Duration of Active and Colostrum-derived Passive Antibodies to Bovine Viral Diarrhea Virus in Calves

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ABSTRACT

Duration of active and colostrum-derived passive antibodies to bovine viral diarrhea virus was studied in 14 calves. Five calves born with actively induced antibodies to bovine viral diarrhea virus retained high titers during the year of observation. Colostrum-derived antibodies to bovine viral diarrhea virus in nine calves declined at an expected rate for the first four to six months of age. However, titers of six of these calves increased at five to eight months of age and either remained constant or increased through one year of age. Bovine viral diarrhea virus antibody titers of the other three calves declined at a constant rate to $< 1:4$ by nine to 12 months of age.

RÉSUMÉ

Les auteurs ont étudié, chez 14 veaux, la durée de l'immunité active et passive à l'endroit du virus de la diarrhée à virus bovine. Cinq de ces veaux, nés avec une immunité active, conservèrent un taux élevé d'anticorps jusqu'à l'âge d'un an. Les anticorps transmis par le colostrum à neuf autres de ces veaux, diminuèrent à un rythme prévu au cours des premiers quatre à six mois après la naissance. Chez six d'entre eux, le taux d'anticorps s'éleva cependant entre l'âge de cinq et huit mois; il y demeura stable jusqu'à l'âge d'un an, ou il enregistra une autre élévation. Chez les trois autres veaux, il diminua de façon constante et atteignit $< 1:4$ entre l'âge de neuf mois et d'un an.

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The possibility that bovine viral diarrhea virus (BVDV) causes a fetal infection was suggested when antibody was found in fetal bovine serum collected in slaughterhouses for cell culture work (14). Subsequent research identified precolostral antibodies to BVDV in calves born to nonimmune cows following artificial exposure to BVDV by various routes (2, 7, 11). These conclusions led to the conjecture that BVDV was capable of crossing the placental wall and inducing fetal infection. It was well established by this time that antibodies did not cross the placental barrier (3), thus neonatal calves not infected *in utero* are dependent on the ingestion of antibody containing colostrum within the first 24 hours of life for immunity to BVDV (4, 5).

The duration of active and passive antibodies to BVDV in calves varies considerably. Calves born to nonimmune cows following intravenous or intramuscular inoculation of BVDV during the second or third trimester of pregnancy maintained high levels of active antibody from birth to 180 days of age in one group (20) and 340 days of age in a second group (12). In studies on passive antibodies to BVDV in calves born to immune cows, antibodies declined to zero by 280 days in nine calves (10) while in another nine calves the maximum duration of any titer was 259 days (13). The latter study was accomplished in calves from a herd where in excess of 80% of the cattle had BVDV antibody titers.

The presence of antibodies to BVDV, either active or passive, are proposed to prevent or hinder further antibody production by live virus (4, 13, 18). It was thereby generally accepted that vaccination to prevent BVDV infection be given to calves when antibodies to this virus were depleted (1).

It was therefore of interest to study the duration of active and passive antibodies to BVDV in young calves in order to determine the best time to initiate a vaccination program.

Calves studied were born to cows used in a study to determine whether killed BVDV could be sufficiently concentrated so that a single injection could stimulate an antibody response in pregnant cattle which would protect them and their fetuses from BVDV infection after an intranasal exposure of the dam (17).

Nineteen BVDV-negative cows were used in the killed BVDV vaccine study. Two of these had severe dystocia and the calves were dead at delivery. The remainder were normal deliveries. Three calves were transferred to other experiments, thus leaving fourteen calves for this study, ten from vaccinated and four from nonvaccinated cows (Table I).

Serum samples were taken from each cow and calf at parturition, along with a colostrum sample before the calf had nursed. Thereafter, calves were bled at two week intervals until 12 weeks of age, then once a month until one year old. BVDV antibodies were determined by the microtiter method (19), using bovine turbinate (BT) cells (16) and the Singer isolate (17) of BVDV at approximately 100 $TCID_{50}$ per 0.025 ml.

Virus isolation was attempted from heparinized blood samples of each calf obtained at birth. Buffy coats were removed, frozen and thawed, then inoculated onto confluent monolayers of BT cells. Each culture was subcultured at least four times onto fresh BT cells, while at the same time unpassaged cells were inoculated with the Singer isolate of BVDV to test for the presence of noncytopathic BVDV by interference (6).

Each calf was left with its dam until weaned at three months of age. From weaning until completion of the observation period the calves were housed two per pen in an isolation building. The pens opened on a common cleaning and feeding corridor.

At birth all calves appeared healthy, except calves 78 and 79 which developed a mild intermittent diarrhea but by two months were gaining weight and appeared normal. BVDV isolation from the buffy coat cells was not successful.

Antibody titers to BVDV in colostrum and serum of the 14 cows and their calves are given in Table I. At parturition, serum titers of the cows ranged from 1:1024 to 1:16386 and colostrum titers from 1:2048 to 1:524,288. In the absence of statistical analysis there does not appear to be any correlation between a cow's serum and colostrum antibody titer nor between the calf's serum and the dam's colostrum antibody titer. The high titer (1:524,288) of one colostrum (cow 69) sample may be due to some additive factor of a nonspecific entity but is most likely BVDV antibody, as serum titers of 1:262,144 and 1:371,000 have been reported for seven day old and newborn calves, respectively (12).

Five calves had precolostral serum BVDV antibodies: four (calves 77, 67, 63, 72) born to nonvaccinated cows and one (calf 71) born to a vaccinated cow (Table I). The presence of serum antibodies at birth indicate an *in utero* infection and thus an active immunity as was expected in calves born to inoculated nonimmune cows (2, 20). However, the calf born to the vaccinated cow was expected to be protected against an *in utero* infection, as were the other calves in that group (Table I) (17). BVDV serum antibody titers of three calves (calf 71, 77, 67) were not affected by ingestion of antibody containing colostrum and any effect of colostrum on the increase between pre- and postcolostral titers of the other two calves (calf 63, 72) would be purely speculative. Active BVDV antibody titers of these five calves ranged from 1:128 to 1:1024 during the latter 11 months of observation (Table II).

The nine remaining calves born to vaccinated cows (Table I) had precolostrum BVDV serum antibody titers of $< 1:4$ and passively acquired BVDV antibody titers that ranged from 1:512 to 1:8192 two weeks postcolostrum. These titers declined during the first four to six months of age at a rate comparable to previous reports (10, 13). However, at five to eight months of age titers of six calves (calf 76, 73, 66, 65, 70, 74) increased from 1:32 and 1:64 to a range of 1:64 to 1:1024 at 12 months of age (Table II). The increase in serum titers of these six calves is suspected to be due to an inapparent infection as clinical illness associated with this disease was not observed. In addition, it has been reported that the most common form of BVDV infection is subclinical (15). Virus isolations from these six calves were not attempted, as it is known to be very difficult in the

TABLE I. Antibody Titers of Killed BVDV Vaccinated and Nonvaccinated Pregnant Cows and their Calves at Described Intervals after Exposure of the Cows to Live BVDV

Cow no.[a]	Gestation when Challenged[b]	Antibody Titer[c]						
		At Time of Challenge	Two Weeks Postchallenge	At time of Parturition	Colostrum	Calf no.	Pre-colostrum	Post-colostrum[d]
Vaccinated								
24	6½	16	8192	16386	65536	71	2048	2048
28	6	32	4096	1024	2048	76	< 4	2048
59	7½	128	8192	8192	32768	73	< 4	1024
64	7½	64	16384	4096	8192	66	< 4	2048
69	7½	64	8192	8192	524288	64	< 4	8192
105	7	8	2048	2048	16348	65	< 4	2048
1747	7	64	8192	2048	32768	70	< 4	4096
1748	6	32	4096	2048	4096	74	< 4	1024
1785	5½	32	4096	2048	8192	79	< 4	1024
2121	5½	32	4096	2948	4096	78	< 4	512
Nonvaccinated								
65	6	< 4	2048	2048	2048	77	2048	2048
102	7	< 4	256	1024	8192	67	4096	4096
106	8	< 4	256	8192	32768	63	128	1024
1419	6½	< 4	512	2048	16348	72	512	2048

[a]All animals were BVDV antibody negative at the beginning of the experiment

[b]Months pregnant

[c]Number represents the reciprocal of the highest dilution of serum and colostrum which would prevent CPE

[d]Serum taken two weeks after birth

TABLE II. Active and Passive BVDV Serum Antibody Titers in Calves from Birth to 12 Months of Age

Calf no.	Pre-colostrum	Post-colostrum[a]	Months of Age 1	2	3	4	5	6	7	8	9	10	11	12
From Vaccinated Cows														
71.....	2048[b]	2048	2048	→	→	→	→	1024	→	512	→	→	→	→
76.....	< 4	2048	256	128	64	32	→	64	→	→	→	→	→	→
73.....	< 4	1024	256	128	→	64	32	64	128	→	→	→	→	→
66.....	< 4	2048	1024	512	128	→	64	32	→	128	64	128	→	→
64.....	< 4	8192	1024	512	256	→	128	64	32	16	→	4	→	< 2
65.....	< 4	2048	1024	512	256	128	→	64	128	→	512	→	→	1024
70.....	< 4	4096	1024	512	256	32	64	256	128	512	256	128	256	→
74.....	< 4	1024	256	128	64	32	64	→	→	256	128	256	128	→
79.....	< 4	1024	256	128	64	→	16	256	4	→	< 2	→	32	128
78.....	< 4	512	512	128	→	32	16	8	→	4	< 2	→	→	→
From Nonvaccinated Cows														
77.....	2048	2048	512	→	256	→	1024	512	→	1024	→	→	2048	→
67.....	4096	4096	2048	512	→	→	→	→	256	→	→	→	→	512
63.....	128	1024	1024	512	→	→	→	→	→	→	→	→	1024	→
72.....	512	2048	512	256	→	512	256	→	128	→	→	→	512	→

[a]Serum taken two weeks after birth

[b]Titer is the reciprocal of the highest serum or colostrum dilution

presence of antibodies (15). Passively acquired BVDV serum antibody of three (calves 64, 79, 78) of the nine calves continued to decline after four to six months of age reaching titers of < 1:2 at nine to 12 months of age (Table II). Calf 79 at 11 months of age had an increase in titer (Table II) but was not clinically ill.

It has been reported that a virus neutralization titer of 1:4 or greater indicated a previous encounter with BVDV or passive immunity (15). It is further indicated that calves with passive immunity titers of 1:4 or greater are not protected against infection, thus resulting in active immunity (9). This latter statement is not known to be supported by published data, therefore, the observations reported here substantiate the premise that calves with passive BVDV serum antibodies can experience an infection that results in higher serum titers. This is in apposition that maternal passive antibodies interfere with any antigenic stimulus (4). As no clinical disease occurred it would appear appropriate to vaccinate calves for BVDV before weaning, thereby increasing the protective antibodies at a generally accepted time of stress and occurrence of a possible natural BVDV infection.

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