer include calves of heifers, calves of thin heifers, calves experiencing dystocia, twins, and calves with metabolic acidosis (usually from peripartum hypoxia associated with dystocia). In some studies higher concentrations of serum immunoglobulins than are traditionally considered adequate were best associated with calf health (Dewell et al., 2006; Waldner and Rosengren, 2009); this supports the concept that, within reason and physiologic limits, at-risk calves should be given as much colostrum as possible. If the dam does not have much or any colostrum, colostrum replacers (not supplements) can be a useful substitute. Some replacers that have been shown through research to support adequate passive transfer or calf health include Land O'Lakes IgG Colostrum Replacement, Calf's Choice Total™ (Saskatoon Colostrum Company, through Alta Genetics), and Secure® (Vita Plus). Replacers that have been effective have 100 to 150 grams of globulin per dose. In some studies 2 doses were needed to support adequate passive transfer, which may be cost prohibitive for some producers. Colostrum supplements do not have adequate concentrations of immunoglobulin to provide adequate passive transfer and should not be used for this purpose.

■ Vaccinating Dry Cows To Improve Health Of Calves

Vaccinating cows late in gestation is sometimes considered as a mechanism to improve calf immunity by increasing calf serum concentrations of passively transferred antibody. This is rational because antibody from the cow's serum is transferred into colostrum in the last month or two of gestation. If a cow's serum antibody titers are increased late in gestation, it follows that colostral antibodies should be increased, and serum antibodies in the calf consuming the colostrum should be increased. While this train of reasoning is logical, relatively little research has confirmed whether vaccinating cows late in gestation improves calf antibody titers, and less has confirmed whether the practice improves resistance of calves to disease. Vaccination of dairy cows with a commercial clostridial vaccine at 6 and 2 weeks before calving significantly increased anti-clostridial antibody titers in calves at 3 days of age (Fleenor and Stott, 1983). Similarly, vaccination of dairy cows with a *Mannheimia haemolytica* vaccine (Presponse®) at 6 weeks and 3 weeks before calving increased antibody titers to *M. haemolytica* in calf serum at 2 – 7 days of age (Hodgins and Shewen, 1994). In a third study, vaccination of beef cows with a *M. haemolytica/H. somni* vaccine at either 4 weeks before calving or 7 and 4 weeks before calving increase serum antibody titers in calves at 28 day of age (Van Donkersgoed et al., 1995). Although all of these studies showed that vaccination of cows in late gestation increased serum antibodies in calves, none evaluated whether disease was decreased in calves. A small study evaluating whether a single dose of inactivated multivalent viral respiratory vaccine given to dairy cows at dry off would increase antibody titers in calves at 2 – 7 days of age showed no effect of vaccination (Osterstock et al., 2003). Two trials evaluated vaccination of late gestation cows to decrease calf diarrhea, with one showing a beneficial effect (Cornaglia et al., 1992), and one showing no effect (Waltner-Toews et al., 1985). In summary, a small number of studies have shown that vaccinating cows late in gestation can improve antibody titers in calves, but more research is necessary to confirm that the practice can decrease disease in calves.

■ Vaccination Of Calves In The Face Of Maternal Antibody

Historically veterinarians have been taught that young calves cannot be effectively vaccinated because maternal antibodies would block vaccine responsiveness. However, many studies have shown that calves can at times have a useful immune response to vaccines given in the face of maternal antibodies. Vaccination of calves with maternal antibodies has been shown to induce an anamnestic (memory) response when they are boosted later in life (Menanteau-Horta et al., 1985); vaccination can prolong the persistence of antibodies (Fulton et al., 2004), and vaccination can prime for T cell responses even when calves do not seroconvert (Ellis et al., 1996). Intranasal vaccination may be superior to parenteral vaccination in calves with high concentrations of circulating antibodies (Kimman et al., 1989); however, the duration of immunity provided by intranasal vaccination of calves with circulating maternal antibodies may not be long lived. A recent study showed that calves vaccinated intranasally with a modified-live BRSV vaccine developed disease following BRSV challenge at 4.5 months after vaccination (Ellis et al., 2010). In general, vaccination of calves with circulating maternal antibodies has been most effective when calves receive 2 doses of vaccine. Modified-live virus vaccines have most often been used successfully to vaccinate calves with maternal antibody. While more variable, some inactivated vaccines have been effective (see review in Woolums, 2007). Vaccination of calves in the first month of life, when maternal antibodies are highest and the calf's immune system is the most immature, is the least likely to be reliable. For example, a large clinical trial recently showed that vaccination of calves with maternal antibodies at 2 and 5 weeks of age did not decrease respiratory disease in the first 90 days of life (Windeyer et al., 2012).

■ Conclusions

Preweaning calf immunity is the sum of positive and negative impacts that include the peripartum cortisol surge associated with the onset of parturition, the concentration of passively acquired antibody from colostrum, the age of the calf, calf nutrition, concurrent stresses such as new introductions, castration/dehorning, and transport; concurrent disease, and the rate of exposure to infectious agents through natural infection or vaccination. The net effect of these impacts is dependent on the timing at which they occur. To optimally manage calf immunity, the goal is to allow exposure to infection or vaccination that induces maximal immune stimulation with minimal disease. The optimal time for this will vary for different operations, based on a variety of management factors, and the infectious agent in question.

■ References

Buddle, B.M., D.N. Wedlock, N.A. Parlane, L.A.L. Corner, G.W. de Lisle and M.A. Skinner. 2003. Revaccination of neonatal calves with *Mycobacterium bovis* BCG reduces the level of protection against bovine tuberculosis induced by a single vaccination. Infect. Immun. 71:6411-6419.

Cornaglia, E.M., F.M. Fernandez, M. Gottschalk et al. 1992. Reduction in morbidity due to diarrhea in nursing beef calves by use of an inactivated oil-adjuvanted rotavirus-Escherichia coli vaccine in the dam. Vet. Microbiol. 30:191-202.

Cortese, V.S. 2009. Neonatal Immunology. Vet Clin Food Anim 25:221-227.

Dewell, R.D., L.L. Hungerford, J.E. Keen, W.W. Laegreid, D.D. Griffin, G.P. Rupp and D.M. Grotelueschen. 2006. Association of neonatal serum immunoglobulin G1 concentration with health and performance in beef calves. J. Am. Vet. Med. Assoc. 228:914-921.

Elhmouzi-Younes, J., A.K. Storset, P. Boysen, F. Laurent and F. Drouet. 2009. Bovine neonate natural killer cells are fully functional and highly responsive to interleukin-15 and to NKp46 receptor stimulation. Vet. Res. 40:54-68.

Ellis, J.A., L.E. Hassard, V.S. Cortese and P.S. Morley. 1996. Effects of perinatal vaccination on humoral and cellular immune responses in cows and young calves. J. Am. Vet. Med. Assoc. 208:393-400.

Filteau, V., É. Bouchard, G. Fecteau, L. Dutil and D. DuTremblay. 2003. Health status and risk factors associated with failure of passive transfer of immunity in newborn beef calves in Québec. Can. Vet. J. 44:907-913.

Fleenor, W.A. and G.H. Stott. 1983. Quantification of bovine IgG, IgM and IgA antibodies to *Clostridium perfringens* B-toxin by enzyme immunoassay. Preparturient immunization for enhancement of passive transfer of immunity. Vet. Immunol. Immunopathol. 4:579-591.

Foote, M.R., B.J. Nonnecke, M.A. Fowler, B.L. Miller, D.C. Beitz and W.R. Waters. 2005. Effects of age and nutrition on expression of CD25, CD44, and L-selectin (CD62L) on T-cells from neonatal calves. J. Dairy Sci. 88:2718-2729.

Foote, M.R., B.J. Nonnecke, D.C. Beitz and W.R. Waters. 2007. High growth rate fails to enhance adaptive immune responses of neonatal calves and is associated with reduced lymphocyte viability. J. Dairy Sci. 90:404-417.

Fulton, R.W., R.E. Briggs, M.E. Payton, A.W. Confer, J.T. Saliki, J.F. Ridpath, L.J. Burge and G.C. Duff. 2004. Maternally derived humoral immunity to bovine viral diarrhea virus (BVDV) 1a, BVDV 1b, BVDV2, bovine herpesvirus-1, parainfluenza-3 virus, bovine respiratory syncytial virus, *Mannheimia haemolytica* and *Pasteurella multocida* in beef calves, antibody decline by half-life studies and effect on response to vaccination. Vaccine. 22:643-649.

Galyean, M., L.J. Perino and G.C. Duff. 1999. Interaction of cattle health/immunity and nutrition. J. Anim. Sci. 77:1120-1134.

Griebel, P.J., M. Schoonderwoerd and L.A. Babiuk. 1987. Ontogeny of the immune response: effect of protein energy malnutrition in neonatal calves. Can. J. Vet. Res. 51:428-435.

Heckert, R.A., L.J. Saif, J.P. Mengel and G.W. Myers. 1991. Isotype-specific antibody responses to bovine coronavirus structural proteins in serum, feces, and mucosal secretions from experimentally challenge-exposed colostrum-deprived calves. Am. J. Vet. Res. 52:692-699.

Hodgins, D.C. and P.E. Shewen. 1994. Passive immunity to *Pasteurella haemolytica* A1 in dairy calves: effects of preparturient vaccination of the dams. Can. J. Vet. Res. 58:31-35.

Kimman, T.G., F. Westenbrink and P.J. Straver. 1989. Priming for local and systemic antibody memory responses to bovine respiratory syncytial virus: effect of amount of virus, virus replication, route of administration and maternal antibodies. Vet. Immunol. Immunopathol. 22:145-160.

Menanteau-Horta, A.M., T.R. Ames, D.W. Johnson and J.C. Meiske. 1985. Effect of maternal antibody upon vaccination with infectious bovine rhinotracheitis and bovine virus diarrhea vaccines. Can. J. Comp. Med. 49:10-14.

Nonnecke, B.J., M.R. Foote, J.M. Smith, B.A. Pesch and M.E. Van Amburgh. 2003. Composition and functional capacity of blood mononuclear leukocyte populations from neonatal calves on standard and intensified milk replacer diets. J. Dairy Sci. 86:3592-3604.

Osterstock, J.B., R.J. Callan and D.C. Van Metre. 2003. Evaluation of dry cow vaccination with a killed viral vaccine on post-colostral antibody titers in calves. Proc. Am. Assoc. Bov. Pract. 36:163-164.

Perino. L.J., T.E. Wittum and G.S. Ross. 1995. Effects of various risk factors on plasma protein and serum immunoglobulin concentrations of calves at postpartum hours 10 and 24. Am. J. Vet. Res. 56:1144-1148.

Van Donkersgoed, J., C. Guenther B.N. Evans, A.A. Potter and R.J. Harland. 1995. Effects of various vaccination protocols on passive and active immunity to *Pasteurella haemolytica* and *Haemophilus somnus* in beef calves. Can. Vet. J. 36:424-429.

Waldner, C.L. and L.B. Rosengren. 2009. Factors associated with serum immunoglobulin levels in beef calves from Alberta and Saskatchewan and association between passive transfer and health outcomes. Can. Vet. J. 50:275-281.

Waltner-Toews, D., S.W. Martin, A.H. Meek, I. McMillan and C.F. Crouch. 1985. A field trial to evaluate the efficacy of a combined rotavirus-coronavirus/*Escherichia coli* vaccine in dairy cattle. Can. J. Comp. Med. 49:1-9.

Windeyer, M.C., K.E. Leslie, S.M. Godden, D.C. Hodgins, K.D. Lissemore and S.J. LeBlanc. 2012. The effects of viral vaccination of dairy heifer calves on the incidence of respiratory disease, mortality, and growth. J. Dairy Sci. 95:1-9.

Woolums AR. 2007. Vaccinating calves: new information on the effects of maternal immunity. Proc. Am. Assoc. Bov. Pract. 40:10-17