IMMUNITY IN NEONATAL CALVES

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Categories : Vets

Date : January 28, 2013

ADAM MARTIN examines the immune defences in newborn calves and the important role of passing on components through the dam’s colostrum

A GENERAL misconception exists that, when born, the neonatal animal’s immune system is incompletely developed. However, the susceptibility of neonatal animals to pathogens has more to do with the fact their immune defences are unprimed, rather than an inherent inability to mount an immune response (Cortese, 2009).

The epitheliochorial placentation present in ruminants exacerbates this problem in neonatal ruminants because transplacental exchange of white blood cells and immunologically active proteins, such as antibodies, does not occur. This increases the importance of innate and passively transferred immunity in neonatal domesticated ruminants.

Generally, thoughts of reduced immunity in the neonatal period are confined to the reduced ability of lymphocytes to produce antibodies in response to non-self antigen exposure, combined with the fact the animals are born agammaglobulinaemic. However, the neonate has reduced specific and non-specific immune mechanisms. The reasons for this are complicated, but are, at least in part, associated with high postpartum cortisol levels and other immunomodulators as the neonate adapts to life postpartum.

Neonates generally have higher numbers of phagocytes compared to adults. However, these phagocytes have a comparatively reduced function for several months compared to adults. The same is true when natural killer cell function is assessed. Reduced complement activity and reduced interferon production also act to limit the ability of a neonate to mount a non-specific immune response. Despite this, it is the antibodies in colostrum that are of most immediate importance to the survival of the neonate.

Immunoglobulins

Colostrum is defined simply as the initial secretions from the mammary gland postpartum. It is a complex nutrient-rich product that has typically taken several weeks to manufacture. Immunoglobulins are one of the major components of colostrum. Approximately 75 per cent of these found in colostrum are of the class immunoglobulin G (IgG), with the remaining 25 per cent largely consisting of equal numbers of immunoglobulin A (IgA) and immunoglobulin M (IgM).

During colostrogenesis in the cow, approximately 500g of immunoglobulins can be transferred from the bloodstream of the dam in its mammary secretions. This transfer is considerable and, after weeks of colostrogenesis, the dam’s level of circulating antibodies has generally decreased significantly, which is one of the reasons for its increased susceptibility to disease in the peripartum period.

Calves that either consume or receive colostrum shortly after birth have significant detectable levels of antibodies present in their blood within hours. In contrast, colostrumdeprived calves have only trace levels of antibodies in their blood for the first three days of their life. Appreciable increases in antibody levels begin on day four. However, functional antibody levels are not reached until day eight.

IgM is the first antibody to be produced by calves. It is produced by B cells and is a large and complex antibody, which, due to its size, primarily remains in the bloodstream. This class of immunoglobulin is particularly effective at stimulating complement release, although, by itself, is a relatively poor opsonin. Smaller, more mobile immunoglobulins, such as IgA and IgG, do not reach significant levels until 16 to 32 days, and take around four months to reach adult levels. IgA is the class of antibodies that defend the mucous membranes. While IgG are most frequently located in the bloodstream and extracellular fluid, these are mobile antibodies capable of moving throughout the body in response to infection. The nature of immunological challenges, which neonates are often exposed to, mean that having appreciable levels of IgA and IgG are essential to protect the individual.

Nutritional value

In addition to immunoglobulins, colostrum has a number of important components – nutritional and otherwise. Colostrum has a high nutritional value and this should not be forgotten when considering neonatal health in animals. Colostrum is an essential source of readily digestible energy that can be of particular importance to small neonates, such as lambs, which are often born into, and live, in an environment below their lower critical temperature. In these circumstances, hypothermia is a real risk to neonatal survival. As it is known the fat content of colostrum can be manipulated by altering the diet of the dam in the weeks preceding partum, under certain circumstances it may be worth considering a feeding strategy that would increase the colostral fat content, thus improving a neonate’s ability to thermoregulate.

Colostral proteins, other than immunoglobulins, play an important role in early development. Interestingly, many vitamins (such as A, D and E) and minerals do not cross the placenta and the neonate is, therefore, entirely dependent on colostrum to supply these early in life. Selenium, however, does manage to make it into the foetus.

Non-nutritional components

A number of important nonnutritional components are believed to play a major role in the initial development and metabolism of newborn animals. These include insulin-like growth factors type one and two, and a number of other growth factors.

Hormones, including insulin, cortisol and thyroxine, are also present in colostrum, although their significance, if any, has yet to be identified. Cytokines are also present in colostrum. The neonate has a reduced complement, interferon and phagocyte production/function, when compared to a mature animal. Neonates that ingest colostrum have a sudden and dramatic increase in their ability to phagocytise bacteria. Work performed in pigs (Nguyen et al, 2007) showed colostral cytokines are absorbed into the bloodstream and that cytokines absorbed from colostrum also have a role in reducing the local secretion of proinflammatory compounds in the intestines, which allows microbial colonisation of the gut to occur.

Colostrum generally contains between 1×10^6 cells/ml and 3×10^6 cells/ml. These cells are almost exclusively leukocytes (approximately 45 per cent macrophages, 30 per cent lymphocytes and 25 per cent neutrophils). Animals receiving colostrum that contains leukocytes develop antigen-presenting cells faster than those that receive colostrum without cells. This is important, as antigen-presenting cells are essential components of acquired immunity to specific pathogens.

There can be no doubt the two single most important factors affecting a calf or lamb’s acquisition of passive immunity from colostrum are the volume of colostrum ingested and the time after birth it was ingested. Repeated surveys have shown inadequate passive transfer of immunity is common and occurs in more than 30 per cent to 40 per cent of calves if good routines are not in place to ensure appropriate colostrum intake.

At birth, a calf’s intestinal epithelium allows for the uptake of immunoglobulins and cells by pinocytosis. At six hours old, this capacity has halved. After eight hours only a third remains, and it is no longer possible 24 hours after birth. Thus, provision of a substantial feed of colostrum (two to four litres for a calf) within the first couple of hours after birth is essential.

Colostral quality has increasingly received attention as it is now known that less than half of dairy cows produce colostrum deemed to be of adequate quality. The vaccination of cows is frequently used in an attempt to increase colostral antibody levels – generally against a specific pathogen. The prevention of calf diarrhoea and sheep clostridial disease would be two good examples of this. However, some caution should be exercised before this approach is employed, as at least one study has shown vaccination caused a decrease in colostral antibodies. Thus, before using prepartum vaccination, it is wise to request data that adequately demonstrates using the product will have the desired effect.

The method of feeding and physiological state of the neonate also affects the efficiency of immunoglobulin uptake. It is known this uptake is better when calves are allowed to suck naturally – worse when bottle fed and lowest after tube feeding. However, as the primary measures of success are volume and timing, it is far more important to provide an adequate volume of colostrum at the correct time with a tube feeder than wait many hours for the calf to suck for itself.

Calves suffering from acidaemia also have less efficient absorption of immunoglobulins than calves with normal blood pH levels. Practically, this means extra attention and care should be given to all neonates born after dystocia, particularly as they are likely to take longer to stand up and locate their dam's teats.

Successful passive transfer of immunity from dam to neonate – while essential to the survival of the calf, and absolutely our primary goal of the first few hours of life – can also negatively interfere with the neonate's ability to mount an immune response. This can pose specific practical problems when planning an efficient vaccination programme for neonatal animals.

A number of protocols advocated involve vaccinating neonates weekly, or almost weekly. However, evidence exists from other species that this can actually lead to antigen tolerance or autoimmunity. Generally, the process – from initial vaccination to achieving homeostasis – takes at least three weeks. Time enough for the development of a primary response, and the culling of B and T cells that failed to respond adequately. This then allows for a booster to be given, which should cement a true anamnestic secondary response (Chase et al, 2008).

References

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