BOVINE VIRAL DIARRHOEA VIRUS

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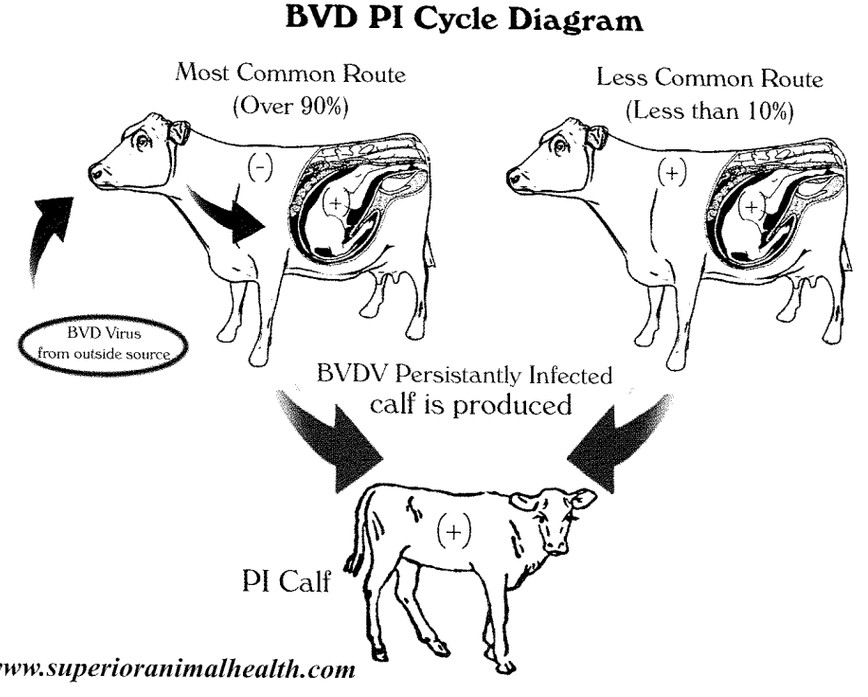
Bovine Viral Diarrhoea virus (BVDV) infection is a viral disease and a member of the Pestivirus genus of the family Flaviviridae. Two biotypes are recognized namely non-cytopathic (does not kill cells it infects) and cytopathic (kills cells it infects). Genotype 1 and 2 also exists and both have cytopathic and non-cytopathic isolates. Type 2 viruses have not been identified in South Africa. Most field isolates are non-cytopathic (Coetzer et al., 2004). This will in part explain the different syndromes caused by this virus infection. If most isolates were cytopathic it would have killed the cells and thus the foetus or animal and persistently infected animals will not develop.

Epidemiology

BVDV infections have been reported from most regions in the world and were first reported in SA in the early 70's. The disease appears to be wide spread in SA.
It is an important disease in cattle as it may cause several different syndromes (please see later), which may result in reproductive losses, diarrhoea, immunosuppression and other diseases.
The most important source of BVDV in nature is immune-tolerant persistently infected animals. High levels of virus are present in their nasal secretions, saliva, tears, milk, semen, urine and faeces. Transiently infected animals may also secrete virus for 10 days, but with much less efficiency (Coetzer et al., 2004).

Persistently infected animals (PI)

PI animals are infected transplacentally (the mother contracts the disease, which then crosses the placenta to infect the foetus) during pregnancy with a non-cytopathic virus between day 43 and 125th day of gestation. At this stage of development the foetus does not die as result of the infection and does not respond with an immune reaction to it (antibody response). The foetus thus recognizes the virus as part of its' own system (immune-tolerant). This results in the birth of a calf which is immune-tolerant to the virus, is consistently viraemic (virus circulates continuously in the body) and is continuously shedding the virus through body secretions as stated above. The calves are immune-tolerant only to the strain of virus which infected it in utero (in the uterus). The calf will not have antibodies to this strain. If another strain infects the calf after birth, it will develop antibodies to that strain. The calf may present unthrifty or may appear as normal as any other calf. The literature varies, but between 50 and 90% PI calves will die in the first year of life. All PI animals are at risk to develop mucosal disease. Mucosal disease only occurs if the PI animal is superinfected with an appropriate cytopathic strain of the virus (antigenically homologous cytopathic virus) or if the non-cytopathic virus in the animal mutates to a homologous cytopathic virus (Coetzer et al., 2004). Diseases caused by BVDV



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Primary post-natal (after birth) infections:

1. **Subclinical infections or mild BVD**
   These are the most common primary post-natal infection in cattle. Seventy to ninety % of cattle will not even show any symptoms. Slight fever, drop in milk production and low white cell count may be observed.
2. **Bovine viral diarrhoea**
   It is normally seen as outbreaks of watery diarrhoea of varying severity in susceptible herds involving 6-12 month old animals. Mortality is normally insignificant, but up to 8% has been reported.
3. **Severe bovine viral diarrhoea/haemorrhagic syndrome**
   Animals show fever, depression, low white and platelet counts, diarrhoea, nasal discharge, salivation, oral ulcers and decreased milk production. Up to 40% animals may die. It is normally seen only with genotype 2 isolates, not present in SA.
4. **Respiratory and miscellaneous diseases**
   BVD is immunosuppressive and may lead to respiratory diseases often associated with Mannheimia haemolytica

(Pasteurellosis/shipping fever). Other infectious diseases that may occur as result of infection includes actinomycosis, enteritis caused by Salmonella, E. coli infections, Babesiosis (red water), verminosis, metritis and mastitis.

Embryonal/foetal disease

1. Fertility
Artificial insemination with contaminated semen or natural service by a BVD-infected bull may result in poor conception rates, embryonal/foetal deaths and impaired embryonal development.

2. Abortions
Transplacental infections at day 50-100 may result in foetal death with stillborn or mummified fetuses. Abortion rates vary between 2 and 7%, but may be as high as 27%.

3. Congenital defects
Infection between day100 and 150 may cause congenital defects. The virus targets the nervous system and eyes and causes a wide array of defects. Some of the defects include hydranencephaly, porencephaly, cerebellar hypoplasia etc. Calves with brain abnormalities have difficulty standing, moving and often have tremors.

Mucosal disease
Only persistently infected animals develop mucosal disease. Mortality is a 100%. An acute and chronic form has been identified. Signs include profuse watery diarrhoea, fever, erosions and ulcers of the lip, tongue, dental pad. Clinical signs in the chronic disease are similar, but less severe and protracted (Coetzer et al., 2004).

Diagnosis
Due to the complex nature of this disease, diagnosis presents a significant challenge.

The main aim of diagnostics in practice is to identify a persistently infected animal as it is the main shedder of virus and source of infection, with the ultimate goal to remove this animal/s from the herd.

The latest research indicates the following two tests to identify PI animals (Cornish et al., 2005):

1. Immunoperoxidase staining of ear notch biopsies
2. Antigen capture ELISA on ear notch biopsies

Immunoperoxidase (IMP) stain

Samples for IMP stains can be collected from ears with an ear notch and placed in formalin. Samples must reach the laboratory within 2-3 weeks for optimal results. Samples are processed and a monoclonal antibody is used to bind to the viral antigen present in various cells of the skin. It is labeled with a color visible to the pathologists. This test is 100% accurate to identify PI animals. Recent research noted that a small number of acutely infected animals may also be identified. It is thus proposed to test all positive animals again after 30 days, to exclude any false positives. This is especially important in valuable/stud animals. A non-valuable animal, which is going to be slaughtered in any case, may be presented to the abattoir, as the virus infection does not influence meat or the use thereof. One may use the same test, but may also use the polymerase chain reaction test on blood (PCR). If positive again the animal is considered to be a PI (Cornish et al., 2005). Personal communication with Dr Dietmar Holm suggests immediate slaughter of all positive animals, as it is not woth the risk to keep them in the herd. Errors may occur and the animal may become part of the herd again with dire consequences.

Antigen capture ELISA

This ELISA detects BVD antigen in skin samples. Samples are placed in a transport medium (can be obtained from the laboratory), but may also be frozen. Samples must reach the laboratory within 2 days.
This method also detects a 100% PI animals, but false positives, detecting acutely infected animals, may also occur. Re-testing after 30 days is recommended for positive animals as discussed above (Cornish et al., 2005).

ELISA testing may be performed on blood for antibodies and antigen, but these tests are not specific for PI animals. A PI animal will be positive on ELISA antigen testing, as they are persistently viraemic, and so would an acutely infected animal. They should not have antibodies, because they are immune-tolerant. If they were infected with another strain after birth, they will however have antibodies and this may skew the results. These are the reasons why blood tests are not used as diagnostic tool to identify PI animals.

PCR tests also detect viral antigen in blood, but are not specific for PI animals. Virus isolation remains the gold standard test to detect virus, but does not discriminate between a PI and acutely infected animal (Coetzer et al., 2004).

Vaccination

It is very important to vaccinate the herd, even after removal of any persistently infected animals from the herd, as the viral infection may be present in a neighbors' herd. Live vaccines must not be used in pregnant animals.

Frequently asked questions

Can an animal become a PI animal after birth?
No, an animal will only become persistently infected during the specific time period in the uterus (day 43 to 125).

How often must the animals be tested?
Only once, as an animal will not become persistently infected at a later stage.

If a cow is not a PI animal, can she have a PI calf?
Yes, if the cow is infected with the virus while she is pregnant during day 43-125, the virus crosses the placenta infecting the calf, which then becomes a PI animal.

If the cow is a PI animal, will all her offspring be PI's?
Yes, a persistently infected cow will transfer the virus to each calf she has and the calf's immune system will also not recognize the virus as foreign. All offspring will be PI's.

How long does the virus live outside the body?
At 35°C the virus survives for 3 hours, at 20°C for 3-7 days and at 5°C for 3 weeks.

Nose to nose contact is the efficient way of spread of the virus.

References

1. Coetzer, J. A. W., Tustin, R. C. 2004. Infectious Diseases of Livestock. 2nd Edition. Oxford: University Press.
2. Cornish, T. E., Van Olphen, A. L., Cavender, J. L., Edwards, J. M., Jaeger, P. T., Vieyra, L. L., Woodard, L. F., Miller, D. R., O'Toole, D. 2005 Comparison of ear notch immunohistochemistry, ear notch antigen-capture ELISA, and buffy coat virus isolation for detection of calves persistently infected with bovine viral diarrhoea virus. Journal of Veterinary Diagnostic Investigation,17:110-117.
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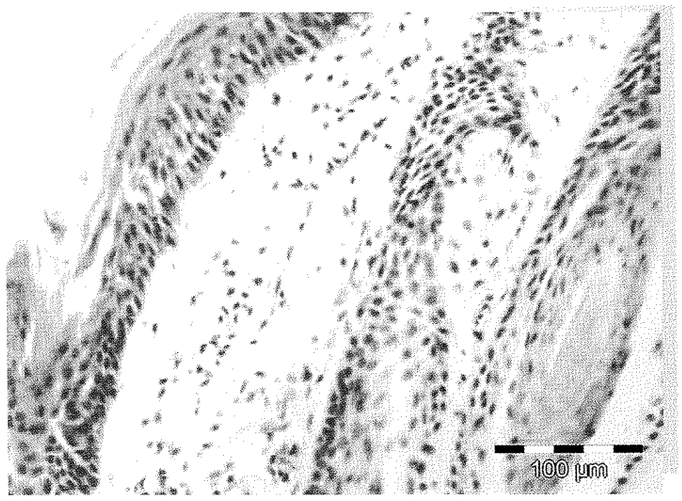


BEES VIRUS DIAREE VIRUS

Bees Virus Diaree Virus (BVDV) is 'n virale siekte en 'n lid van die Pestivirus genus van die familie Flaviviridae. Twee biotipes word herken naamlik nie-sitopaties (maak nie selle dood wat dit infekteer) en sitopaties (maak selle dood wat dit infekteer). Genotipe 1 en 2 bestaan ook, en beide het sitopatiese en nie-sitopatiese isolate. Tipe 2 virusse is nog nie in Suid Afrika geïsoleer nie. Die meeste veld isolate is nie-sitopaties (Coetzer et al., 2004.) Dit verklaar gedeeltelik die verskillende sindrome wat deur hierdie virusinfeksie veroorsaak word. Indien meeste isolate sitopaties was, sou dit die selle en dus ook die fetus gedood het, en permanente besmette draers sou nie ontwikkel het nie.

Epidemiologie

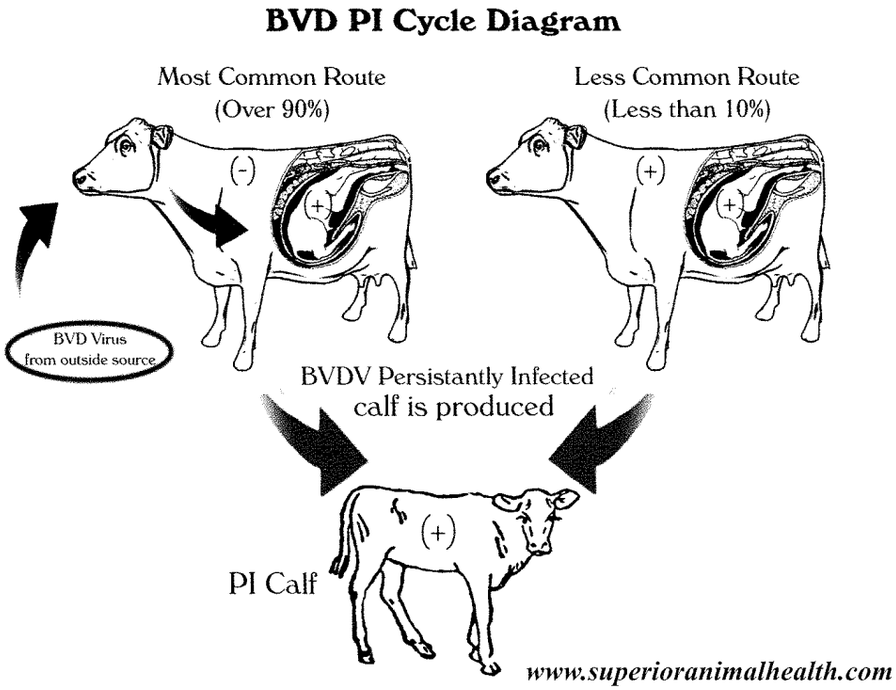
BVDV infeksies is in die meeste gedeeltes van die wêreld gerapporteer en is vir die eerste keer vroeg in die 70's in Suid-Afrika gerapporteer. Die siekte kom wydverspreid in Suid-Afrika voor.
Dit is 'n belangrike siekte in beeste, aangesien dit verskeie verskillende sindrome veroorsaak (sien asseblief later), wat mag lei tot reproduksie verliese, diaree, immuunonderdrukking en ander siektes.
Die mees belangrikste bron van die virus in die omgewing is immuuntolerante permanente besmette draers. Hoë vlakke van die virus is teenwoordig in hulle neus uitloopsels, spoeg, trane, melk, semen, uriene en mis. Tydelike besmette diere kan ook die virus vir 10 dae uitskei, maar glad nie so effektief soos PI diere nie (Coetzer et al., 2004).

Permanente besmette draers (PI)

PI diere word deur die plasenta geinfekteer (die koei word aangesteek en die virus gaan deur die plasenta na die fetus) tydens dragtigheid deur 'n nie-sitopatiese virus tussen dag 43 en 125 van dragtigheid. Op hierdie stadium gaan die fetus nie dood nie en reageer nie met 'n teenliggaam respons op die virus infeksie nie. Die fetus herken dus die virus as deel van sy eie sisteem (immuuntolerant). Dit lei tot die geboorte van 'n kalf wat immuuntolerant is tot die virus, konstant viremies is (die virus sirkuleer die hele tyd in die liggaam) en konstant die virus uitskei deur

liggaamsekskresies soos bo gelys. Die kalf is net immuuntolerant tot die virus wat dit in die baarmoeder besmet het en sal geen teenliggaampies tot hierdie isolaat hê nie. Indien 'n ander isolaat die kalf na geboorte infekteer, sal hy wel teenliggaampies teen daardie isolaat ontwikkel. Die kalf kan 'n krummel kalf wees of net so normal soos enige ander kalf lyk. Die litteratuur verskil, maar tussen 50% en 90% PI diere gaan in die eerste jaar van hul lewe dood. Alle PI diere het die risiko om mukosa siekte te ontwikkel. Mukosa siekte ontwikkel net as die kalf verder aangesteek word deur 'n antigeniese identiese sitopatiese virus of as die nie-sitopatiese virus muteer na 'n identiese sitopatiese virus (Coetzer et al., 2004).

Siektes wat deur BVDV veroorsaak word



Primêre nageboorte infeksies

1. **Sub-kliniese infeksie of ligte BVDV**
   Hierdie is die mees algemeenste infeksie in beeste. Sewentig tot 90% van die beeste sal nie eers simptome wys nie. Ligte koors, verlaging in melk produksie en lae witbloedseltelling mag waargeneem word.
2. **Bees virus diaree**
   Dit word gewoonlik gesien as uitbrake van waterige diaree van varieerende graad in vatbare kuddes in diere tussen 6 en 12 maande oud. Mortalitiet is gewoonlik baie min, maar kan tot 8% styg.
3. **Erge bees virus diaree/bloedingssindroom**
   Diere toon koors, depressie, lae witbloedsel en plaatjie telling, diaree, neusuitloopsels, verhoogde spoeg produksie, mondsere en verlaagde melk produksie. Tot 40% geaffekteerde diere mag vrek. Hierdie kondisie word gewoonlik net met tipe 2 uitbrake, wat nie in Suid-Afrika teenwoordig is nie, gesien.
4. **Respiratoriese en ander siektes**
   BVDV is immuunonderdrukkend en mag lei tot respiratoriese siektes geassosieerd met Mannheimia haemolytica (Pasteurella/shipping fever). Ander infeksieuse siektes wat mag volg sluit in actinomycosis, enteritis as gevolg van Salmonella, E. coli infeksies, Rooiwater, verminose, baarmoeder infeksie en mastitis.

Embrioniese/fetale siektes

1. **Vrugbaarheid**
   Artifisiële inseminasie met besmette semen of natuurlike diens deur 'n BVDV besmette bul (PI), kan lei tot swak bevrugting, embrionale/fetale dood en verswakte embrionale ontwikkeling.
2. **Aborsies**
   Transplasentale infeksie tussen dag 50 en 100 kan lei tot dood van die fetus, stil geboortes en gemummifiseerde fetusse. Die aborsie getalle varieër van 2 tot 7%, maar kan so hoog soos 27% wees.
3. **Kongenitale defekte**
   Infeksie tussen dag 100 en 150 mag lei tot kongenitale defekte. Die virus fokus op die senuweestelsel en die oë en veroorsaak 'n wye verskeidenheid defekte. Defekte sluit in hydranenkefalie, porenkefalie, serebellum hipoplasie ensovoorts. Kalwers met brein abnormaliteite sukkel om te staan, beweeg en het tremors.

Mukosa siekte

Net PI diere kan mukosa siekte ontwikkel. Mortaliteit is 100%. 'n Akute en kroniese vorm word geidentifiseer. Tekens sluit in 'n erge waterige diaree, koors, erosies en ulsers van die lippe, tong en mond. Kliniese tekens in die kroniese siekte is soortgelyk, minder erg en kom oor 'n langer tydperk voor.

Diagnose

As gevolg van die komplekse natuur van die siekte is diagnose 'n uitdaging. Die hoof doel van diagnose in die praktyk is om PI diere te identifiseer, aangesien hulle die mees effektiewe uitskeier van die virus en bron van infeksie is en die hoofdoel is om hierdie diere uit die kudde te verwyder.

Die nuutste navorsing dui op die volgende 2 toetse om PI diere te identifiseer (Cornish etal. 2005):

1. Immunoperoksidase kleuring op oorknipbiopsies
2. Antigeen ELISA op oorknipbiopsies

Immunoperoksidase (IMP) kleuring

Monsters vir IMP kleuring kan geneem word van ore met oorknippe en in formalien geplaas word. Monsters moet die laboratorium in 2-3 weke bereik vir optimale resultate. Monsters word geprosesseer en 'n monokloniese teenliggaam word gebruik om te bind met die virus antigeen in verskeie selle in die vel. Dit word dan met 'n kleur gemerk wat sigbaar is vir die patoloog. Die toets is 100% akuraat om PI diere te identifiseer. Onlangse navorsing dui daarop dat 'n klein hoeveelheid akuut geinfekteerde diere ook so geidentifiseer kan word. Daar word voorgestel dat sodanige diere weer binne 30 dae getoets word om vals positiewe diere uit te skakel. Dit is van belang in waardevolle diere. In nie-waardevolle diere kan positiewe diere dadelik geslag word, aangesien die infeksie nie die vleis beinvloed nie. Dieselfde toets of Polimiriserende Ketting reaksie (PKR) toetse kan gebruik word. Indien weer positief word die dier as 'n PI beskou (Cornish et al., 2005). Persoonlike kommunikasie met Dr Dietmar Holm dui egter daarop dat 'n positiewe resultaat in praktyk as positief beskou moet word en dat die dier dadelik uitgeskot moet word. Die risiko verbonde daaraan om 'n dier terug te hou en mootlik te vergeet is net te groot.

Antigeen ELISA

Hierdie ELISA tel BVDV antigeen op oorknipbiopsies op. Monsters word in transportmedium geplaas (by laboratorium beskikbaar), maar kan ook gevries word. Monsters moet die laboratorium binne 2 dae bereik.

Hierdie metode identifiseer ook 100% PI diere en vals positiewe diere mag ook geidentifiseer word. Die literatuur beveel weereens hertoetsing na 30 dae aan, maar soos reeds genoem meen veeartse in die praktyk dat die dier dadelik uitgeskot moet word.

ELISA toetse kan ook op bloed uitgevoer word vir antigeen en teenligaampies, maar die toetse is nie spesifiek vir PI diere nie. 'n PI dier sal positief wees op ELISA antigeen toetse omdat hulle konstant viremies is, maar 'n akuut geinfekteerde dier sal ook positief wees. 'n PI dier sal negatief wees vir teenliggaampies, maar as hulle na geboorte geinfekteer word met 'n ander stam van die virus sal hulle teenliggampies hê, wat die resultate sal verwar. Hierdie is die redes waarom bloedtoetse nie gebruik word om PI diere te identifiseer nie.
PKR toetse word ook gebruik om antigeen in bloed te identifiseer, maar is nie spesifiek vir PI diere nie. Virus isolasie is die standaard toets, maar diskrimineer nie tussen 'n PI dier en akuut geinfekteerde dier nie (Coetzer et al., 2004).

Enting

Dit is baie belangrik om 'n kudde te ent. Selfs al is alle PI diere uitgeskot kan 'n buurman se beeste die kudde infekteer. Lewendige entstof moet nie in dragtige diere gebruik word nie.

Algemene vrae

Kan 'n dier 'n PI word na geboorte?
Nee, 'n dier kan net 'n PI dier word as dit in die spesifieke fase geinfekteer word in die baarmoeder (dag 43 tot 125).

Hoe gereeld moet diere getoets word?
Net een keer, aangesien 'n dier nie nageboorte 'n PI kan word nie.

As 'n koei nie 'n PI dier is nie, kan sy 'n PI kalf hê?
Ja, as die koei geinfekteer word deur die virus tussen dag 43-125, kan die virus deur die plasenta gaan en die kalf infekteer wat dan 'n PI dier word.

As die koei 'n PI dier is, sal al haar kalfies PI wees?
Ja, al die koei se kalfies sal PI diere wees. Sy dra die virus aan die fetus oor, wat dit sal herken as deel van homself en sal 'n PI dier word.

Hoe lank leef die virus buite die liggaam?
Teen 35°C oorleef die virus 3 ure buite die liggaam, teen 20°C 3-7 dae en teen 5°C 3 weke.

Verwysings

1. Coetzer, J. A. W., Tustin, R. C. 2004. Infectious Diseases of Livestock. 2nd Edition. Oxford: University Press.
2. Cornish, T. E., Van Olphen, A. L., Cavender, J. L., Edwards, J. M., Jaeger, P. T., Vieyra, L. L., Woodard, L. F., Miller, D. R., O'Toole, D. 2005. Comparison of ear notch immunohistochemistry, ear notch antigen-capture ELISA, and buffy coat virus isolation for detection of calves persistently infected with bovine viral diarrhoea virus. Journal of Veterinary Diagnostic Investigation,17:110-117.
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