Clinical, Serological and Virological Findings in Cattle With Acute, Sub-acute and Chronic Mucosal Disease

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Introduction

The bovine viral diarrhea virus (BVDV) is a single strand, encapsulated RNA-virus. Taxanomically it is a pestivirus of the family Flaviviridae (Wengler; 1991). According to its behavior in homologous cell cultures, cytopathogenic (cpBVDV) and non-cytopathogenic (ncpBVDV) strains of BVDV are identified. The major difference between these two strains is the cytopathogenic virus capability of cleaving the 125 kD protein into a 54 kD and an 80 kD protein. A mutation (insertion) of the viral RNA which encodes the 54 kD protein and perhaps other proteins seems to be responsible for the difference (Meyers *et al.,* 1989; De Moerlooze *et al.,* 1990). It is assumed that Mucosal Disease (MD) develops after a superinfection with a cpBVDV occurs. According to examinations by Howard *et al.,* (1987) or Moennig *et al.,* (1990) the superinfection must exhibit an epitope-homology to the former antigen. A mutation of a persistent ncpBVDV into a cpBVDV exhibiting an antigen epitope-homology is also discussed (Brownlie *et al.,* 1987; Howard *et al.,* 1987; Corapi *et al.,* 1988; Moennig and Liess, 1988; Moennig, 1992). Depending on the time of infection, the BVDV may either lead to a latent infection or to a wide range of clinical manifestations such as abortions, stillbirths, deformations, fertility disorders, pneumo-enteric diseases, stunted growth, bovine viral diarrhea and mucosal disease (Gründer *et al.,* 1981; Stöber, 1983; Duffel and Harkness, 1985; Doll, 1986; Gründer, 1986a, b and 1990; Schuller and Cerny-Reiterer, 1989; Heckert *et al.,* 1990; Moennig, 1992). An *in utero* infection of a fetus within its immune incompetent stage of development (up to the fourth month of gestation) with a ncpBVDV is of special epidemiological importance. Such an infection leads to a persistent, tolerated infection or perpetuity of the virus which eventually leads to the fatal mucosal disease (Brownlie *et al.,* 1984 and 1986; McClurkin *et al.,* 1984; Bolin *et al.,* 1985). The predominant clinical signs in mucosal disease are diarrhea with characteristic mucosal lesions (erosions) of mucous membranes and the interdigital skin. Less characteristic forms of MD however present considerable diagnostic difficulties. This article will primarily deal with the different chronical manifestations of MD.

Own Investigations

Material and Methods

The study is based on 158 cattle with MD, which were in-patients at the Medizinische und Gerichtliche Veterinaerklinik II of the Justus-Liebig-University in Giessen, Germany from 1986 through 1991. The clinical examination was conducted according to Rosenberger *et al.,* (1990). Special attention was given to the duration, characteristic clinical symptoms, fecal consistency, age, BVD-antibody concentration or virus isolation and seasonal occurrence of the disease in the given cattle with MD. The postmortem investigations were conducted at the Institute for Veterinary Pathology in Giessen, Germany.* The determination of BVDV and specific BVD-antibody concentrations from intra vita and postmortem samples (nasal swabs, EDTA-blood samples, fecal samples and diverse tissue samples) were conducted at the Institute for Hygiene and Infectious Diseases of Animals in Giessen, Germany.** Current tissue culture techniques and virus neutralization tests were applied according to Frey *et al.,* (1991).

Results

Number of MD Cases and Duration of Disease

Of the 158 cattle with MD, 103 animals (65%) showed acute MD; 19 (12%) showed sub-acute MD; and 36 (23%) animals showed chronic MD (Fig. 1). The mean duration of the disease was eight days in the acute form, twenty days in the sub-acute form, and fifty days in the chronic form.

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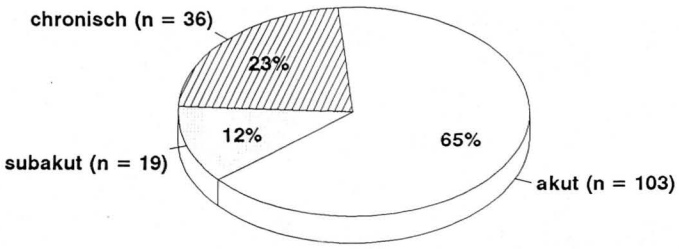
Figure 1. Duration of disease in 158 cattle with mucosal disease.



Occurrence Frenquency of Distinguishing Clinical Findings

Diarrhea was the most frequent clinical finding, occurring in 80% of the acutely and sub-acutely ill cattle and in 60% of the chronically ill cattle. Approximately 65% of the acutely and sub-acutely ill animals showed reddening and erosions of the oral and nasal mucosa. Fifty percent of the chronically ill exhibited these clinical signs. Lesions of the interdigital skin were seen more often in sub-acutely ill than chronically ill patients, 43% and 37% respectively. Acutely ill animals showed interdigital lesions in only 27% of the cases. Those animals exhibiting stunted growth were also less widely spread among the acutely ill, averaging a mere 4% in comparison to 10% and 36% among the sub-acutely and chronically ill. A similar distribution is observed with regard to bronchopneumonia. Chronically ill animals have a high occurrence of this disease with an incidence of 31%. In acutely and sub-acutely ill animals, bronchopneumonia was diagnosed in 15% and 16% respectively. Nasal discharge was similarly observed in 29% of the acutely ill and 31% of the chronically ill animals. A much higher incidence, however, was observed among the sub-acutely ill animals, with nasal discharge being observed in 57% of the cases. Furthermore, bronchopneumonia was diagnosed as the sole clinical symptom in only very few of the animals. These were again more widely spread among the chronically (9%) and sub-acutely (6%), than among the acutely ill (Fig. 2). Encrusted exanthema was merely observed in 3 chronically ill animals. In observing fecal consistency, it was evident that 16% of the acutely ill, 21% of the sub-acutely ill, and 55% of the chronically ill animals showed varying consistencies from watery to highly viscous. Watery, brown-red, bloody, or fibrinous excrements were observed in 22% of the acutely ill, 11% of the sub-acutely ill, and 9% of the chronically ill animals. Watery brown to gray-green colored excrements were seen in 65% of the acutely and sub-acutely ill and in only 37% of the chronically ill (Fig. 3).

BVD-Virus and Antibody Detection

BVDV was isolated in 140 animals overall. Isolation was performed in tissue culture by testing nasal swabs, fecal samples, EDTA blood samples, and various

Figure 2. Distinguishing clinical signs in 158 cattle with mucosal disease.

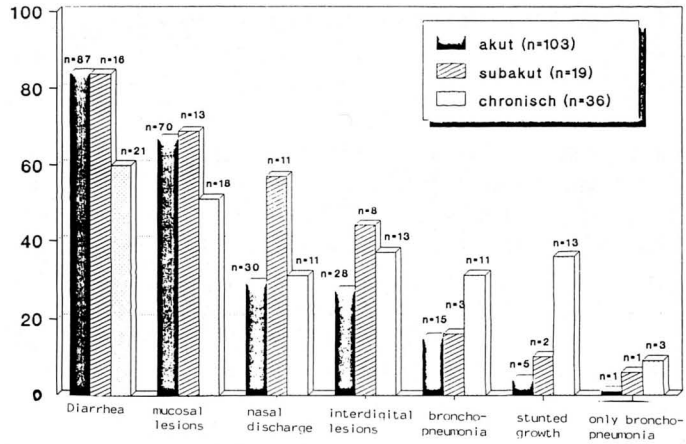
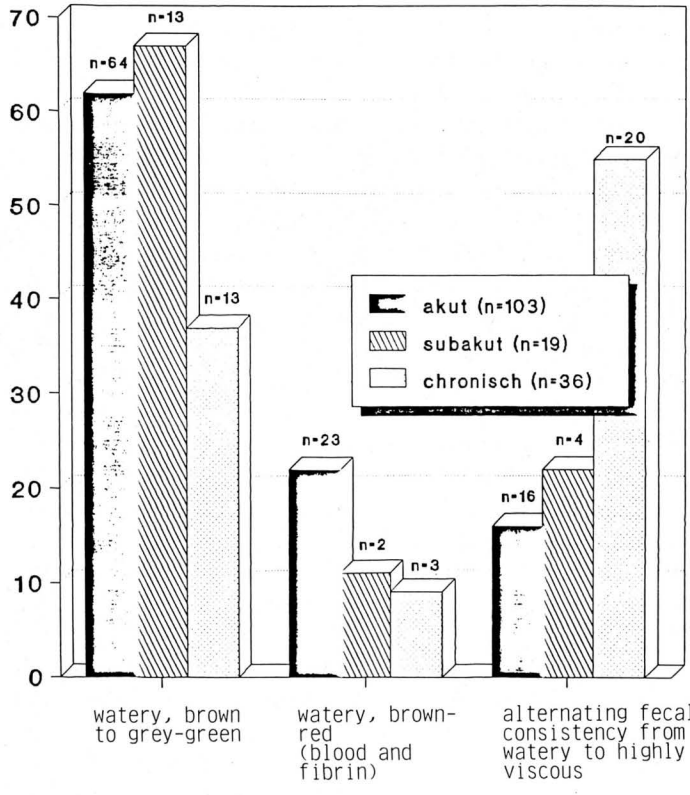


Figure 3. Fecal consistency in 158 cattle with mucosal disease.



tissue probes. Only one of the listed probes was required to test positive in order for the animal to be listed as BVDV-positive. Seventy-nine of these isolations rendered cpBVDV. Thirty-seven showed ncpBVDV. In 24 cases both cp and ncpBVDV were able to be isolated (Table 1). 155 animals were serologically tested. 149 animals rendered a neutralizing antibody titer below the detectable limit of <1:10. Six animals tested positive (>1:10). One animal which had tested negative in

all virus-isolation-tests rendered an antibody-titer of 1:640. Three animals were not tested (Table 2).

Table 1. Detection of cytopathogenic and non-cytopathogenic BVDV in 158 cattle with acute, sub-acute and chronic mucosal disease.

Duration of disease	zpBVDV		nzpBVDV		zp- u. nzpBVDV		negative	
	(n)	%	(n)	%	N	%	(n)	%
acute (n=103)	57	55.3	21	20.4	16	15.6	9	8.7
subacute (n=19)	5	26.3	6	31.6	3	15.8	5	26.9
chronic (n=36)	17	47.2	10	27.8	5	13.9	4	11.7
TOTAL	79	50	37	23.4	24	15.2	18	11.4

zpBVDV = zytopathogenes BVD-Virus
nzpBVDV = nichtzytopathogenes BVD-Virus

Table 2. Detection of BVDV neutralizing antibody in 158 cattle with acute, sub-acute and chronic mucosal disease.

Duration of disease	BVD-Virus-Neutralizationstiter		
	<1:10 (n)	>1:10 (n)	not tested
acute (n=103)	98	2	3
subacute (n=19)	19	-	-
chronic (n=36)	32	4	-
Total	149	6	3

Age Distribution

By observing the age of the animals with MD it can be concluded that most of the cattle fall ill between four and twelve months of age (Fig. 4). The youngest calf with MD merely reach an age of two weeks. Eleven animals (7%) were over 2.5 years of age, the oldest being six years old.

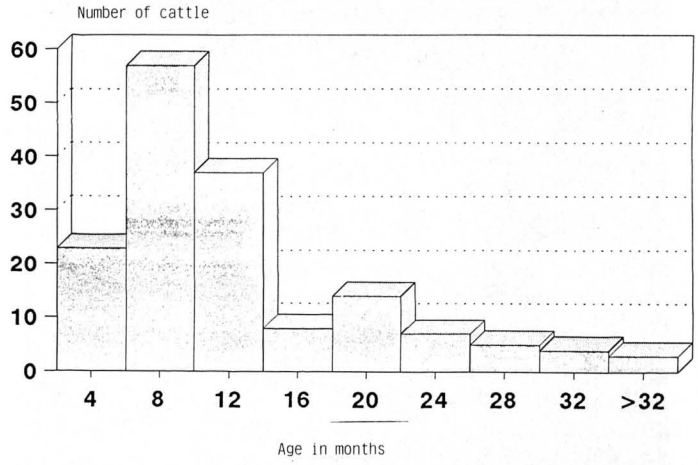
Seasonal Occurrence

In examining the seasonal distribution of MD-cases, specific seasonal peaks were not observed.

Discussion of Results

By nature, Mucosal Disease is an acutely progressing disease marked by diarrhea and occasional lesions of mucous membranes and the interdigital skin (Stöber, 1983; Brownlie *et al.*, 1985; Duffel and Harkness, 1985). Based on the clinical records of 158 cattle with MD, a chronic course of the disease was determined in 36 animals (23%). It must be noted that in most of these cases (86%), the anamnesis was used to classify the cattle into the group of chronically ill. In 1986a and 1990 Gründer

Figure 4. Age distribution of 158 cattle with mucosal disease.



had already pointed out the occurrence of chronic MD cases. These are rarely diagnosed on account of MD's characteristic symptoms such as diarrhea and mucosal lesions. According to the given investigation, diarrhea is still the most frequent clinical finding in MD. It is, however, noticeable that the frequency of diarrhea of approximately 80% in acutely and sub-acutely ill animals sinks to 60% among the chronically ill. On the other hand, the percentage of animals with both diarrhea and bronchopneumonia rise from approximately 15% among acutely and sub-acutely ill to 31% among the chronically ill. In fact, 9% of the chronically ill show only respiratory tract affections. Those animals with anamnestic descriptions such as "loses weight" or "lags behind age group" and clinical findings such as scruffy coat and poor physical appearance were classified as runts. Their classification accounted for 4% of the acutely ill, 10% of the sub-acutely ill, and 36% of the chronically ill. Doll and Gerbermann (1988) came up with even higher numbers (28% with bronchopneumonia and 61% runts) among their patients. The frequency of mucosal lesions falls from 68% among acutely ill to 50% among the chronically ill; a tendency which has already been observed by Gründer (1988a, 1990). Of interest appears to be the increasing incidence of epithelial swelling and a light reddening of the muzzle and nasal orifices in cattle with chronic MD in the recent past (Fig. 5-9). The occurrence frequency of interdigital lesions ranging from 27% to 43% are in accordance with past publications, which state similar results (Doll, 1986; Gründer, 1986a, Doll and Gerbermann, 1988). Animals lacking these characteristic symptoms pose great diagnostic difficulties when a virus examination is not available to the called veterinarian. Increasingly difficult are those cattle with MD that lack the main symptom of diarrhea, or that merely show an alternating fecal-consistency (Gründer, 1986a; Doll and Gerbermann, 1988; Gründer,

Figure 5. Erosions on the hard palate of a young Holstein.

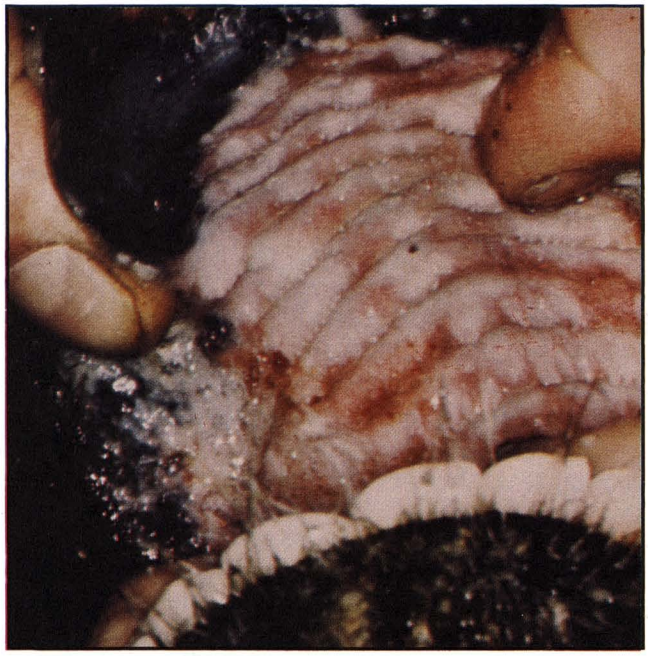


Figure 6. Pin-head sized reddings on the hard palate of a young red Holstein heifer with acute mucosal disease.

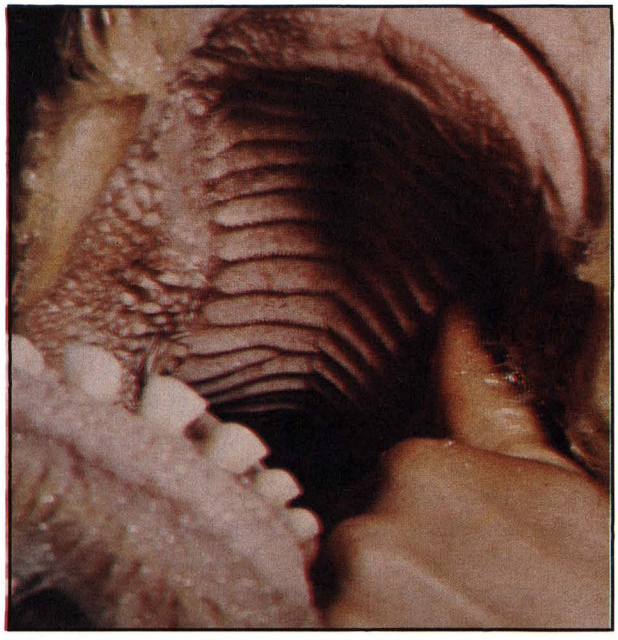


Figure 7. Epithelial swelling and reddened muzzle in a twenty-one month old Limousin cow with chronic mucosal disease.

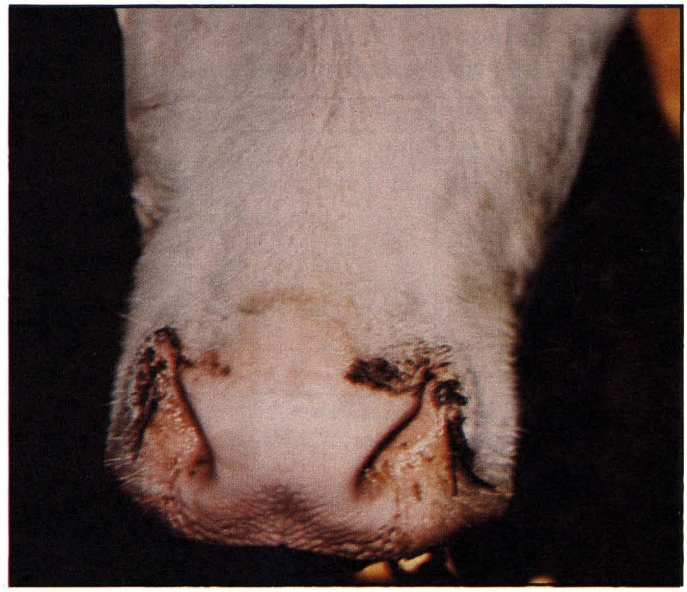
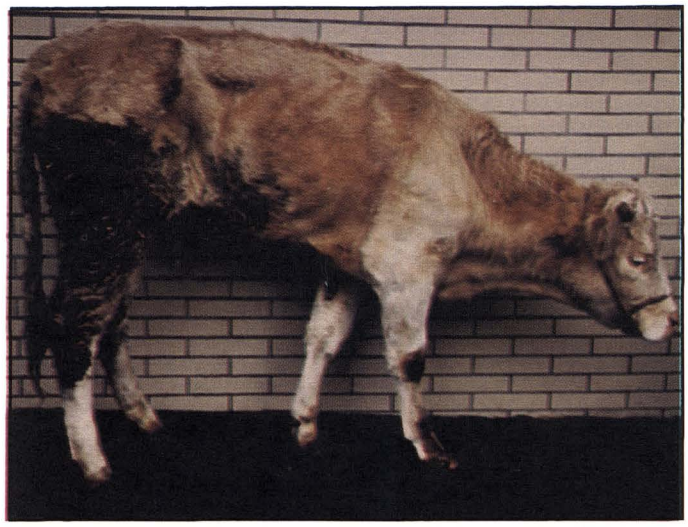


Figure 8. Epithelial swelling and slightly reddened nasal orifices in a twenty-one month old Simmental cow with mucosal disease.

1990). The very high incidence (55%) of the chronically ill cattle showing alternating fecal-consistency highlights this point. In order to set apart possible differential diagnosis the Bovine Leukocyte Adhesion Deficiency - BLAD - (Stöber, 1991) should be brought to mind. Of further importance are strong manifestations of infectious bovine rhinotracheitis, salmonella infections in older cattle, bovine malignant catarrhal fever and outside of Europe, the "Rinderpest" (Gründer, 1986a) and solar dermatitis, especially of the muzzle. Suspicious cases and especially the chronic forms must lead to virological examinations of all sick animals. Should laboratory examinations verify the initial suspicion, an

Figure 9. Highly emaciated, one year old Charolais heifer with chronic mucosal disease.



examination of the whole herd in regard to persistent, viraemic cattle should be conducted. It is of further importance then to vaccinate all heifers in the herd before breeding commences. The laboratory diagnosis should be supported by virus isolation, due to the varying interpretation of results derived from serological testing. An acceleration of diagnostic measures can be reached by turning to recently developed techniques such as continuous flow cytometry (Wolf, *et al.,* 1991) or the Antigen Capture (AgC) - ELISA for verification of the BVDV-antigen in the blood of viraemic cattle (Gottschalk, 1991). The various disease fighting measures brought forth by different authors in the recent past will not be further discussed in this paper. It remains to be said, however, that the most important measures are the identification and elimination of persistent viraemic cattle and the prevention of an intra-uterine virus transmission (Liess *et al.,* 1983; Stöber, 1983 and 1991; Duffel and Harkness, 1985; Gründer, 1986a; Liess *et al.,* 1987; Stahl *et al.,* 1987; Moennig and Liess, 1988; Gerbermann *et al.,* 1990; Moennig, 1992).

BVD-virus isolation was possible in approximately 90% of the cases, similar to the results obtained by Gründer (1986a). This is possible due to the animals showing persistent viraemia and virus shedding until death. The differentiation of BVDV in cattle with MD or having died thereof into cpBVDV and ncpBVDV does not pose a diagnostic advantage. Both strains are repeatedly found in these cases. The same conclusion has been brought forth in many publications throughout the literature (Brownlie *et al.,* 1984; Bolin *et al.,* 1985b; McClurkin *et al.,* 1985). Virus neutralizing antibodies were absent in almost all cases of MD. It should be noted that neutralizing antibodies may be found in persistent viraemic or MD stricken cattle nevertheless. These are usually directed toward heterologous BVDV (Steck *et al.*, 1980; Liess *et al.,* 1983). The finding of neutralizing BVDV-antibodies therefore does not eliminate the possibility of the animal being persistently viraemic. By far, most patients fall ill to MD at an age between four and twelve months. Most authors similarly conclude that most MD cases arise in young heifers (Doll, 1986; Gründer, 1986a; Doll and Gerbermann, 1988; Stöber, 1991). Even further it should be mentioned that adult cattle can also contract MD in occasional cases (Cutlip *et al.,* 1985; Doll, 1986; Gründer, 1986b; Doll and Gerbermann, 1988; Stöber, 1991). According to the data, 11 cattle (7%) were older than 2.5 years, with one individual reaching an age of six years. The specific importance of those animals showing no clinical symptoms until the outbreak of the disease at a later point of time, in conjunction with virus persistence, has been described by different authors and will not be discussed here (Liess, 1988; Stöber, 1991). By analyzing the seasonal occurrence of MD it can be concluded, in accordance with Doll (1986), that there are no seasonal peaks. The incidence of MD is therefore not greater in any specific season as Gründer (1986a) had originally stated for spring. Overall, it was determined that chronic forms of MD are not rarely observed. These chronic forms exhibit indistinct symptoms such as alternating fecal consistency and mild mucosal lesions to none at all.

Summary

Clinical, serological and virological findings in cattle with acute, subacute and chronic Mucosal Disease are recorded. In a retrospective study, clinical findings of 158 cattle with Mucosal Disease (MD) were evaluated for duration of disease, main clinical symptoms, structure of faeces, serological and virological findings, age and seasonal distribution of disease. 65% of the animals had acute, 12% subacute and 23% chronic MD. The latter did not always show typical symptoms of MD. BVD-virus could be isolated from 90% of the patients, whereas only 6% had virus-neutralizing antibodies. Most animals fell sick between four and twelve months of age. No seasonal peaks could be determined.

Acknowledgement

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