BRITISH CATTLE VETERINARY ASSOCIATION

P R O C E E D I N G S
FOR 1984 - 1985

Produced for B.C.V.A. by
BEECHAM ANIMAL HEALTH

BVD - UNDERSTANDING THE NATURE OF INFECTION

J BROWNLIE BVSc PhD MRCVS
AFRC Institute for Research on Animal Diseases, Compton, Newbury, Berkshire RG16 ONN

Bovine viral diarrhoea virus (BVDV) is widespread in the national herd. In most herds, exposure of cattle to the virus is before pregnancy. This results in an inapparent infection and good immunity to reinfection.

In certain individuals and herds (particularly closed herds) the first exposure is during pregnancy. This can result in foetal death, abortions or in the birth of calves persistently infected with virus.

This viral persistence into adult life is associated with a specific immunotolerance; antibodies are consistently lacking, although the virus is present throughout post-natal life. For this tolerance to develop, the infection with the virus must be in early gestation before 180 days. It is these persistently viraemic animals which later succumb to Mucosal Disease. Clinically the disease is characterised by anorexia, profuse diarrhoea and leucopenia. Post-mortem examination demonstrates the extensive erosion and necrosis of the gut lymphoid tissue. Clinical disease is invariably fatal.

The trigger for onset of clinical disease was not understood. At the IRAD, Compton, we have been looking at this problem starting by examining three field outbreaks of disease.

Blood samples were taken from all of the animals within those groups with clinical disease and examined for the presence of BVD. Antibody was determined initially by virus neutralisation and latterly by an ELISA for BVDV antibody that has been developed at the IRAD. It was a consistent finding that animals could be divided into the three groups summarised in Table 1; (a) healthy animals with antibody and no virus, (b) those with undetectable or low levels of antibody but persistently infected with non-cytopathic virus and finally (c) animals clinically sick with Mucosal Disease. Blood samples from the latter group again had little or no antibody but contained both cytopathic and non-cytopathic strains of BVDV.

Table 1: Presence of BVDV and antibody in blood from groups of cattle on three farms with Mucosal Disease

Description of cattle	No. in group	BVDV antibody	Non-cytopathic BVDV	Cytopathic BVDV
a) In contact health	50	+	-	-
b) Healthy persistently infected	47*	-**	+	-
c) Clinically sick Mucosal Disease	4	-**	+	+

* Subsequently 40 of these animals have died of Mucosal Disease.
** Antibody may be present at low level. <1/20 by neutralisation or <1/200 by ELISA.

These findings led us to propose the following hypothesis. Clinical Mucosal Disease in cattle requires a persistent infection with non-cytopathic BVDV and a subsequent infection with cytopathic virus. The non-cytopathic virus infection is established *in utero* before immunocompetence develops. It is tolerated and although there is no specific immune response, there is also no clinical disease. However, on subsequent infection with cytopathic virus unlimited growth is permitted in these immunotolerant animals. The virus multiplies rapid and death invariably follows 2-3 weeks later.

Within a closed herd, which is BVDV-antibody free, non-cytopathic virus could readily spread amongst cattle in early pregnancy and later produce a number of persistently infected calves. Then, about 6-24 months later, if these calves are exposed to a second virus, that is cytopathic, an explosive outbreak of Mucosal Disease would be seen.

To test this hypothesis the following experiment was performed.

From an animal (Pe 515) on Farm 1 that died from Mucosal Disease, cytopathic (Pe 515c) and non-cytopathic virus (Pe 515nc) were isolated. The cytopathic virus was cloned by three cycles of plaque purification. Three further animals (Pe 605, Pe 606 and Pe 628) from the same farm were identified as persistently infected with non-cytopathic virus only. They were brought into isolation facilities at the Institute and kept for periods of 4-6 months without developing clinical signs. Regular sampling revealed consistently high levels of non-cytopathic virus in the blood (10^5-10^6 TCD_{50}/g). Two animals (Pe 605 and Pe 606) were infected intranasally with 5 ml of cloned Pe 515c (10^7 TCD_{50}/ml) and within 2-3 weeks both developed anorexia, diarrhoea and were killed *in extremis*. At post-mortem examination, there were characteristic gut erosions and an accompanying pathology of the gut-associated lymphoid tissue that were typical of Mucosal Disease. Cytopathic virus was recovered from gut lesions and mesenteric lymph nodes (10^6-10^7 TCD_{50}/g) and both cytopathic (10^2 TCD_{50}/ml) and non-cytopathic (10^5-10^6 TCD_{50}/ml) strains from blood.

The third persistently infected animal (Pe 628) was inoculated with fluid from uninfected cell culture and was killed at four weeks although it showed no clinical signs of disease. There was no evidence of any gut lesions and no recovery of cytopathic virus from gut tissue or blood. Four further seronegative animals, not infected with non-cytopathic BVDV, were inoculated with the cytopathic strain, Pe 515c. They showed no clinical response and by four weeks had produced antibody to the virus. The post-mortem examination at four weeks revealed no gross pathology in the small intestine and cytopathic virus was not isolated. This contrasts with the growth of cytopathic virus (10^7/g) in the intestinal tissue of the dual infection of cows Pe 605 and Pe 606.

These results provide evidence that in cattle, persistently infected with non-cytopathic virus, subsequent challenge with cytopathic virus will reproduce fatal Mucosal Disease (Brownlie *et al*, 1984).

The only advice presently available to clinicians faced with a Mucosal Disease problem is:

1. To bleed all animals in the group and also the dams of any with clinical disease.

2. Check bloods for both BVDV antibody and virus.

3. Those animals that are diagnosed as persistently viraemic are best slaughtered as soon as possible.

4. All animals, particularly bulls, newly introduced to closed herds should advisably be checked for BVD virus and antibody.

Research is continuing into this complex disease at IRAD and those practitioners wishing to discuss a particular BVDV problem could contact us at IRAD, Compton.

REFERENCES

Brownlie J, Clarke M C and Howard C J (1984). Experimental production of fatal Mucosal Disease in cattle. Veterinary Record, 114, 535-536.