Neonatal Immunity in Cattle

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Introduction

Neonatal mortality associated with infection by a variety of pathogens is a major problem in the cattle industry. The increased susceptibility of the newborn calf to disease is primarily associated with its immunologic status at birth. Management practices before and at the time of parturition represent major determinants in the survival capacity of the newborn ruminant. This article will review some of the main characteristics of the immune system of the newborn calf as well as possible strategies that are available for the prevention of neonatal morbidity and mortality.

The bovine immune system

The immune system consists of cellular and humoral factors involved in cellular and humoral immunity.[15 16 80] The main cellular components of the immune system are the lymphocytes and macrophages. Although all lymphocytes appear to be similar morphologically, they are quite different in their functional characteristics. According to their site of origin and functional capacities, two major subpopulations of lymphocytes are recognized, namely the T lymphocytes and the B lymphocytes[80]. The T lymphocytes develop from stem cells under the influence of the thymus, while the B lymphocytes develop in the fetal liver and bone marrow.[66 67]

Due to their important role in regulating the production and differentiation of lymphocytes the thymus, the fetal liver and the bone marrow are designated as primary lymphoid organs. During their development the B and the T lymphocytes will leave their site of primary differentiation to localize at specific sites in the secondary lymphoid organs. The main function of the secondary lymphoid organs is to facilitate trapping of foreign material or antigens, to process these antigens and to mediate the clonal expansion of effector lymphoid cell populations. The secondary lymphoid organs will therefore provide a suitable environment for efficient interaction between antigen sensitive B and T lymphocytes, macrophages and antigens. Appropriate cell interaction will result in the production of either mature plasma cells secreting specific antibodies which represents the humoral arm of the immune response or specific effector T lymphocytes which represents the cellular arm of the immune response.

Based on morphologic and functional features, the secondary lymphoid organs are further subdivided into local and systemic sites. The systemic immune system consists of the peripheral lymph nodes, the spleen and hemal lymph nodes. In contrast the local immune system is represented by the lymphoid tissue lining the mucosal surfaces together with their associated lymph nodes.[7 47]

The primary function of the systemic immune system is the elimination of infectious agents or antigens that have gained access to the blood stream or interstitial tissues of the host. Conversely, the local immune system is responsible for preventing or stopping infectious agents or antigens from gaining access to the general circulation. Examples of lymphoid tissue involved in local immunity are the gut associated lymphoid tissue (GALT) and mesenteric lymph nodes, the bronchus associated lymphoid tissue (BALT) and bronchial lymph nodes, the organized lymphoid tissue scattered along the lamina propia of the gut, respiratory tract and genitourinary tract mucosae, the salivary glands, the lacrimal glands and ocular mucosa and finally the mammary glands.[30 55 61]

When examining those two systems, there appears to be some degree of compartimentalization.[62] As a result these two branches of the immune system will often function independently from one another. Thus, following an infection localized at the level of the host intestinal or respiratory tract mucosa a good local immune response may become apparent without evidence of serum or systemic response. The reverse is also possible, for example, following parenteral immunization the host may develop a good systemic response without evidence of local immunity to the antigen that was used for the parenteral immunization. Segregation of immune responses within the systemic or the local immune system is seen with both arms of the immune response, the cellular as well as the humoral arm.

Recent developments in the field of cellular immunology have yielded some evidence as to the heterogeneity of the lymphocyte population. Thus, the T cell population can be subdivided into two broad categories, the effector T cells and the regulator T cells. The effector T cells consists of those T cells that are responsible for various cell mediated immune reactions. They include T cells that mediate cytotoxic functions. The cytotoxic T lymphocytes (CTL) and T cells responsible for delayed type hypersensitivity reactions (T_{DTH}). The cytotoxic T lymphocytes play a major role in

recovery from viral infections by specifically destroying the virus infected cells.[65] Conversely the T delayed type hypersensitivity cells (T_{DTH}) cause non-specific increased resistance to many infectious agents, particularly those that act as intracellular parasites such as *Mycobacterium* sp., *Brucella* sp., *Listeria* sp. and *Salmonella* sp. These cells are also involved in graft rejection and hypersensitivity reactions to many chemicals and drugs.

The second major group of T cells, the regulator T cells, are those T cells which are capable of regulatory functions. They are either called T helper or T suppressor cells and they are responsible for controlling the magnitude of the response to specific antigens during the development of the immune response. In this respect, the differentiation of other lymphoid cells such as the B lymphocytes or the T effector cell subsets will either be helped or suppressed by the regulator T cells.

In summary, available data suggest that for a humoral immune response to occur the antigen first has to be trapped by the macrophage located in the secondary lymphoid tissue The macrophage will then process and present the immunogen to the circulating antigen sensitive B and T helper cells. Following the secretion of soluble factors called lymphokines by the T helper cells, the B cells will start to proliferate and mature into antibody forming cells, the plasma cells. The resulting clone of daughter B cells which are committed to synthesize and secrete immunoglobulin with antibody activity specific for the antigen will then be responsible for the humoral immune response of the host.

The immunoglobulin molecule consists of two heavy and two light chains. The heavy chains determine the class of the immunoglobulin and in combination with the light chains form the antigen combining sites of the immunoglobulin molecule. This portion of the immunoglobulin molecule which varies tremendously determines the specificity of the antibody for a particular antigen that has initiated its production. The antigen combining site of the antibody molecule is therefore called the variable region, whereas the opposite end of the immunoglobulin molecule which consists only of the heavy chains is called the constant region or the Fc (crystallizable fragment) portion of the immunoglobulin molecule. The constant region of the immunoglobulin molecule is in part responsible for the capacity to fix complement.

Four classes of immunoglobulin are present in bovine serum: the IgG, the IgM, the IgA and the IgE[16]. In the mucosal secretions of the adult bovine we find mostly IgG, and SIgA antibodies.[15 16]

The concentration of serum immunoglobulin varies with age, breed, and the degree of stimulation of the immune system following either vaccination or infection. The calf will show a gradual increase in serum immunoglobulin from birth to 3 to 5 months of age at which time it will reach adult concentrations of serum immunoglobulin.[16]

If we examine the main classes of immunoglobulins in cattle and describe some of their particularities and functions, we first recognize the IgG. The IgG antibodies are the most prevalent immunoglobulins in the blood and interstitial fluid. They represent 90% of the total serum immunoglobulins and their half-life in serum is approximately 20 days.

Two subclasses of IgG are recognized; IgG_1 and IgG_2 with the majority of the IgG's being IgG_1. They are synthesized primarily by plasma cells found in the systemic sites and play a major role in the phagocytosis of bacteria and neutralization of viruses. They are also capable of fixing complement. Three to five weeks before parturition massive amounts of IgG_1 are selectively transported into the mammary secretions where they serve as the major source of antibodies in the colostrum[15 16 17 21 44] (Fig 1). It has been reported that up to 500 gms of IgG_1 are transferred to the mammary gland each week during the last 3 weeks of gestation in the cow.[12] This explains why during the last few weeks of gestation the total serum IgG_1, level in the cow may decrease by 50%.[12 21 45 79 85] The selective transport of IgG_1 molecules into the colostrum is mediated by the presence of specific receptors for the Fc portion of the IgG_1 antibody molecule on the cell surface of the glandular epithelium of the mammary gland.[31 39 71]

The IgM antibodies represent about 10 to 12% of the total serum immunoglobulins and are characteristic of the initial antibody response to an antigen. They consist of a polymer of 5 immunoglobulin molecules attached by covalent and noncovalent bonds to a glycoprotein called the J chain (J stands for joining). They have the capacity to fix complement and represent the best agglutinating antibody. Their half-life in serum is approximately four days.[15]

The IgA antibodies make up approximately 3% of the total serum immunoglobulins. Most of them originate from plasma cells located along the mucosa of the small intestine.[8 46] In bovine serum the majority of the IgA antibodies consists of dimers of 2 IgA molecules attached by a J chain.[15] They have a half-life of 2 to 3.5 days in circulation. The greatest concentration of IgA antibodies is found in the secretions such as colostrum, milk, saliva, tears and secretions of the upper airways, urogenital and intestinal tracts.[53] Together with the IgG_1 the IgA antibodies represent the major immunoglobulin isotypes present in colostrum and milk (Fig 1)[17 29].

At the level of the mucous membranes the dimeric IgA antibodies are synthesized and secreted by plasma cells found in the lamina propria. As the dimeric IgA molecules are produced and accumulate in the interstitial space they are selectively transported through the epithelial cells lining the mucosa. The IgA dimers reach the luminal side of the lining epithelium via their attachments to an epithelial cell surface membrane receptor. After being transported through the epithelial cell the receptor is cleaved and the dimers of IgA antibody are released in the form of secretory IgA molecules which have an extra glycoprotein called the secretory component (SC). The SC is synthesized by the epithelial cells lining the mucosa and it acts as a specific

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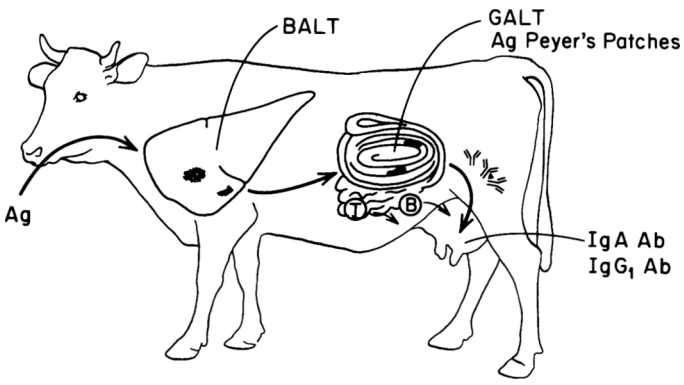
Figure 1. Selective transport of humoral immunity from mucosal sites into the colostrum.



receptor for the transport of the dimeric IgA molecule across the epithelium into the secretions.[41 42]

In addition to acting as a receptor for the transport of the IgA dimer the SC increases the resistance of the SIgA antibodies to the action of the proteolytic enzymes present on the surface of the mucous membranes, especially the gut. The SIgA antibodies play an important role in the regulation of the microbial flora present at the mucosal surfaces by preventing the adherence and colonization of the mucous membranes by microorganisms to which they are specifically directed.

Neonatal immunity in bovine animals

With this review of the current concepts of bovine immunology as a background the factors that makes the bovine neonate unusually susceptible to disease can be examined.

A number of factors associated with either specific or non-specific defense mechanisms are lacking in the neonate. Two factors are of particular importance: firstly the functional capacity of the mucosal surfaces and secondly the status of the immune system of the neonate ruminant.

The mucosal surfaces of the gastrointestinal and respiratory systems are bathed throughout fetal life with sterile amniotic fluid. *In utero* the lung acts as a secretory organ whereas the intestine has a fluid absorptive function. A major change occurs at birth since the lungs are required to perform gaseous exchanges and the intestine has to digest and absorb large quantities of nutrients.

The mucous membranes of the neonate are in direct contact with the environment. They are completely lacking a normal microbial flora which by itself is an important non-specific protective mechanism, especially for the gastrointestinal tract. In addition, during the first 24 hours of life the gastric pH of the newborn ruminant is near neutral and few parietal cells can be seen within the abomasal lining mucosal epithelium.[9 25 33 84] There is also a reduced intestinal digestive capacity at birth and the absorptive activity of the gut epithelium is unusually receptive to the uptake and transport of macromolecules from the lumen to the circulatory system.[11 14 23 34 35 40 71]

Those physiologic factors present in the gastrointestinal tract of the newborn are essential for the absorption of colostral immunoglobulins. However, dependent upon the level of environmental contamination, variable numbers of microorganisms will have direct access to the intestinal mucosa for colonization.[84] Therefore, at the time of birth and for the first 12 hours of life, the mucosal surfaces of the neonate appear exquisitely susceptible to the presence of any pathogenic organism.

As far as the status of the immune system is concerned, the newborn calf is deficient in both cellular and humoral components of the systemic and local immune systems.[18 37 63 68]

Since there is no transplacental transfer of immunoglobulins from the maternal to the fetal circulation in ruminants, the newborn calf is born agammaglobulnemic.[10 51] All of the systemic and local humoral immunity of the newborn is therefore dependent upon the passive transfer of maternal antibodies through the colostrum. The cells lining the mucosa of the small intestine of the newborn are capable of nonselective absorption of colostral immunoglobulin for the first 24 hours after birth[14 20 33]. The greatest absorption occurs in the first few hours after birth and declines thereafter [14 18]. Factors regulating the absorptive process are poorly understood.

The local immune system represented by the lympoid cells scattered along the lamina propria of the mucosal surfaces is absent at birth.[36] Some IgA and IgM containing plasma cells will begin to infiltrate the lamina propria of the enteric mucosa only 3 or 4 days after birth.[3] The IgM producing plasma cells will predominate during the first week of life followed by the IgA producing cells after the first month. In other words, the mucosal IgA system is absent at birth and will slowly mature during the first 30 days of life.

The cellular components of the immune system are also markedly reduced in functional capacity and degree of development. Thus, the peripheral blood lymphocytes of the newborn consists of almost 90% T cells with very few B cells in circulation.[83] The number of B cells in circulation gradually increases until at 20 weeks of age when values similar to adult levels are reached.[83]

A marked increase in serum cortisol levels is seen in the newborn ruminant usually beginning 10 to 15 days before parturition and persisting 10 to 12 days after birth.[2 6 22 50 68 91] This production of cortisol by the fetal adrenal is a normal physiologic event in the initiation of parturition in ruminants. However, in addition to triggering parturition, the high serum cortisol levels causes a marked change in the

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leukocyte parameters of the newborn.[18 22 38 43 68] Those changes which are consistent with a stress pattern are characterized by a marked neutrophilia together with an eosinopenia, a lymphopenia and a variable monocyte response. The lymphocyte: neutrophil ratio, which is about 0.6 to 0.7 at birth, will not reverse until the fourth day after birth.[22 38] Even though the absolute number of circulating polymorphonuclear leukocytes is increased in newborn calves, these cells do not function as do those in the adult.[43 54 66 67]

In addition to being lymphopenic, colostrum fed newborn calves show some degree of suppression of the cell mediated response to mitogens.[18 68 77] The cytotoxic capacity of peripheral blood lymphocytes from newborn lambs appears similarly reduce during the neonatal period.[28]

Another important component of the humoral defense mechanism is represented by the complement system. The complement activity of the newborn ruminant is about half of that of the adult at birth and decreases even further to one fourth of the adult level 24 hours after the ingestion of the colostrum.[66 67 76] Adult levels of complement activity will not be reached until at least 1 to 2 months after birth.[63 76] Since the complement system is important for opsonization and bacteriolysis, reduced levels in the neonatal period may significantly contribute to the impaired resistance manifested by the neonate.

Maternal role in Passive Immunity

An important maternal contribution to the survival of the neonate comes through the passive transfer of acquired maternal mucosal immunity. Most of this immunity is directed towards microorganisms likely to be present in the environment of the neonate. This represents a major means of vertical transfer of immunological experience in ruminants.

Although humoral and cellular elements are present throughout lactation, the colostrum is particularly rich in elements associated with the maternal immune system. Those factors are especially concentrated in the first milking and decrease significantly to reach very low levels after the third milking post partum. In addition to the factors associated with specific immunity the colostrum contains a number of non immune effector mechanisms presumably capable of providing additional sources of protection for the neonate.[73 74 75]

These non immune effector mechanisms may play an important protective function in the gut lumen before the immune response and mucosal barrier of the neonate become effective. Among other factors, the enzyme lysozyme may be responsible for reducing the local concentration of susceptible bacteria by hydrolyzing the glycopolysaccharides of the bacterial cell wall. Lactoferrin, an iron binding protein which is bacteriostatic, is also present in significant concentrations in colostrum. Very small amounts of this protein are found in the milk.

The lactoperoxidase/thiocyanate/hydrogen peroxide system represents another non specific antimicrobial factor present in the colostrum. The lactoperoxidase, like the lactoferrin, is present in high concentration in colostrum and decreases to lower levels in milk. The lactoperoxidase/thiocyanate/hydrogen peroxide system which is somewhat similar to the antimicrobial myeloperoxidase/halide/hydrogen peroxide system of the neutrophils has been shown to have a significant antistreptococcal activity as well as a marked bacteriostatic and bacteriocidal activity against gram negative bacterias particularly some of the enteropathogenic serotypes of *Escherichia coli.*[73]

Other non immune effector mechanisms present in colostrum may either participate in bacteriolysis or regulate bacterial colonization of the gastrointestinal mucosa of the neonate. A trypsin inhibitor which is thought to play a role in protection of the immunoglobulins from enzymatic digestion is also present in the colostrum.[5 48 72]

In addition to the antibodies, large numbers of cellular elements are found in the mammary secretions.[29 56] One to 10 x 10^6 cells/ml of colostrum are present at the time of parturition. Ten days later the number of cells in the milk represents less than 1 x 10^5 cells/ml. Although most of the cells present in colostrum are macrophages, the exact function of these cells in passive transfer of cellular immunity remains unknown.

Factors leading to neonatal disease

The environmental conditons and defective passive transfer immunity are determinant factors associated with neonatal calf morbidity and mortality. Changing husbandry practices are leading to more animals in confinement; as a consequence, the number of pathogens increases in the environment. Most agents responsible for neonatal disease will affect the calf either *in utero* or shortly after birth. As we saw earlier, most of the antigenic challenge to the newborn calf will occur at the level of the mucosal surfaces. In the absence of passive local resistance to organisms common to the environment, systemic spread or septicemia by organisms of relatively low virulence for immunologically mature animals will occur.[85]

Serum immunoglobulin levels derived from passive transfer of colostral immunity are usually protective against neonatal septicemia in calves.[51] Serum antibody levels in calves do not always correlate with protection against infection or reinfection of the gastronintestinal tract by many pathogens.[49 60 89 95] Adequate protection against neonatal diarrhea is dependent upon the continuous presence of sufficient amount of specific antibodies in the gut lumen.[60 86 87 88 89]

Passive Transfer of Immunity Colostrum Feeding

Passive protection of the newborn against specific pathogens present in the herd environment requires the presence

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of specific antibodies in the colostrum. This can only be achieved by appropriate sensitization and development of active immunity to the herd pathogens by the dam before parturition.

To assure appropriate passive protection for the neonate, newly introduced pregnant replacement animals should be exposed to the herd environment a minimum of 3 weeks prior to their expected calving time. When this is not possible the feeding to neonates of frozen colostrum obtained from an adult cow raised on the farm can be used.

Studies on passive transfer of humoral immunity by the colostrum have shown that the time at which the colostrum is obtained from the dam plays an important role in determining its lactoglobulin concentration. The total immunoglobulin content of colostrum taken on the second milking represents only one third of that level of immunoglobulin present in the first milking.[29 52] Thus, cows that leak colostrum before parturition will often yield inadequate amounts of protective immune lactoglobulin for their calves.

Adequate immunoglobulin protection is obtained when two feedings of first milked colostrum are provided; the first feeding should be given within the first 6 hours after birth with the second feed 4 to 6 hours later.[24] A minimum of 10% of the body weight of colostrum in 2 feedings will provide adequate immunoglobulin protection.

No difference in either colostral intakes or serum immunoglobulin levels is seen whether the colostrum is fed using nipple bottles or buckets.[24] In the case of force feeding with esophageal feeders or stomach tubes the results are somewhat contradictory. Whether the colostrum is fed at room temperature or body temperature does not appear to influence the colostral intake or serum immunoglobulin levels.[24]

The presence or absence of the dam does not significantly affect the quantity of colostrum consumed by the calf during its first two feedings. However, the levels of Ig obtained by the neonate in the presence of the dam are significantly greater than those levels obtained by newborn fed in the absence of the dam.[24 81 82] Therefore, the efficiency of absorption of immunoglobulin by the calf is greatly improved in the presence of the dam.

Management during the neonatal period

As a general recommendation, the pregnant dam should be transferred to a clean loose box stall near the expected calving time. After parturition, the calf should be kept with its dam for at least 24 to 48 hours after birth. Since the majority of the calves are capable of obtaining their first feeding within 2 to 6 hours after birth, particular attention should be given to those situations in which delayed or inadequate colostrum intake is likely to occur. Examples of such instances are listed in Table 1. Delayed colostrum intake will often occur in nulliparous heifers especially, of dairy breeds, following dystocia or poor maternal behavior.

TABLE 1. **Factors associated with delayed or failure of colostral intake by newborn calves.**

Nulliparous vs Multiparous dam
dystocia, weak calf, exhausted dam, poor maternal behavior.
Poor udder conformation
Udder edema and congestion
Pre partum leakage of colostrum
Mastitis
Downer cow
Premature calving

Dams with big, low hanging udders will often influence the pattern and time spent by the calf actively teat-seeking after birth. This is due to the fact that the teat seeking activity in newborn calves is naturally oriented toward places about the level of their head when standing.[32] Although teat-seeking of the calf is usually directed at the hind quarter, mostly in the udder region, in cases in which the udder and teats are low hanging the calf will often search for a long time without locating the teats. It may eventually direct its attention somewhere else onthe cow's body or sometimes it may end up in the corner of the calving pen without having sucked its dam.[32]

In the remaining examples, where inadequate colostrum intake are expected, frozen colostrum from an adult cow raised on the farm may become very helpful. In cases where the immunoglobulin status of the calf is thought to be responsible for neonatal loss quantitative assessment of colostral intake may be indicated. Many different tests are available, some being more easily accessible in the field than others.[26 64 69 70 90 93] The zinc sulfate precipitation of globulin in which correlation between the degree of turbidity and total serum IgG/IgM is made, has some practical value. The refractometer reading for total protein can also be of value as an index of susceptibility.

Vaccination programs

Vaccination programs specifically designed at protecting newborn calves should be included in the general herd health management program. In considering the type of vaccine and the choice of a particular strategy, considerations need to be given to the pathogen(s) shown to be a problem in the herd or in the area under consideration. The route and frequency of administration of the vaccine i.e. whether orally to the calf at birth or intramuscular in the dam before parturition should be determined. Also of importance are the types of vaccine available; modified live or killed viral preparations, or bacterins and toxoids in the case of bacterial vaccines.

The factors associated with maximal passive transfer of immunity by the colostrum and the requirements for adequate overall calf management practices are just as important as the vaccination program of the herd.

Calf management program should include reducing environmental exposure to pathogens. Since the incidence

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and severity of disease is dependent upon the exposure dose to pathogens and the immune status of the host, and provided that adequate passive transfer of specific immunity is present at mucosal surfaces, lowering the exposure to pathogens by controlling environmental contamination will have a significant impact on overall preventive measures. Minimizing the exposure of the calf to pathogens can be brought about by improved housing conditions including control of humidity and temperature through ventilation. Improvement of general sanitation using effective disinfection procedures will also be helpful.

Failure of vaccination programs specifically designed at protecting the newborn calf will result from the appearance of new etiologic agents in the herd. Since most vaccines, particularly those designed to protect against enteric colibacillosis will stimulate specific immunity directed against a limited number of pathogenic organisms, it is likely that in the case of mixed infections, the protection afforded by vaccination will be incomplete. The efficacy of vaccines has received considerable attention in the past few years.[78] Most field studies especially those involving vaccines specifically designed to protect against viral gastroenteritis of calves have demonstrated their ineffectiveness in preventing diarrhea under field conditions.[1 13 19 94]

Failure of passive transfer of immunity varies with the type of management and the breed of animals whether they be beef or dairy cattle. It may vary between 10% and 40% depending upon husbandry conditions.[27] This emphasizes the importance of adequate intake and absorption of colostral immunoglobulins by the neonatal calf. Despite early feeding of sufficient amount of colostrum some 20 to 30% of calves will show evidence of failure of passive transfer (serum IgG < 8 mg/ml).[4 27 58 59 92] Seasonal factors have been associated with this condition.[4 27 57] Thus, maximum absorption occurs during the summer and early fall months whereas minimum absorption occurs in winter months. Factors other than seasonal that could explain such failure in passive transfer of immunity by the colostrum have not been described.

Conclusion

From all the experimental data available, it becomes quite clear that the cow-calf relationship represents a unique challenge to the large animal practitioner. The veterinarian, with his/her current medical knowledge, represents the best qualified individual capable of educating the herdsman on this matter. Any recommendations designed at improving or correcting existing herd health management practices will rely in large part upon the clinician's understanding of the natural phenomenon occuring during the neonatal period. In some situations however, even in the presence of skillful management practices, problems will occur that will only find their answer after logical analysis of the husbandry practices used on the farm. A critical examination of the actual situation will then allow the veterinarian to provide a reasonable approach to managing neonatal health.

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Abstracts

Roming, L.G.P. (1984): Tolazolin als Xylabin-Antagonist beim Rind. Dtsch. tierarztl. Wschr. 91, 154-157.

The antagonistic properties of Tolazoline given 15 minutes after administration of Xylazine were ascertained in respect to the degree of analgesia, sedation, and myorelaxation, as well as heart rate, breathing rate and rate of rumen contraction obtained by clinical examination of 24 cattle. In addition to that, the hyperglycemic effect of Xylazine could be reduced or even revoked by Tolazoline. The quick return of rumen-movements to normal through Tolazoline treatment after Xylazine-induced reduction of ruminal activity was also recorded by measurement of prestomachal pressure

Multiple Use of Progesterone Releasing Intravaginal Devices for Synchronisation of Oestrus and Ovulation in Cattle, S. R. McPhee, M. W. Doyle, I. F. Davis, and W. A. Chamley, Aust. Vet. J. 60:40.

Experiments were conducted to investigate the possibility of using progesterone releasing intravaginal devices (PRIDs) more than once, for the purpose of synchronising oestrus and ovulation in dairy cows. In an initial study, PRIDs were inserted into 6 ovariectomised cows for 12 days on 3 separate occasions and blood samples were collected for progesterone assays. After removal, 3 PRIDs were sterilized by autoclaving and the other 3 by gassing with ethylene oxide. After PRID insertion progesterone concentration in plasma rose rapidly. Autoclaved PRIDs which were reused once and then twice, maintained blood progesterone profiles which were comparable to the release of progesterone from a new PRID. This was not the case when PRIDs were re-used after gas sterilization.

In a second study, PRIDs were inserted into 41 dairy cows for 9 days and an injection of prostaglandin F2a was given one day before PRID removal. Onset of oestrus was determined by observation at intervals of 3 h for 30 min and time of ovulation was determined by endoscopy approximately 30 h after onset of oestrus. PRIDs were autoclaved after removal and re-used twice.

In cows which received new PRIDs, 85% came into oestrus between 30 and 60 h after removal. When PRIDs were used for the second time, 100% of cows showed oestrus within 30 to 60 h. When PRIDs were used for the third time the interval between PRID removal and onset of oestrus was highly variable. Only 29% of cows showed oestrus within 30 to 60 h whereas 59% showed oestrus between 12 and 42 h after PRID removal.

The distribution in estimated time between PRID removal and ovulation followed closely the distribution of onset of oestrus for each insertion of PRIDs. The synchrony of ovulation was most concentrated for the second use of PRIDs and least for the third use. A few cows did not follow the general pattern of response.

Indications that the PRID may be used more than once for synchronising oestrus and ovulation in the dairy cow, and the adoption of a 9-day PRID insertion interval in any synchronisation schedule should result in a significant reduction in the cost of this technology.

A Necropsy Technique for Cattle to Eliminate Contamination of Lymph Nodes by Mycobacteria. J. H. Norton, B. J. Duffield, A. J. Coward, R. W. Hielscher, and R. F. Nicholls, Aust. Vet. J. 61:75-76.

A field necropsy technique for cattle is described which avoids contamination by environmental mycobacteria of tissues intended for bacteriological examination. Settling the dust by hosing on and around the carcase, using sterile instruments for the collection of each tissue, excising lymph nodes without incising the capsule and submitting the nodes to the laboratory intact in saturated tetraborate solution resulted in uncontaminated samples even under adverse field conditions. The procedure is recommended for future investigations into the role of mycobacteria other than *Mycobacterium* bovis in the sensitization of cattle to the intradermal test for tuberculosis.