The role of management and the use of vaccines in the control of acute undifferentiated diarrhea of newborn calves

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Introduction

The health management of dairy and beef calves has not received the attention it deserves from cattle producers and veterinarians, compared to the emphasis placed on reproductive performance, milk production, mastitis control, and the nutrition of the cow herd.

Acute undifferentiated diarrhea of calves from a few days of age up to 30 days of age accounts for a major portion of the economic loss due to diseases of calves in that age group. I will review the principles of control of acute undifferentiated diarrhea of newborn calves including the use of some of the commonly available vaccines. The emphasis will be on the diarrheas associated with enterotoxigenic *Escherichia coli* (ETEC), rotavirus, and coronavirus.

In the last 10 years there has been considerable interest in the use of vaccines given to the pregnant dam to stimulate the production and concentration of specific antibody in the colostrum and milk which when transferred to the calf may provide protection against diarrhea.

The principles of control

When a livestock producer seeks advice on the clinical management and control of a herd epidemic of acute diarrhea in calves, the veterinarian should request to visit the herd to conduct a clinical and epidemiological investigation with the objective of identifying the risk factors which need to be corrected to control the outbreak at the present time and to control the disease in the future.

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Because of the complex nature of the disease, it is unrealistic to expect total prevention; control at a low incidence should be the major goal. Effective control of calf diarrhea can be accomplished by application of three principles:

1. *Reduce the degree of exposure of newborn calves to the infectious agents.*
2. *Provide maximum non-specific resistance with adequate colostrum and good animal management.*
3. *Increase the specific resistance of the newborn calf by vaccination of the pregnant dam.*

1. Reduce the degree of exposure of newborn calves to the infectious agents.

Dairy calves. These comments are particularly relevant for calves born inside barns where contamination is usually higher than outside on pasture.

— Calves should be born in well-bedded calving box stalls which were previously cleaned out.
— The perineum and udder of dirty cows should be washed shortly before calving.
— Calves should be reared in clean individual pens until at least three weeks of age.
— Calves affected with diarrhea should be removed from the proximity of other calves if possible and treated in isolation.

Beef calves. In large beef herds the calves are usually born outside on pasture or on confined calving grounds. First-calf heifers are sometimes placed in a barn to calve when severely cold weather is anticipated. Calving indoors can be a major risk factor because of the high level of contamination with enteropathogens. Calving indoors is common in small beef herds and sanitation and hygiene are critical to reduce infection pressure.

— Calving grounds should have been free of animals previous to the calving period; the grounds should be well drained, dry and scraped free of snow if possible. The population density is critical. It is suggested that at least 1000 square feet per cow are necessary to minimize infection pressure. Up to 2000 square feet would be ideal. A top dressing of the calving grounds with straw or wood shavings will provide a comfortable calving environment.

— In a few days following birth when the calf is nursing successfully, the cow-calf pair should be moved to a nursery pasture to avoid overcrowding in the calving grounds. The details of the management of the beef herd at calving time to control calf diarrhea have been described elsewhere (1). In beef herds with more than 100 cows, it is recommended that the herd be subdivided into calving groups of 50 to 75 head which are confined to a calving area which is separate from the wintering grounds. When each calf is 24 hours of age and has been accepted by its dam, the cow-calf pair is moved to a nursery pasture or corral. Such a system allows the regular inspection of the calving group and the nursery group (1).

The principle of reducing infection pressure is also effective when outbreaks of diarrhea occur in beef herds. The cows yet to calve are moved to a new calving ground previously not occupied by cattle. Often the outbreak will cease.

The practice of fall calving on open pasture in August and September will minimize the exposure of the calf to infectious agents and is being successfully adopted by some cow-calf producers.

2. Provide maximum non-specific resistance with adequate colostrum and good livestock management.

This begins with the provision of adequate nutrition to the pregnant dam which will result in a vigorous newborn calf and adequate quantities of colostrum. The next most important control measure is to ensure that colostrum is ingested in liberal quantities within minutes and no later than a few hours after birth. While the optimum amount of colostrum which should be ingested by a certain time after birth is well known, the major difficulty under practical conditions is to know how much colostrum a particular calf has consumed. In one study, in large dairy herds, 42% of calves left with their dams for one day following birth had failed either to suck sufficient colostrum or to absorb sufficient colostral immunoglobulins. This problem can be alleviated by bottle feeding one liter of pooled colostrum to all calves at approximately one hour after birth. Encouraging and assisting the calf to suck colostrum to satiation within one hour after birth will result in high concentrations of absorbed immunoglobulins in the majority of calves. The ingestion of 80–100 g of colostral immunoglobulins within a few hours after birth is so effective in achieving high levels of colostral immunoglobulins in calves that either leaving the calf with the cow for the next 12–24 hours or encouraging the calf to suck again at 12 hours will not result in a significant increase in absorbed immunoglobulins.

There are several commercially available milk- or colostrum-derived oral supplements intended for newborn calves which have not received an adequate amount of colostrum early enough after birth. The concept is excellent. However, some colostral supplements contain low immunoglobulin concentrations compared to those which are found in high-quality first-milking colostrum (2). Fresh colostrum contains about 100 g/L of total immunoglobulins, thawed frozen colostrum about 24 g/L, and Colostrx about 18 g/454 g bag of product (2). To meet the requirement of 80 to 100 g, using Colostrx, the calf would have to consume at least 4 to 5 bags of the product.

Dairy calves. Immediately after birth, unless the calf is a vigorous sucker, colostrum should be removed from the cow and fed by nipple-bottle or by stomach tube at the rate of at least 50 mL/kg body weight in the first two hours. Encouragement and assistance to suck to satiation within the first hour after birth is also highly effective as described above. The calf should be left with the cow for at least two days. This contact will improve the absorption of immunoglobulin.

Following the colostral feeding period, dairy calves are usually placed in individual stalls until weaning. Feeding of fermented colostrum to newborn calves up to three weeks after birth provides a source of lactoglobulins in the intestinal tract and reduces the incidence of neonatal diarrhea of calves due to rotaviruses and the coronavirus.

Beef calves. Beef calves should be assisted at birth, if necessary, to avoid exhaustion and weakness from a prolonged parturition. Normally beef calves will make attempts to stand and suck within 20 minutes after birth but this may be delayed for up to 8 hours or longer if they have had a difficult birth or are weak for a variety of reasons. Beef calves which do not suck within two hours should be fed colostrum by nipple bottle or stomach tube. Whenever possible they should be encouraged and assisted to suck to satiation within one hour after birth. The mean volume of colostrum and colostral immunoglobulins produced in beef cows and the absorption of colostral immunoglobulins by their calves can vary widely. Beef calves deserted by indifferent dams need special attention. Constant surveillance of the calving grounds is necessary to avoid overcrowding, to detect diarrheic calves which should be removed, to avoid mismothering, and to ensure that every calf is seen to nurse its dam. Although up to 25% of beef calves may not achieve adequate serum levels of immunoglobulins, the provision of excellent management can minimize the incidence of diarrhea. The recently developed practice of corticosteroid-induced parturition in cattle may result in a major mismothering problem if too many calves are born too quickly in a confined space. Every management effort must be used to establish the cow-calf bond as soon as possible after birth.

3. Increase the specific resistance of the newborn calf by vaccination of the pregnant dam (lactogenic immunity)

The passive immunization of calves against some of the causative agents of calf diarrhea by vaccination of the pregnant dam with those agents has received considerable research attention in recent years and the results appear promising (3–9). The pregnant dam is vaccinated during the third trimester of pregnancy or earlier to stimulate the production of specific antibodies to particular strains of enterotoxigenic K99+ *E. coli*, rotaviruses and the coronavirus, which

Table 1. Vaccines available for the control of acute undifferentiated diarrhea of newborn calves

Vaccine	Constituents	Directions for Use
Ecolan *Escherichia coli* Bacterin.	K99 and F41 pilus antigens and capsular antigens, K17, K28, K30, K35, and K85.	In first year vaccinate at time of pregnancy diagnosis and second injection 2–4 weeks before calving; 2 mL SC or IM. For subsequent calving give booster 2 weeks before calving.
Ecolan RC	Same bacterial components as in Ecolan plus 2 serotypes of rotavirus and one type of coronavirus.	In first year vaccinate at time of pregnancy diagnosis and second vaccination 4–6 weeks before calving; 4 mL IM; in subsequent years vaccinate once 4–6 weeks before calving.
Jencine K99	Purified and concentrated inactivated K99 pili antigens in white, oily emulsion.	One intramuscular injection 6 months to 2 weeks before parturition; revaccinate during same time period annually and thereafter.
Scour Guard 3 (K) Bovine rota-coronavirus vaccine. *Escherichia coli* bacterin.	Inactivated bovine rota- and coronavirus and K99 *E. coli* bacterin.	In first year vaccinate twice IM at least 2 weeks apart; second dose 2–3 weeks before calving. Revaccinate annually 2–3 weeks before calving.
Scour Guard 3 (KC)	Bovine rota- and coronavirus, *E. coli* bacterin, *Clostridium perfringens* type C.	In first year vaccinate twice IM at least 2 weeks apart; second dose 2–3 weeks before calving. Revaccinate annually 2–3 weeks before calving.
Calf Guard. Bovine rota-coronavirus vaccine.	Bovine rota- and coronavirus (modified live virus).	Vaccinate calf orally immediately after birth and no later than 1 day of age. Can also vaccinate pregnant cow, IM, twice 3 to 6 weeks apart with second dose at least 30 days before calving. Revaccinate twice annually.
Genecol	Specific monoclonal K99 *E. coli* antibody.	Administer orally to newborn calf within 12 hours of birth.

antibodies are then passed on to the newborn calf. This is also known as lactogenic immunity.

The vaccines and their components which are available in Canada are summarized in Table 1.

It must be emphasized that vaccination is an aid to good management and not a replacement for inadequate management.

Vaccination of pregnant cattle with either purified *E. coli* K99$^+$ pili or whole cell preparation containing sufficient K99$^+$ antigen can significantly reduce the incidence of naturally occurring enterotoxic colibacillosis in calves nursing vaccinated cows (4). Good protection is also possible when the dams are vaccinated with a four-strain *E. coli* whole cell bacterin containing sufficient K99$^+$ pilus antigen and the polysaccharide capsular K antigen. There is a highly significant correlation between the level of colostral antibodies to the K99$^+$ antigen and the prevention of severe diarrhea or death in calves challenged with enterotoxic *E. coli*. The colostral levels of K99$^+$ antibody are highest during the first two days after parturition, which is the most susceptible period for enterotoxic colibacillosis to occur in the newborn calf. The continuous presence of the K99$^+$ antibody in the lumen of the intestine prevents adherence of the bacteria to the intestinal epithelium. The K99$^+$ antibody is also absorbed during the period of immunoglobulin absorption and may be excreted into the intestine during diarrhea. This may be one of the reasons that mortality is inversely proportional to the level of serum immunoglobulins achieved within the first 24 hours after birth. For most *E. coli* vaccines, the pregnant dams are vaccinated twice in the first year, six and two weeks prior to parturition. Each year thereafter they are given a single booster vaccination. One vaccine containing an inactivated K99+ pilus antigen in an oil emulsion will provide protection when the first dose is given as early as six months before calving.

Two different immunization approaches have been used to control rotavirus and coronavirus diarrhea in calves. One is the stimulation of active immunity by vaccinating the newborn calf with an oral vaccine containing the modified live viruses. The other is the stimulation of lactogenic immunity by vaccinating the dam during pregnancy as with the *E. coli* vaccines.

A modified live virus rotavirus vaccine designed for oral administration to calves immediately after birth has been available commercially for many years and good results were claimed initially. Recent controlled evaluations of the oral vaccine indicate a failure of protection of calves against rotavirus infection and rotavirus-coronavirus infection (9). Effective oral vaccination of calves in the field against diarrhea caused by rotavirus or coronavirus is hindered by the presence of specific antibodies in the colostrum — *the colostrum barrier* (10). This may explain the failure of the vaccine under field conditions. Most of the efficacy trials with the vaccine were done on colostrum-deprived gnotobiotic calves which were vaccinated orally at birth and experimentally challenged a few days after birth. It is probably futile to vaccinate calves orally immediately after birth, particularly in herds where the disease is endemic. The colostrum of cows may contain high levels of specific antibodies from natural infection.

The second approach to control relies on lactogenic immunity. The success of this method depends on the presence of a sufficient amount of specific antibody to the rotavirus and coronavirus in the colostrum and milk of the dam which will neutralize the infection in the intestine of the calf. However, a major problem with this method of control is the rapid decline in the concentration of colostral antibodies, commonly to below protective levels, which occurs within 24–48 hours following parturition (3,6). Recent evidence supports earlier suggestions that the circulating antibody which the newborn calf acquires in the first 24 hours of life is excreted into the lumen of the intestine, which may provide some additional protection (11).

Effective oral vaccination of calves in the field against diarrhea caused by rotavirus or coronavirus is hindered by the presence of specific antibodies in the colostrum — *the colostrum barrier*

Numerous vaccination trials have been used to show that immunization of the pregnant cow with rota and coronavirus vaccines will protect the calf against diarrhea due to those viruses.

The daily feeding of colostrum, from cows vaccinated with a rota-coronavirus vaccine, to calves will reduce the incidence of diarrhea and shedding of the viruses in the feces (12,13). This can be applied practically in dairy herds, where calves are usually hand-fed, to control a problem with rotaviral diarrhea. The daily feeding of stored colostrum from cows of the affected herd will reduce the incidence of clinical disease in the calves (14). In affected herds the colostral antiviral antibody may be sufficient to prevent the disease if colostrum is fed daily for up to 30 days. If a large number of cows are calving over a short period of time, the colostrum can be pooled and fed to the calves daily. Even small amounts of colostrum from immunized cows are efficacious if mixed with cows' whole milk or milk replacer.

The parenteral vaccination of the pregnant dam before parturition with a rotavirus and coronavirus vaccine will increase the level and duration of specific antibody in the colostrum compared to the control unvaccinated cows (3,6). However, the major effect of vaccination is to increase the titer in the colostrum. There is much less effect on the duration of the antibody level in the post-colostral milk (13). The challenge for the researchers and manufacturers of rotavirus and coronavirus vaccines has been to develop a vaccine which when given to pregnant cattle will result in protective levels of specific antibody in the colostrum initially, and then be maintained at protective levels in the post-colostral milk for a sufficient period such as up to 10 days to three weeks, the period in which calves are most susceptible to these viral diarrheas. In some of the original trials, the use of a modified live rotavirus-coronavirus vaccine stimulated a small but insignificant increase in colostral and milk antibodies. However, by three days after parturition the rotavirus and coronavirus antibody titers in the milk of vaccinated heifers had declined to low or undetectable levels (8). The use of an inactivated rotavirus vaccine resulted in significantly increased antirotavirus antibody in colostrum and milk from vaccinated dams compared to controls but the severity of diarrhea was the same in calves from both groups. The increased milk antibody delayed the establishment of infection but did not reduce the severity of clinical disease which was experimentally induced.

Lactogenic immunity can be effective if sufficiently high titers of antiviral antibodies can be achieved in the colostrum

Experimentally, the use of a rotavirus vaccine, containing an adjuvant, given simultaneously intramuscularly and by the intramammary route significantly enhanced serum, colostrum and milk rotavirus antibody titers, whereas intramuscular vaccination with a commercial modified live rotavirus-coronavirus vaccine did not. Small quantities of colostrum from the cows vaccinated by the intramammary and intramuscular routes fed to rotavirus-challenged calves provided protection against both diarrhea and shedding of the virus in the feces (5,7). This illustrates that lactogenic immunity can be effective if sufficiently high titers of antiviral antibodies can be achieved in the colostrum but more importantly, if this were possible in the post-colostral period when the calves are most susceptible to the virus infections. The 30-day milk antibody titers from these cows were considered to be protective, by which time calves should have developed a high degree of age-specific resistance to rotavirus infection. The use of an inactivated rotavirus vaccine in an oil adjuvant given to pregnant cows 60–90 days before calving and repeated on the day of calving resulted in a significant increase and prolongation of protective titers of colostral antibodies for up to 28 days after calving. Diarrhea in calves from vaccinated cows was less common and less serious. Similar results have been obtained with combined inactivated adjuvanted rotavirus and *E. coli* vaccine (15–19).

Vaccines containing various combinations of the K99+ and related antigens of enterotoxigenic *E. coli*, the rotaviruses, and the coronavirus are now available and have been evaluated with variable results (17,19).

As a general principle, if high antibody titers to the enteropathogens can be achieved in the colostrum and in the postcolostral milk for long enough, *and if the calf ingests liberal quantities of the colostrum within several hours after birth*, the incidence of diarrhea caused by those pathogens will be reduced. The *E. coli* and the rotavirus and coronavirus vaccines have been evaluated by two methods. In the first, calves are fed colostrum daily from vaccinated cows and experimentally challenged with the viruses. The antibody titers of the colostrum and the milk for up to three weeks are also measured which provides an indication of the titers required to provide protection.

In the second method, which is more difficult to conduct and interpret the results, the vaccine is evaluated by comparing the incidence of naturally occurring diarrhea in calves nursing vaccinated cows with the incidence in calves nursing unvaccinated cows in the same herd. The major problem in this kind of evaluation is to determine the cause of diarrhea in both groups of calves. At the present time, I am unaware of the availability of any multiple component vaccines (*E. coli*, rotavirus, coronavirus) in Canada which have been shown to be effective based on field trials where the vaccines have been tested, with concomitant unvaccinated controls, against naturally occurring diarrhea in calves from birth to 30 days of age.

The oral administration of a $K99^+$-specific monoclonal antibody to calves during the first 12 hours after birth may be an effective method of reducing the incidence of fatal enterotoxigenic colibacillosis particularly when outbreaks of the disease occur in unvaccinated herds. Clinical trials indicate that the severity of dehydration, depression, weight loss and duration of diarrhea were significantly reduced in calves which had received the $K99^+$ specific monoclonal antibody (20). However, the preparation if too expensive for routine use in commercial cattle herds.

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