The pathogenesis of bovine virus diarrhoea virus infections

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Summary: Bovine virus diarrhoea virus (BVDV) disease in cattle ranges from the transient acute infections, which may be inapparent or mild, to mucosal disease which is inevitably fatal. On occasions the acute infections can lead to clinical episodes of diarrhoea and agalactia but as these syndromes cannot be reproduced experimentally, the pathogenesis remains unclear. The immunosuppressive effect of acute BVDV infections can enhance the clinical disease of other pathogens and this may be an important part of the calf respiratory disease complex. Although BVDV antigen has been demonstrated within the lymphoid tissues, for prolonged periods, the evidence for viral latency remains to be proven.

Venereal infection is shown to be important in the transfer of virus to the foetus and congenital infections can cause abortions, malformations and the development of persistently viraemic calves.

The two biotypes of the virus, non-cytopathogenic and cytopathogenic, are described. Their sequential role in the pathogenesis of mucosal disease arises from the initial foetal infection with the non-cytopathogenic virus and the subsequent production of persistently viraemic calves. These calves may later develop mucosal disease as a result of superinfection with a "homologous" cytopathogenic virus. The possible origin of this biotype by mutation is discussed.

Chronic disease is defined as a progressive wasting and usually diarrhoeic condition; it is suggested that this may develop following superinfection of persistently viraemic cattle with a "heterologous" cytopathogenic biotype.


INTRODUCTION

The pathogenesis of any disease reveals the balance between the ability of the host to resist microbial invasion and the capacity of the microbe to inflict damage. The wide variety of clinical signs, observed during bovine virus diarrhoea virus (BVDV) infections, demonstrates the complexity of this balance and thereby poses an equal
complication for any description of pathogenicity. The severity of BVDV disease ranges from acute infection which may be inapparent or mild to mucosal disease which is inevitably fatal.

An emerging tenet of BVDV pathogenesis now appears to be the different roles taken by the two biotypes of the virus; one of which is non-cytopathogenic and the other cytopathogenic and distinguishable by their cytopathology in cell culture. The separate and yet interacting roles of these biotypes have emerged over the last six years and have fascinated both the clinician and the researcher interested in BVDV pathogenesis. A detailed description of the pathogenesis is now given which will complement other chapters in this Review.

**ACUTE DISEASE**

**Acute BVDV infections**

Acute BVDV infection in cattle is generally mild if not inapparent to the stockman. It is a common infection with an estimated 70% of cattle within the UK seroconverting to BVDV by 4 years of age (32). However, close clinical scrutiny will often disclose a rise in body temperature, a leukopenia from about days 3 to 7 post-infection and occasionally a mild nasal discharge (21, 58). The BVDV isolated from acute infections is non-cytopathogenic and illustrates that this biotype is the one normally circulating within the cattle population. Characteristic of acute infections is the limited recovery of virus from both blood and nasal secretions during the first 3-10 days whereas there appears to be a slow and prolonged increase in specific antibody for 10-12 weeks post-infection.

The pathogenesis of acute infection has not been clearly described. It is likely that the initial infection is within the oronasal mucosa and that spread from this site is systemic. Virus may be isolated from nasal swabs during the first few days post-infection but only in low titre. There is now preliminary evidence that certain field strains appear to be well adapted to growth in the nasal mucosa (Howard, Clarke and Brownlie, unpublished results). Those capable of rapid growth within the oronasal mucosa may account for the limited oculonasal discharge and shallow ulcerations seen in some of the acute infections (2). Systemic spread of infection may occur as virus free in serum or as virus associated with the cells within the buffy coat fraction of blood; the lymphocytes and monocytes are generally regarded as being particularly sensitive to BVDV infection (65). A decrease in the B-lymphocytes following acute BVDV infection has been reported (54) and a decreased T-cell responsiveness to mitogens (59). However, these findings were not confirmed in subsequent work on a group of 4 to 6-month old calves (19). Changes in the lymphocyte populations have also been examined by the use of fluorescent antibody assays (7). This study has shown that during the leukopenia following BVDV infection, there is a transient decrease in both the B and T-cell lymphocytes but there was effective recovery by 11-17 days post-infection. It would appear that such reductions in lymphocytes do not prejudice the ability of the normal young calf to recover from infection. BVDV will also multiply in non-lymphoid cells, e.g. calf kidney and calf testes cell cultures, under laboratory conditions, but there is limited information about the relevance of this for the pathogenesis of acute disease.
It would be simplistic to discount the pathogenic effect of BVDV during the course of all acute infections. It is clearly evident from clinical observations that BVDV can, under certain circumstances, cause disease. Episodes of agalactia and diarrhoea have been recorded in adult cattle from which BVDV has been identified as the causal organism (52). The original description of disease was of a transmissible diarrhoea in adult cattle (49) and in many of the early studies severe lesions were produced (21, 66). The reason for the severe experimental disease of yesteryear and the failure of present day researchers to reproduce it, is not clear. It may, in part, be the result of a confusion with the acute disease that leads to a clinical manifestation and mucosal disease; recently, the pathogenesis of mucosal disease was clarified (8, 14) and will be explained in detail below. The virus may also have altered in virulence over the years but this is not easy to quantify. Many of the early BVDV isolates have become laboratory-adapted (i.e. NADL) and there is recent evidence that these have become altered in antigenicity (23), perhaps by host nucleic acid insertion into the viral genome (44). There is also the possibility of differences in tissue tropisms between field isolates, some of which may be better adapted to multiply in either the respiratory mucosa or the general systemic tissues. It is interesting to note that in a study of 21 animals, aged between 53 and 440 days, the titre of virus recovered from nasal secretions was age-related and highest in the younger animals whereas the differences in viraemia were not (Clarke, Howard and Brownlie, unpublished results). This may help explain the variation in experimental disease when animals of different age are used. However, the pathogenesis of the severe clinical disease following acute infection will remain unresolved until it can be reproduced experimentally. The pathology of acute infections does not appear to have received attention and this may reflect both the lack of interest in examining mild infections and the failure to reproduce the severe acute disease.

Mixed BVDV infections

A further complication of acute infections occurs when there is invasion of BVDV along with another pathogen. It has been well documented that a mixed infection of BVDV with infectious bovine rhinotracheitis virus (31, 55), bovine respiratory syncytial virus (Dr E.J. Stott, personal communication) or Pasteurella haemolytica (56) produces a more severe disease than with either pathogen alone. It is particularly interesting to note that all those dual infections mentioned above are respiratory and, therefore, it is not surprising that field surveys have implicated BVDV as a causal agent in the calf respiratory disease complex (64). Furthermore, mixing BVDV with an enteric pathogen, such as rotavirus and coronavirus (68) or Salmonella spp. (72), has been demonstrated to exacerbate enteric disease.

The basis for the pathogenesis of mixed infections would appear to be the immunosuppression consequent on the transient leukopenia (see above) and possibly on a neutrophil dysfunction (61) following acute BVDV infections. There is also the suggestion that BVDV may stimulate the release of prostaglandins from blood mononuclear cells and that the prostaglandins in turn would depress lymphocyte blastogenesis (43). Unfortunately, there has been, as yet, no documented research into the effect of BVDV infections on the local immune response. This would have particular relevance for respiratory and enteric infections which are essentially mucosal invasions. Epithelial cells appear to be affected during the acute phase and this may promote the establishment of these surface pathogens.

The outcome of infecting cattle, that are persistently viraemic with BVDV (see below), with other pathogens has been reported. Infecting such animals with bovine
leucosis virus reduced the ability of 4 out of 6 to make strong antibody responses as measured by immunodiffusion (60).

The pathology of these mixed infections is highly dependent on the nature of the second pathogen. In the case of Pasteurella haemolytica, there is a fibrinopurulent pneumonia and pleuritis (56) but from the other reports, there is a lack of descriptive pathology.

**BVDV latency**

An aspect of BVDV pathogenesis that has received little attention is the possibility of viral latency. Under normal conditions, the progress towards recovery following acute infections lies in the development of a specific neutralising antibody response and possibly a cell-mediated response. These immune responses are described in a later chapter of this Review. However, what is striking about this response is the slow rise in antibody over the first 10-12 weeks after infection and yet the failure to recover virus after the first 3-10 days (Fig. 1) (34).

![Graph](image)

**FIG. 1**

**Typical virus detection and specific antibody response following acute BVDV infection of calves**

The failure to isolate virus from either nasal swabs or blood after about day 10 is perplexing for two reasons. Firstly, there is often undetectable antibody by this stage and secondly the antibody response continues in the apparent absence of virus for a further 10-11 weeks. Explanations for this observation may be either that non-
infectious virus (i.e. viral antigen) is being continually presented to the immune cells during these 10-11 weeks or that infectious virus is sequestered in lymphoid tissues. It has been shown that viral antigen is present in the macrophages within the lymphoid tissues of foetuses following experimental infection (4) and this may be a mechanism for continual stimulation of the antibody response. The persistence of viral antigen has been suggested to occur also in the ovaries of cattle for at least 60 days after intramuscular inoculation (63). However, it is uncommon to recover infectious virus from tissues later than 14-21 days post-infection (see the chapter in this issue on diagnosis of BVD/MD in cattle). In earlier years BVDV was reported to be present in various tissues after prolonged periods following infection; virus was isolated from mesenteric and bronchial lymph nodes on days 39 and 56 post-inoculation (46) and from blood and the nares on days 72 and 102 after infection (40). In recent times, this has not been observed and may reflect the closer attention now paid to adventitious virus infecting experimental calves or cell cultures. Experiments to attempt the recrudescence of virus from convalescent animals have not been reported but a summary of our present knowledge suggests there is little evidence for BVDV latency.

Venereal infections

The major interest in any BVDV invasion of the urogenital tract is the possibility of subsequent congenital infection; this risk is greater with the persistently viraemic animal and will be dealt with below. Acute infections of the urogenital tract of seronegative cattle with BVDV can produce clinical disease and may be a greater cause of loss to the national herd than results from the persistently viraemic animal.

The virus can infect both ovarian and testicular tissues and can be recovered from semen of acutely infected bulls (57, 71). The semen is often of poor quality (70) and has the potential to spread infection to sero-negative heifers (45). However, the pathogenesis of urogenital infection during acute disease is poorly described.

**IN UTERO AND CONGENITAL INFECTIONS**

BVDV rarely infects the foetuses of sero-positive cattle. Maternal antibodies appear well able to prevent the access of virus through the placentome. Whether maternal antibody prevents the virus from becoming viraemic has not been determined. It appears that the problem of in utero and congenital infections is restricted to the BVDV sero-negative dam. In these animals, foetal infection can follow from either acute or persistent viraemias.

During acute infection the virus invades the placentome, replicates and may cross to the foetus without producing lesions (22). In sheep, BVDV has been shown to damage the maternal vascular endothelium within 10 days of infection and the resulting cellular debris is ingested by the foetal trophoblast (3). This could be a mechanism of virus transfer from dam to offspring but may also account for the placentitis that leads to the high level of abortion following BVDV infection. It is well recorded that early embryonic death, infertility and “repeat breeder” cows are often the sequel to pestivirus infection during pregnancy (67). In a herd infected with BVDV, the conception rates were reduced from 78.6% in the immune cows to 22.2% in infected cattle (69).
In cattle that are persistently viraemic, there is less certainty about the pathway and timing of foetal invasion because all tissues, including the uterus, are continually infected. However most, if not all, foetuses born of viraemic dams become likewise persistently viraemic. Whether infection of these foetuses occurs at the level of the germ cell or subsequent to the rupture of the zona pellucida upon implantation is still to be clarified. It has been reported that Border disease virus antigen can be found in the germinal cells of the sheep ovary (28) but similar reports in the cow are lacking.

Whether, following acute or persistent infection, the virus infects the foetus by either direct cell to cell transmission or systemic spread is not clear. The time taken for the passage of virus from dam to foetus is variable but it has been recorded that abortions due to BVDV can occur within 10-18 days after intramuscular infection (69). Our own experience has shown that abortions can take place several months after foetal infection.

The outcome of foetal infection is dependent on two main variables: the age of the foetus at the time of infection and the biotype of the infecting virus. There is uncertainty about the pathogenesis of infection during the first 30 days of pregnancy. There is good evidence that BVDV will reduce the conception rate during this period (69) and that the virus will replicate freely in the maternal placenta (50). However, there is also the view that limited transplacental infection occurs during this early stage (71) because the contact between maternal epithelium and foetal trophoblast is not sufficiently intimate for vertical transmission until the “bridge” formation at around 30 days (3, 39). This has implications for the use of infected semen or even during embryo transfer (45).

There is little doubt that foetal infection will occur after this 30-day period and the outcome depends on whether the virus establishes during the first (up to about 110-120 days), the second (to about 180-200 days), or third trimester (to full term, about 280 days). Infection during the first two trimesters can result in abortions (29) whereas infection during the first trimester can also produce calves that remain persistently viraemic for life (see below). Calves infected during the last trimester are able to mount an active immune response (11).

Abortions

The outcome of infection with the non-cytopathogenic biotype during the first and second trimesters is frequently death, abortion or mummification of the foetus (22, 35, 38). Foetal death can follow directly from viral invasion but damage of the maternal placenta may contribute by disrupting its vascular supply of nutrients. Experimental infections during this period have shown that more than 30% of foetuses are aborted (18) but recovery of virus from aborted tissues is poor. However, experimental infection of cattle during the first trimester of pregnancy with the cytopathogenic biotype does not give abortions and there is some doubt whether this biotype can even establish in the early foetus (17).

Teratogenesis

Viruses that establish in the early foetus during organogenesis can have the distinction of causing bizarre malformations that permanently affect the animal. BVDV has a well documented teratogenic effect, in common with other nonarbo togaviruses (67). When the lesions induced by BVDV infection are particularly severe, the foetus will die and be aborted. However, it is evident that the non-cytopathogenic
biotype can replicate in the early foetus, often causing damage to selected tissues but not sufficient to cause death. Such calves are born with a variety of clinical signs that range from apparently normal to weak, unthrifty calves or occasionally brain-damaged calves (see the chapter in this issue on clinical aspects of BVDV infections).

The pathogenesis of this wide range of lesions is unlikely to be due to a single defect. The virus appears catholic in its choice of cells in which to replicate. It has a preference for mitotically active cells, particularly those of the central nervous system (CNS) and lymphoid tissues (5, 10, 26, 27). Whether the pathogenic event is an inhibition of normal cell division and differentiation or due to a direct lytic action of the virus is difficult to determine. Certainly, BVDV causes significant intrauterine growth retardation in many tissues of the foetus, particularly in the CNS and the thymus (26) and a direct cytolitic effect has been suggested for the hypoplasia in the germinal layer of the cerebellum (10) and other tissues (22). Hypomyelination of the CNS, which is often associated with thymic hypoplasia, has also been observed (1, 6). A further consistent finding within the group of pestiviruses is the localisation of the virus in the vascular endothelium and from the resulting vasculitis, there can be inflammation, oedema, hypoxia and cellular degeneration (67).

Persistent viraemia

Another outcome of foetal infection during the first trimester is the establishment of a viraemia that persists for life (22, 37). The basis for this persistence is that the bovine immune system, before 110-120 days, has not developed sufficient immunocompetence to recognise the BVDV within the foetus as foreign. When "self" antigens are recognised, soon after this 110-120 day period, the virus is accepted as a "self" tissue and there is immunotolerance. It is this immunotolerance, reflected by the lack of specific antibody to the persisting virus, that allows the virus to persist in the blood and tissues for the lifetime of the animal. It is worthy of mention that in all the recorded field and experimental data there is no evidence for persistence with the cytopathogenic biotype; only with the non-cytopathogenic (17).

There is considerable variation in the signs and pathology described for these persistently viraemic cattle. Their identity is based on the recovery of non-cytopathogenic virus in high titre on successive occasions and the lack of antibody to the persisting virus. Their clinical appearance can range from normal to grossly abnormal. Why some are more damaged than others can, at present, only be a speculation about the age, size, and timing of viral challenge for the early foetus. The pathogenesis of the grossly abnormal calf reflects the viral tropism for the CNS, lymphoid and epithelial cells. Within the CNS, the predilection sites for viral persistence are the cerebral cortex and the hippocampus (27). Lesions in such tissues are often more severe when the foetus is infected during the second trimester (6, 62) and account for the depression and incoordination seen in some newborn calves. Frequently these calves fail to survive and grossly abnormal brain lesions, such as cerebellar hypoplasia (10, 26), can be seen at post-mortem.

Lesions within the lymphoid tissues, apart from the reduced size of organs, such as the thymus (26), are not so evident. The gross changes, seen in the Peyer’s patches of the small intestine during mucosal disease, are not observed (14). However, there are cellular changes that are said to account for the immunosuppression seen in persistently viraemic animals. There is a reduction in the recirculating B-cells (48) and also in T-cells (59). There are preliminary data to show that the recirculating
gamma/delta T-cells are also depressed (Howard, Clarke and Brownlie, unpublished results). It has been estimated that 4.4% of blood leukocytes, 5.4% of T-cells and 2.1% of B-cells are infected with virus (9). Interestingly, in sheep persistently infected with Border disease virus, it was demonstrated that B-cells were significantly increased whereas the T-cells and lymphocytes expressing class I MHC antigen were decreased (20).

Several epithelial tissues sustain BVDV replication. BVDV antigen can be demonstrated within the keratinocytes of the tongue, skin and labia (4) and this may account for the erosive oral lesions which characterise clinical disease.

**MUCOSAL DISEASE**

Mucosal disease was first reported in 1953 and described as a fatal condition of cattle, characterised by severe erosive lesions in the intestinal mucosa (57). The clinical signs are described elsewhere in this *Review*. The virus isolated from this condition was understandably called mucosal disease virus (MDV) but reinoculation into cattle did not reproduce the fatal mucosal disease. Later, it was demonstrated that BVDV and MDV were serologically similar and gave the same mild illness in response to acute infection (30). Over the next thirty years a series of observations were made about these viruses, reviewed by Brownlie (13) and most of which have been identified above. Finally, two significant findings led to the proposal for the aetiology of mucosal disease. The first was that only persistently viraemic animals succumbed to mucosal disease (41). Secondly, that persistently viraemic animals had only the non-cytopathogenic virus whereas those that died of mucosal disease were infected with both biotypes, non-cytopathogenic and cytopathogenic (14).

These observations were refined into a hypothesis (14), as shown in Fig. 2, which requires that cattle, sero-negative to the virus, become infected during early pregnancy with the non-cytopathogenic biotype. The virus, infecting the dam, transfers across the placenta to the foetus and can result in the birth of a persistently viraemic calf, due to the immunotolerance described above. Some time after birth, usually when the animal is 6-18 months of age, superinfection of these viraemic animals with the cytopathogenic biotype may occur. This results in the rapid development of fatal mucosal disease.

The truth of this hypothesis was demonstrated by the experimental production of mucosal disease in exactly the manner predicted (8, 14). Subsequently, the need for antigenic "homology" between the persisting and superinfecting biotypes has been recognised as crucial to the development of mucosal disease and has illustrated the precision of the immunotolerance (15). The origin of the cytopathogenic virus continues to fascinate us; it has been suggested that this may arise by a molecular event, such as mutation, from the persisting non-cytopathogenic virus (15, 33). Further speculation is presented elsewhere in this *Review*.

Mucosal disease has been described as a sequel to vaccination with modified-live virus (42). These vaccines are mostly derived from cytopathogenic virus strains and our hypothesis would suggest that such vaccines may be acting as the superinfecting challenge.
nc = non-cytopathogenic BVDV

c = cytopathogenic BVDV

FIG. 2
Pathogenesis of mucosal disease

The pathology of mucosal disease has been described, particularly the characteristic erosive lesions seen in the gut lymphoid tissues (36). It has now been demonstrated that the cytopathogenic biotype has a particular tropism for the gut-associated lymphoid tissue (24) and that, in the sequential development of lesions, this biotype rapidly homes to the Peyer’s patch tissue (16). Although, the reason for the gross lesions visible over the Peyer’s patches is likely to be a result of the direct lytic action of the virus, there is now preliminary evidence that a synergism between the two biotypes is required for the full expression of mucosal disease (25).

Prominent in mucosal disease is the lesion that develops after the destruction of the lymphoid tissue in the Peyer’s patches and the collapse of its overlying intestinal mucosa. This gives the characteristic erosions along the small intestine. The ultimate question for pathologists, the cause of death, has a less certain answer. In studies on the sequential development of mucosal disease it was evident that these Peyer’s patch lesions occurred both late and rapidly in the course of superinfection with
cytopathogenic virus and coincided with clinical disease (16). However, there were animals that died without clinical diarrhoea. This would suggest that the diarrhoea and any resulting dehydration was not an essential part of the syndrome. It has not been assessed whether, in the destruction of the lymphoid tissue, there is a release of toxic factors or an excess of inflammatory products. The cause of death still remains an enigma.

**CHRONIC DISEASE**

The aspect of BVDV pathogenesis, above all others, that gives rise to confusion is the "chronic" disease. It is used to describe not only animals that are continually or "chronically" infected with BVDV but also animals that are clinically ill for prolonged periods. A clearer definition is required nowadays in order to make progress in its understanding.

There is no doubt that a clinical entity exists where cattle become progressively cachectic following long-lasting bouts of diarrhoea. The course of disease may be several weeks or months and ultimately the animal dies or it may apparently recover. There is little disagreement that this could be described as chronic disease. From some field cases of this syndrome, non-cytopathogenic BVDV has been isolated. Should this biotype be isolated on repeated occasions, in absence of specific antibody to the virus, then the animal would accurately be described as persistently viraemic. The problem of definition arises from the knowledge that all persistently viraemic animals do not have a chronic clinical disease and that the syndrome has not been experimentally reproduced.

In 1985, we suggested that chronic disease may occur as a result of superinfection of persistently viraemic animals with cytopathogenic isolates that have partial antigenic "homology" with the persisting virus (15). Our understanding of partial "homology" was not defined but was intended to indicate an antigenic position between "homology" and "heterology", as shown in Fig. 3. "Homology" was conferred by the immunotolerance which allows the non-cytopathogenic virus to persist and also enables the superinfecting cytopathogenic virus to survive. The failure of the immune system to recognise the superinfecting cytopathogenic virus was taken to mean antigenic homology. It is now understood that the two biotypes isolated from cases of fatal mucosal disease are antigenically similar (33, 53). Furthermore, it has been shown that those cytopathogenic viruses that are antigenically different, i.e. against which antibody is made, do not cause mucosal disease. These can be said to be "heterologous".

Our proposal for chronic disease suggested that immunotolerant animals were superinfected with cytopathogenic isolates that were "heterologous" but only partially recognised by the immune system and therefore not eliminated. Recently, we have superinfected a series of persistently viraemic cattle with "heterologous" cytopathogenic virus (18). In two animals there was, several months after superinfection, a slow onset of disease with bouts of diarrhoea and progressive wasting. During this period, both animals preferred roughage and refused "concentrate" food. They had periods of several days when their condition appeared to ameliorate, only to relapse into further clinical disease. The animals were finally killed, and at post-
mortem, gut erosive lesions typical of mucosal disease were revealed. These preliminary experiments may be the first to reproduce chronic disease.

The pathology of field and experimental chronic disease has not been described.

FIG. 3
Pathogenesis of chronic disease
CONCLUSIONS

Few viruses appear to have so diverse and complex a pathogenesis as BVDV. Our recent understanding only serves to highlight the ingenious ways in which the virus subverts the host’s defences. Like certain other viruses that are able to persist for long periods, it invades the lymphoid tissue and disables the recognition and effector functions of immunity. In his book, Mims examines the mechanisms of viral persistence (47) and, from this, it is evident that BVDV is the pathogen par excellence for persistence (17). The clear definition we are now able to give to the biological roles of the two biotypes has opened up new areas in our immunological and molecular biology research. It is possible that the apparent unique pathogenesis of mucosal disease will later be shown to be in the vanguard of new understanding of other infections.

As a comment of caution, this Review highlights the salutary benefit to be gained from detailed examination of the pathology of BVDV infections; we must not miss opportunities by ignoring this basic science in favour of the exclusive use of new technologies.

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PATHOGENÈSE DES INFECTIONS PAR LE VIRUS DE LA DIARRHÉE VIRALE BOVINE. — J. Brownlie.

Résumé: Le virus de la diarrhée virale bovine peut provoquer chez les bovins une maladie aiguë passagère, inapparente ou bénigne, ou encore la maladie des muqueuses, qui est toujours mortelle. L’infection aiguë se manifeste parfois par des épisodes cliniques de diarrhée et d’agalactie, mais la pathogenèse de ces syndromes n’est pas éclucidée car on ne peut pas les reproduire expérimentalement. L’effet immunodépresseur des infections aiguës peut exacerber les manifestations cliniques provoquées par d’autres agents infectieux ; son rôle peut être important dans le complexe des affections respiratoires du veau. Bien que la présence du virus ait été reconnue dans les tissus lymphoïdes, sur des périodes prolongées, l’éventualité d’une virulènce latente n’a pu jusqu’ici être démontrée.

L’infection vénérienne apparaît jouer un rôle important dans la transmission du virus au fœtus et les infections congénitales peuvent entraîner des avortements, des malformations et une virémie persistante chez le veau.

L’auteur décrit le rôle des deux biotypes du virus, non-cytopathogène et cytopathogène dans la pathogenèse de la maladie des muqueuses. L’infection du fœtus par le virus non-cytopathogène se prolongeant par la virémie persistante chez le veau en est le point de départ. La maladie des muqueuses peut apparaître plus tard chez le veau, à la suite d’une surinfection par un virus cytopathogène «homologue». L’auteur examine l’hypothèse d’une mutation qui peut être à l’origine de ce biotype.

La maladie chronique se traduit par un amaigrissement progressif, généralement accompagné de diarrhée. On peut penser qu’elle apparaît chez les bovins présentant une virémie persistante à la suite d’une surinfection par un biotype cytopathogène «hétérologue».

**PATOGÉNESIS DE LAS INFECCIONES POR VIRUS DE LA DIARREA VIRAL BOVINA.**

– J. Brownlie.

Resumen: El virus de la diarrea viral bovina puede provocar en los bovinos una enfermedad aguda, pasajera, no aparente o benigna, así como también la enfermedad mucosa, que siempre es mortal. La infección aguda se manifiesta a veces mediante episodios clínicos de diarrea o agalactia, pero no se ha determinado la patogénesis de estos síndromes porque no se han podido reproducir experimentalmente.

El efecto inmunodepresor de las infecciones agudas puede exacerbar los síntomas clínicos provocados por otros agentes infecciosos y desempeñar un papel importante en el complejo de las afecciones respiratorias en el ternero. Aun cuando se ha reconocido la presencia del virus de la diarrea viral bovina en tejidos linfoides durante períodos prolongados, no se ha podido probar su virulencia latente.

La infección venérea parece ser un factor importante en la transferencia del virus al feto y las infecciones congénitas pueden causar abortos, malformaciones o una viremia persistente en el ternero.

El autor describe el papel de los dos biotipos del virus: no citopatógeno y citopatógeno en la patogénesis de la enfermedad mucosa. El inicio de aquélla es la infección del feto por el virus no citopatógeno y la persistencia subsecuente de la viremia en el ternero. Estos terneros pueden sufrir posteriormente la enfermedad mucosa, tras una sobreinfección por un virus citopatógeno «homólogo». El autor examina la hipótesis del origen de este biotipo por mutación.

La enfermedad crónica se caracteriza por un estado de decaimiento progresivo, generalmente acompañado de diarrea. Cabe pensar que aparece tras una sobreinfección de animales con viremia persistente, provocada por un biotipo citopatógeno «heterólogo».


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