Current situation of bovine virus diarrhoea-mucosal disease (BVD-MD) virus infections and their antigenic diversity in Hokkaido, Japan

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Summary: The current situation of bovine virus diarrhoea-mucosal disease (BVD-MD) virus infections is briefly reviewed, with special reference to problems arising from fetal infection in the Hokkaido district, a northern island of Japan. The results of some investigations on BVD-MD virus carried out in Japan are also described. Although bovine congenital anomalies caused by BVD-MD virus and mucosal disease may be late sequelae to fetal infection and occur sporadically, it appears that their incidence and importance in the Hokkaido district have increased in recent years. The results of antigenic characterisation of the recent isolates and serologic survey on bovine sera suggested that BVD-MD viruses with various antigenic properties are widespread among cattle in the district. There is also a possibility that clinical manifestations in infected cattle may differ with the antigenicity of the viruses. In addition, the virological investigations on experimental and naturally occurring mucosal disease suggested that persistently infected cattle are populations at high risk of developing mucosal disease. The antigenic homology of non-cytopathogenic persistent virus and cytopathogenic virus is probably an important factor in the pathogenesis of mucosal disease.

KEYWORDS: Antigenicity - Bovine virus diarrhoea - BVD-MD virus - Congenital infection - Epidemiology - Hokkaido - Incidence - Japan - Mucosal disease - Pathogenicity - Persistent infection.

INTRODUCTION

Although bovine virus diarrhoea-mucosal disease (BVD-MD) virus was first recognised in the United States in 1946 in association with acute and often fatal disease (39), the initial discovery of the virus in Japan was made accidentally in the beginning of the 1960's by Omori and co-workers (21, 41, 42). They prepared many cell cultures of bovine origin at that time and detected several non-cytopathogenic (NCP) BVD-MD viruses in bovine testicle and kidney cell cultures. The virus had nationwide distribution in cattle herds, with a prevalence of serum neutralisation antibody ranging from 50 to 100%. A febrile response was induced with a characteristic pattern of two peaks in cattle following experimental inoculation. The significance of NCP BVD-MD virus in bovine diseases, however, remained obscure.

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Subsequently, isolation of cytopathogenic (CP) BVD-MD virus from a calf with chronic diarrhoea (26) and calves fatally affected with severe diarrhoea (17, 22), that resembled mucosal disease (44), have been reported. In addition, outbreaks of congenital neurological defects caused by NCP BVD-MD virus have been reported by several workers (12, 16, 38, 47, 48, 49). However, BVD-MD virus infections were not thought to be major diseases of cattle in Japan until the beginning of the 1980's because the problems associated with these infections were only recognised sporadically.

In the 1980's the situation has taken a new turn. Various improvements of laboratory technology contributed to bringing the attention of many veterinary diagnosticians to BVD-MD virus infections. Especially with the application of bovine fetal muscular (BFM) cell cultures to BVD-MD virus (18), the routine isolation and identification of virus and detection of its neutralising antibody were facilitated. In consequence, various diseases associated with BVD-MD virus infection were reported and the virus was recognised as one of the important pathogens for cattle (25).

BVD-MD virus is recognised as a causative agent of multiple bovine diseases that include transient fever, leukopenia, respiratory disease with or without diarrhoea, immunosuppression, breeding problems, abortion, fetal mummification, malformations of the central nervous system, persistent infection of calves and mucosal disease (1). Congenital anomalies and mucosal disease seem to be the more important problems in Japan. However, there is insufficient data to make a nationwide survey of the current situation. In this brief review, therefore, some aspects of BVD-MD virus infections are described as they occur in the Hokkaido district, a northern island of Japan. These aspects include incidence, epidemiology, pathogenesis and antigenic diversity of the recent isolates of BVD-MD virus. The Hokkaido district, covering 83,513 km², is the most developed area of animal husbandry in Japan and has approximately 800,000 dairy and 20,000 beef cattle.

**INCIDENCE OF BVD-MD VIRUS INFECTIONS**

**Technical comment**

It seems beneficial to describe BFM cell cultures before the main subject because their use led to great progress in the investigation and diagnosis of BVD-MD virus infections in Japan.

Before 1980, bovine testicle and kidney cell cultures had almost always been used for research and diagnostic work on BVD-MD virus infections. These cells were often contaminated with NCP BVD-MD virus and this had troubled many workers for a long time. The problem was overcome by Hashiguchi and Murakami (18) who developed a new assay system using BFM cells. These cells are susceptible to both CP and NCP BVD-MD viruses and support good growth of both. CP virus can induce a distinct cytopathic effect and NCP virus can be assessed by its ability to interfere with multiplication of CP virus (50, 51, 52), by the END (exaltation of Newcastle disease virus) method (21, 41, 42) or immunofluorescent staining. For the practical application of BFM cell cultures to research and diagnostic work, a seed-lot system is recommended. Primary BFM cultures prepared by an ordinary cell culture method are examined thoroughly for contamination with NCP BVD-MD virus. When the
absence of contamination is confirmed, cells are freeze-stored as the seed-lot. BFM cells reconstituted from one ampoule of the seed-lot can be used for at least five to six months or over at least 30 passages without considerable decrease in susceptibility to BVD-MD virus. Other advantages of BFM cell cultures are their high multiplication rate and easiness of passage, maintenance and large-scale cultivation.

The following investigations on BVD-MD virus infection in Japan depended greatly on the BFM cell culture system.

Viruses associated with bovine congenital anomalies in Japan

Several viruses are recognised or suspected as the causative agents of bovine congenital anomalies in Japan. They include Akabane and Aino viruses of the Shimbu group of the *Bunyaviridae* genus, Chuzan virus of the Palyam subgroup and bluetongue virus of the bluetongue subgroup of the *Orbivirus* genus, and BVD-MD virus of the *Pestivirus* genus (35).

Akabane virus is well known as the most hazardous virus for pregnant cattle in Japan, and epizootic congenital anomalies of calves occur periodically at intervals of about ten years; approximately 40,000 and 9,000 calves were affected in outbreaks during 1972-1975 and 1985-1986 respectively (27, 28, 29, 30, 37, 40).

Chuzan virus was recently recognised as one of the teratogenic viruses. An epizootic of congenital anomalies of calves characterised by hydronencephaly and cerebellar hypoplasia broke out in the Kyushu district, a southern island of Japan, from November 1985 to April 1986. About 2,000 beef cattle, along with a few cases in dairy cattle, were affected with the disease. Many attempts were made to investigate the aetiological agent of this hazardous disease. Based on serological and epidemiological evidence and the results of experimental infection, Chuzan virus was established as the causative agent (13, 14, 36).

A few cases of bovine congenital anomalies associated with Aino virus have been reported in south-western Japan but the disease has not been reproduced experimentally (35, 37).

Although bluetongue virus and its antibody have been detected in Japanese cattle, the suspected cases of congenital anomalies have not been reported.

The diseases associated with Akabane and Chuzan viruses often take epizootic forms since they are both arthropod-borne. These viruses are considered the most dangerous teratogenic viruses for bovines in Japan. However, Akabane and Chuzan viruses are not serious problems in the Hokkaido district, probably because there are no insects capable of their transmission. In the Hokkaido district, BVD-MD virus is regarded as a more important teratogenic virus and the diseases associated with it have become considerably more important in recent years.

Incidence of congenital anomalies caused by BVD-MD virus

Fetal infection with NCP BVD-MD virus between 100 and 150 days of gestation often results in malformations of the central nervous system characterised by cerebellar hypoplasia, hydronencephaly, internal hydrocephalus, optic neuritis, etc. (1). Table I shows the numbers of reported cases of congenital neurological defects caused by BVD-MD virus in the Hokkaido district. The frequency of congenital defects
caused by BVD-MD virus has increased remarkably in recent years. One explanation for this is that many veterinarians have recently begun to pay attention to BVD-MD virus infections. The other possibility is that a new type of virus more liable to cause congenital neurological defects has appeared in the past decade. This possibility is discussed in the section on epidemiology and antigenic diversity of BVD-MD virus.

### Table I

Reported cases of bovine congenital neurological defects caused by BVD-MD virus in the Hokkaido district

<table>
<thead>
<tr>
<th>Year</th>
<th>Dairy cattle</th>
<th>Beef cattle</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1979</td>
<td>23</td>
<td>0</td>
<td>23</td>
</tr>
<tr>
<td>1980</td>
<td>3</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>1981</td>
<td>3</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>1982</td>
<td>25</td>
<td>0</td>
<td>25</td>
</tr>
<tr>
<td>1983</td>
<td>16</td>
<td>0</td>
<td>16</td>
</tr>
<tr>
<td>1984</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>1985</td>
<td>139</td>
<td>0</td>
<td>139</td>
</tr>
<tr>
<td>1986</td>
<td>134</td>
<td>6</td>
<td>140</td>
</tr>
<tr>
<td>1987</td>
<td>136</td>
<td>3</td>
<td>139</td>
</tr>
<tr>
<td>1988</td>
<td>57</td>
<td>0</td>
<td>57</td>
</tr>
</tbody>
</table>

However, the exact incidence of congenital defects caused by BVD-MD virus is not known because diagnosis of the diseases involves great difficulties. The demonstration of neutralising antibody in pre-colostral sera is the only available diagnostic method for congenital defects; usually BVD-MD virus cannot be isolated from affected calves. It is questionable, therefore, whether the data in Table I indicate the actual numbers of congenitally affected calves, and more are probably present in the field.

**Incidence of persistent infection and mucosal disease**

It is well known that fetuses may become immunotolerant to the infecting virus. Persistently infected calves may be born when pregnant cattle are infected with NCP BVD-MD virus in early gestation up to 90 days and occasionally up to 125 days (32, 46).

In the Hokkaido district, persistently infected cattle are often found in farms or areas with a recent history of outbreaks of congenital neurological defects caused by BVD-MD virus (24, 51). However, the prevalence of persistently infected cattle in the entire population is not known. In Japan, there has been one report dealing with the prevalence of persistently infected cattle in the areas where outbreaks of congenital anomalies occurred within the previous one to two months (51). Of 154 cattle from such areas, 18 (11.7%) were positive for NCP BVD-MD virus. Second blood samples were obtained from 13 of 18 calves, that were viraemic in the first test, one to two months after the initial sampling. NCP BVD-MD virus was re-isolated from 12 of 13 cattle indicating that they were persistently infected. At least 8.1% (12/149) of calves were, thus, considered as persistently infected. About half of the persistently infected cattle were clinically normal but the others appeared to be weak and undersized.
These results agree approximately with those reported in Denmark by Meyling (34) who has demonstrated that 0.9% of apparently healthy cattle going to slaughter, and 10.5% of those from 13 herds with a history of BVD-MD virus infection, were viraemic. According to reports so far (2, 20, 34, 43, 51), it seems likely that the prevalence of persistently infected cattle varies widely among herds and may be estimated at less than 1% in the general population but considerably higher in herds or areas with a recent history of BVD-MD virus infection.

Mucosal disease is the sporadic but fatal form of BVD-MD virus infection. The hypothesis that persistently infected cattle, induced \textit{in utero} by infection with NCP BVD-MD virus, are populations at high risk of developing and later succumbing to mucosal disease, has been supported by many workers (1, 7). Although both acute and chronic forms of mucosal disease have been reported in the Hokkaido district the prevalence is unknown. Some characteristic features in the epidemiology of mucosal disease are sporadic occurrence of low morbidity and high mortality. However, outbreaks of mucosal disease in which more than ten cattle were affected within one to two months have occasionally been reported (17, 22; S. Murakami, personal communication).

**PATHOGENESIS OF BVD-MD VIRUS INFECTION**

Pathogenesis of mucosal disease

In Japan, there are few reports on the experimental analysis of mechanisms involved in the pathogenesis of congenital anomalies caused by BVD-MD virus. In the meanwhile, some studies on the pathogenesis of mucosal disease have been reported (17, 22, 50, 52).

Hashiguchi \textit{et al.} (17) produced experimental mucosal disease in one apparently healthy calf by inoculating a CP BVD-MD virus that was isolated from naturally occurring mucosal disease (22). This is probably the first report on the experimental production of mucosal disease. At present the assumption that mucosal disease is a late sequel to fetal infection with NCP BVD-MD virus is accepted by many workers (1, 7), since both CP and NCP viruses are frequently isolated from naturally occurring mucosal disease (19, 31, 50) and the disease is reproduced experimentally in persistently infected cattle by inoculation with CP virus (3, 5, 6, 45, 52). Although there is no detailed description of the calf used in the experiment of Hashiguchi \textit{et al.} (17), the virological and serological responses of the affected calf were similar to those in cases of experimental mucosal disease produced in persistently infected cattle (52). It seems reasonable, therefore, to consider the calf that developed mucosal disease in their experiment as persistently infected.

One of the interesting results of recent studies on mucosal disease has been the suggestion that antigenic homology of CP and NCP BVD-MD viruses is related to pathogenesis of the disease (50, 52). In a field survey of naturally occurring mucosal disease, both CP and NCP viruses could be isolated from almost all cases and antigenic similarity in both viruses was demonstrated (50). This coincides with the results reported by Bolin and co-workers (2, 31) and Howard \textit{et al.} (19). In addition, in three of four cattle persistently infected with NCP BVD-MD viruses, either mucosal disease or chronic diarrhoea appeared after challenge with CP viruses that were antigenically
different from the persistent viruses (52). Interestingly, the CP viruses recovered from
the affected cattle at necropsy were antigenically different from the challenge viruses
but similar to the NCP persistent viruses. These facts seem to indicate that antigenic
homology of CP and NCP BVD-MD viruses may be an important factor in the
pathogenesis of mucosal disease as suggested by other workers (6, 7, 19). Little is
known, however, about the origin of CP virus that can be recovered from mucosal
disease and that is antigenically identical to NCP persistent virus, although a mutation
of the NCP form, causing persistent infection, to the CP form has been suggested
(7, 19). Further studies on the genetics and mutations of BVD-MD virus and on the
interactions between NCP and CP viruses in the course of mucosal disease may be
expected to elucidate the origin of CP virus and pathogenesis of the disease.

EPIDEMIOLOGY AND ANTIGENIC DIVERSITY OF BVD-MD VIRUS

Epidemiology

Outbreaks of congenital problems caused by BVD-MD virus are characteristically
sporadic and non-seasonal in occurrence, with a few exceptional cases of the epizootic
form. This is probably because, in part, BVD-MD virus is not arthropod-borne and
the prevalence of immune cattle in the general population is high. BVD-MD virus
seems to be transmitted directly from either acutely or persistently infected to
susceptible cattle. BVD-MD virus is quite different from Akabane and Chuzan viruses
in the means of transmission. The latter viruses are arthropod-borne and occasionally
cause hazardous and epizootic bovine congenital anomalies in Japan. There is also
likely to be considerable variation in the incidence of congenital problems caused
by BVD-MD virus among herds or areas. This is probably due to the fact that the
populations of immune cattle vary widely among herds or areas although in the general
population the incidence is usually high.

When BVD-MD virus invades a farm or area with a low population of immune
cattle, the virus spreads readily and rapidly and raises serious problems in pregnant
cattle. The occurrence of such a case is rare but once this happens, various noteworthy
events start in the herd. Kimura et al. (24) observed such a case and reported the
events which followed the introduction of BVD-MD virus into a farm. From
November 1986 to May 1987, various congenital anomalies occurred in a large farm,
located in the northern part of the Hokkaido district, where about 400 dairy cattle
were reared. During that period, 32 dams were pregnant and congenital anomalies
occurred in 25 (78%). They include five aborted fetuses, four persistently infected
cattle and sixteen calves with malformations of the central nervous system. Virological
and serological examinations indicated that BVD-MD virus was the causative agent
of the outbreak. The time of spread of the virus among cattle in the farm was
epidemiologically considered as the end of October 1986. The relationship between
gestational days at that time and the outcome of fetuses was of great interest and
indicated clear variations of sequelae with fetal maturation (Table II). Infections before
90 days of gestation induced mostly abortion and persistently infected cattle, while
those between 90 and 150 days caused congenital neurological defects. These
observations are similar to those reported by Roeder et al. (46). It appears, thus, that
BVD-MD virus causes considerable loss to cattle production when herds with a low
population of immune cattle are invaded.
TABLE II

Serious congenital problems caused by BVD-MD virus
in a large farm of dairy cattle (a)

<table>
<thead>
<tr>
<th>Gestational days at infection (b)</th>
<th>No. of pregnant cattle</th>
<th>Outcome (no. of cattle) (c)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Normal</td>
</tr>
<tr>
<td>&lt;90</td>
<td>14</td>
<td>3</td>
</tr>
<tr>
<td>90-150</td>
<td>14</td>
<td>0</td>
</tr>
<tr>
<td>&gt; 150</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Total</td>
<td>32</td>
<td>7</td>
</tr>
</tbody>
</table>

a) Modified from the report of Kimura et al. (24)
b) Epidemiologically estimated
c) AB : abortion
PI : persistently infected cattle
CND : congenital neurological defects

Although it is evident that BVD-MD virus is transmitted from acutely and persistently infected to susceptible cattle, there are only a few cases of outbreaks in which the route of introduction of virus into new herds or areas has been elucidated. In Japan as well as in other countries, however, the view that persistently infected cattle play a more significant role in the transmission and maintenance of BVD-MD virus, than acutely infected cattle, is now supported by many workers.

Antigenic properties of Japanese isolates

Although all BVD-MD viruses, whether CP or NCP in cell cultures, share common antigen(s), antigenic differences among the strains have been demonstrated by many workers (8, 11, 15, 19, 23). More recently, attempts have been made to use monoclonal antibodies for differentiation of BVD-MD viruses (4, 9, 10, 33).

In the initial investigations, Japanese isolates of BVD-MD virus were shown to be related antigenically to some strains originating in the United States (17, 26, 41). Subsequently, Itoh et al. (23) reported that Japanese isolates of NCP BVD-MD virus were antigenically identical to one another but distinguishable from the American strains in a cross-neutralisation test. More recently, antigenic diversity among Japanese isolates was reported (51). NCP viruses isolated from persistently infected cattle in 1986 were compared antigenically, with the reference strains that were isolated previously in Japan, in the cross-neutralisation test. As shown in Table III the new isolates, KS86-1 and OS86-1, were found to be distinguishable from the reference Nose, T-20 and No. 12 strains (51). The virus groups were tentatively designated as the KS86-1 (K) and Nose (N) groups, respectively (53). These seem to indicate that BVD-MD viruses with various antigenicities are spread widely among Japanese cattle. This was also confirmed by a serological survey on sera from Japanese cattle. Serum samples collected from 713 cattle between 1974 and 1988 were tested for neutralising antibody to BVD-MD virus using antigenically different viruses from groups N and K. The type of virus that was suspected of infecting seropositive cattle was presumed according to the reaction patterns of sera to both viruses (53). As shown in Table IV, the prevalence of BVD-MD virus antibody was high, ranging from 50 to 100%.
### Table III

**Antigenic comparison of Japanese isolates of BVD-MD virus in the cross-neutralisation test**

<table>
<thead>
<tr>
<th>Virus (b)</th>
<th>Antisera to virus</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Nose</td>
<td>T-20</td>
</tr>
<tr>
<td>Nose (CP, 1974)</td>
<td>100</td>
<td>—</td>
</tr>
<tr>
<td>T-20 (CP, 1978)</td>
<td>50</td>
<td>100</td>
</tr>
<tr>
<td>No. 12 (NCP, 1967)</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>KS86-1 (NCP, 1986)</td>
<td>8</td>
<td>6</td>
</tr>
<tr>
<td>OS86-1 (NCP, 1986)</td>
<td>4</td>
<td>4</td>
</tr>
</tbody>
</table>

All data are expressed as “R” values that were calculated using the following formula: 

\[ R = 100 \times \frac{r_1}{r_2} \]

where \( r_1 \) and \( r_2 \) are heterologous titre of virus 1/homologous titre of virus 2, and heterologous titre of virus 2/homologous titre of virus 1, respectively.

a) Modified from the report of Shimizu and Sato (51)

b) CP : cytopathogenic

NCP: non-cytopathogenic

Year of isolation is indicated in brackets

### Table IV

**Serologic survey using antigenically different BVD-MD viruses in the Hokkaido district**

<table>
<thead>
<tr>
<th>Year</th>
<th>No. of sera tested</th>
<th>No. of sera positive for antibody (%)</th>
<th>Virus suspected of infection (b)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>N group (%)</td>
</tr>
<tr>
<td>1974</td>
<td>50</td>
<td>49 (98)</td>
<td>45</td>
</tr>
<tr>
<td>1976</td>
<td>50</td>
<td>29 (58)</td>
<td>17</td>
</tr>
<tr>
<td>1978</td>
<td>50</td>
<td>50 (100)</td>
<td>32</td>
</tr>
<tr>
<td>1981</td>
<td>63</td>
<td>50 (79)</td>
<td>50</td>
</tr>
<tr>
<td>1982</td>
<td>50</td>
<td>31 (62)</td>
<td>29</td>
</tr>
<tr>
<td>1983</td>
<td>50</td>
<td>44 (88)</td>
<td>23</td>
</tr>
<tr>
<td>1984</td>
<td>20</td>
<td>17 (85)</td>
<td>12</td>
</tr>
<tr>
<td>1985</td>
<td>20</td>
<td>10 (50)</td>
<td>30</td>
</tr>
<tr>
<td>1986</td>
<td>95</td>
<td>54 (57)</td>
<td>13</td>
</tr>
<tr>
<td>1987</td>
<td>119</td>
<td>96 (81)</td>
<td>14</td>
</tr>
<tr>
<td>1988</td>
<td>146</td>
<td>86 (59)</td>
<td>19</td>
</tr>
<tr>
<td>Total</td>
<td>713</td>
<td>516 (72)</td>
<td>25</td>
</tr>
</tbody>
</table>

a) From the report of Shimizu et al. (53)
b) Groups of infected virus in seropositive cattle were presumed by the reaction patterns of sera to the reference viruses of groups N and K

Before 1981, infections with BVD-MD viruses other than group K were prominent and there were no suspected infections with group K virus. Such cattle were first detected in 1982 and increased in number thereafter, thus suggesting that this type
of virus appeared at the beginning of the 1980's and then spread gradually among cattle in the Hokkaido district. However, there is no information on the origin of group K BVD-MD virus. One possible explanation is that an antigenic mutation might occur in existing viruses. Alternatively, group K virus might have been introduced from a foreign country. In fact, cattle persistently infected with NCP BVD-MD viruses have been found in the herds imported from foreign countries, although the viruses isolated from those cattle were antigenically different from group K virus (Oh-Ike, personal communication).

Antigenic comparison of BVD-MD viruses isolated from persistently infected cattle and mucosal disease and its relationship to pathogenicity are described in the next section.

Antigenic properties of viruses isolated from different sources

An interesting result obtained from the recent studies is that antigenic properties of BVD-MD virus differ with the source of virus isolation. Twenty-nine recent isolates, 17 from persistently infected cattle and 12 from mucosal disease, were characterised antigenically by the neutralisation test using antisera to the reference viruses of groups K and N (53). As shown in Table V, 17 isolates from persistently infected cattle were divided into three groups; 12 and 2 were considered as the possible members of groups K and N respectively, and the others were classified into neither group. Twelve cattle in which group K viruses were isolated came from farms with a recent history of outbreaks of congenital neurological defects, and the others were found in farms with no history of the disease. In contrast, the majority (10/12) of BVD-MD viruses isolated from mucosal disease were considered as being classified in group N. Interestingly, no group K viruses were isolated from any cases of mucosal disease. In addition, almost all cattle with mucosal disease were derived from farms with no history of congenital neurological defects. If a bold speculation is allowed on the basis of these results, it would be possible to consider that the pathogenicity of BVD-MD viruses may differ with their antigenicity. It appears that BVD-MD viruses of both groups

<table>
<thead>
<tr>
<th>Source of isolation</th>
<th>History of herd</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>K</td>
</tr>
<tr>
<td>PI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>0</td>
<td>12</td>
</tr>
<tr>
<td>No</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>MD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>No</td>
<td>10</td>
<td>0</td>
</tr>
</tbody>
</table>

Table V

Antigenic characterisation of BVD-MD viruses isolated from persistently infected cattle and mucosal disease

a) Modified from the report of Shimizu et al. (53)
b) PI : persistently infected cattle
MD: mucosal disease
c) Recent history of outbreaks of congenital neurological defects caused by BVD-MD virus
may induce immunotolerance in fetuses when infected in early gestation but group K virus may be more liable than group N virus to cause congenital neurological defects when infected thereafter. In this regard, it is of great interest that congenital anomalies have shown an increasing tendency in the Hokkaido district since the appearance of group K virus at the beginning of the 1980’s. In addition, the evidence that no group K virus was recovered from any cases of mucosal disease suggests the possibility that cattle persistently infected with NCP virus with a particular antigenicity, like group N, may be more liable to succumb to mucosal disease than cattle with others.

The relationships between antigenicity and pathogenicity of BVD-MD viruses appears to be an interesting research subject for the future.

CONTROL OF BVD-MD VIRUS INFECTIONS

Two control measures have now been adopted to prevent BVD-MD virus infections in Japan. One is test-and-removal of persistently infected cattle and the other is the application of a vaccine. Because it is impossible to test all cattle for BVD-MD virus, the veterinary officials of the Livestock Hygiene Centres, located in the fourteen areas of the Hokkaido district, concentrate their efforts on inspecting cattle in the farms or areas where outbreaks of congenital anomalies have recently occurred.

The vaccine used for control of BVD-MD virus infections in Japan is a cell culture adapted living vaccine. Dams are recommended to be vaccinated before insemination, since transplacental transmissibility of the vaccine virus has been reported. Development of a more effective and secure vaccine for BVD-MD virus infection is anticipated.


Résumé : Cet article présente brièvement la situation actuelle des infections dues au virus de la diarrhée virale bovine-maladie des muqueuses (BVD-MD), en évoquant plus spécialement les problèmes de l'infection fœtale dans l'île de Hokkaido, au nord du Japon. Les résultats de quelques travaux effectués au Japon sur le virus BVD-MD sont également présentés. Bien que les anomalies congénitales dues à ce virus et la maladie des muqueuses puissent faire partie des séquelles tardives de l'infection fœtale et avoir une incidence sporadique, il apparait que leur fréquence et leur importance ont augmenté à Hokkaido depuis quelques années. Les résultats de la caractérisation antigénique des souches récemment isolées et d'une enquête sérologique portant sur des sérums de bovins font penser que des virus BVD-MD ayant des propriétés antigéniques diverses sont largement répandus dans le cheptel bovin de l'île. Il est possible, également, que les manifestations cliniques chez les bovins infectés soient différentes en fonction de l'antigénicité des virus. Par ailleurs, les études virologiques sur la maladie des muqueuses expérimentale et naturelle font
penser que les bovins infectés de manière persistante sont exposés à un risque élevé de développer la maladie des muqueuses. L’homologie antigénique entre le virus persistant non cytopathogène et le virus cytopathogène est probablement un facteur important de la pathogénie de la maladie des muqueuses.


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Resumen: Este artículo presenta brevemente la situación actual de las infecciones debidas al virus de la diarrea viral bovina-enfermedad mucosa (BVD-MD), con especial referencia a los problemas de la infección fetal en la isla de Hokkaido, al norte de Japón, así como los resultados de algunos trabajos realizados en Japón sobre el virus BVD-MD. Aunque las anomalías congénitas causadas por este virus y la enfermedad mucosa pueden formar parte de secuelas tardías de la infección fetal y tener una incidencia esporádica, su frecuencia y su importancia han aumentado en Hokkaido desde hace algunos años. Los resultados de la caracterización antigénica de las cepas recientemente aisladas y de una investigación serológica de sueros de bovinos permiten pensar que virus BVD-MD con propiedades antigénicas diversas están vastamente difundidos en el ganado bovino de la isla. También es posible que las manifestaciones clínicas en los bovinos infectados sean diferentes en función de la antigenicidad de los virus. Por otra parte, los estudios virológicos sobre la enfermedad mucosa experimental y natural permiten pensar que los bovinos infectados de manera persistente corren un gran riesgo de desarrollar la enfermedad mucosa. La homología antigénica entre el virus persistente no citopatógeno y el virus citopatógeno es, probablemente, un factor importante de la patogenia de la enfermedad mucosa.


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REFERENCES


