Impact of bovine herpesvirus-1 infection on fertility in dairy cattle

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Impact of subclinical bovine herpesvirus-1 infection on fertility in dairy cattle

Bovine herpesvirus-1 (BoHV-1) is endemic in the UK dairy herd and subclinical infection can have an important negative impact on fertility. As well as being the cause of infectious pustular vulvovaginitis and infectious balanoposthitis, BoHV-1 can reduce conception rate following introduction of the virus in contaminated semen at the time of artificial insemination. Its ability to cause abortions, particularly in the last trimester, is well-documented and the incidence of abortions can be high following the introduction of infection to naïve herds. The impact of BoHV-1 on herd fertility will depend on the degree of herd immunity, route of infection and strain of BoHV-1. Vaccination has been shown to reduce spread of BoHV-1 within and between herds, and to significantly reduce the risk of abortion. In light of the cost of a single abortion, and the impact of BoHV-1 on milk yield, routine vaccination against BoHV-1 offers a cost-effective control strategy suitable for most UK dairy herds.

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Bovine herpesvirus-1 (BoHV-1) is an important pathogen of cattle throughout the world. It is an alpha-herpesvirus that can be subdivided into types 1.1, 1.2a and 1.2b (Muylkens et al, 2007), but only types 1.1 and 1.2b are thought to occur in the UK (Nettleton and Russell, 2017). Subtype 1.1 and 1.2a are associated with respiratory disease (infectious bovine rhinotracheitis) and abortion, while type 1.2b has been isolated from genital lesions (infectious pustular vulvovaginitis and infectious balanoposthitis) (Raaperi et al, 2014). However, this distinction is not absolute, and is influenced by the route of infection with either subtype able to establish infection in either the reproductive or the respiratory tracts (Nettleton and Russell, 2017).

Infection is widespread and is present on all continents (Ackermann and Engels, 2006). While there has been no national herd prevalence survey carried out in Great Britain, surveys of herds in England and Wales in 1970–1972 and 1984–1986 found the proportion of herds with antibody positive animals increased from 18% to 48% (Edwards, 1988) with a subsequent increase to 69% in 1996 when bulk tank milk was examined (Paton et al, 1998). These studies were limited by the lack of information on the BoHV1 vaccinal status of the surveyed herds, but nevertheless were taken together to indicate a long-term trend of increasing herd seroprevalence that was considered likely to continue (Paton et al, 1998). In a survey conducted in the southwest of England that excluded herds that had been vaccinated, but where the vaccinal status of purchased animals was unknown, 83% of 114 herds had at least one animal that was seropositive to BoHV1 (Woodbine et al, 2009), and a national survey completed in 2015 found that of 118 unvaccinated herds 62% had bulk tank antibody to BHV1 (Velasova et al, 2017). There is therefore a lack of information on the proportion of dairy herds in Great Britain that currently have endemic BoHV1 infection or the rate at which outbreaks of BoHV1 occur. This lack of information has not prevented the creation of formal control programmes for this infection, firstly by the Ministry of Agriculture Fisheries and Food in the 1980s and subsequently by the Cattle Health Certification Standards (2023) in 1999. However, pedigree beef cow herds have been the predominant participants in these programmes. In contrast, in 2021 there were 15 countries in the European Union with compulsory control programmes and 8 countries were officially free from BoHV1 infection (Hodnik et al, 2021). An initial low herd level prevalence was an important factor in the decision of some countries to pursue eradication, but experience has shown that herd vaccination with BoHV1 glycoprotein-E deleted vaccines can be an effective tool for those herds with endemic infection that are required to progress to freedom from infection (Raaperi et al, 2014). Therefore, while the limited survey work indicates that a high herd seroprevalence should be expected in Great Britain, this is not necessarily a barrier to achieving effective control of BoHV1 either through formal control or herd vaccination programmes.

This article examines the impact of BoHV-1 infection on fertility at an individual and herd level, and the role vaccination may have on preventing or mitigating losses associated with this virus.

Pathogenesis

Primary infection with BoHV-1 results in local dissemination as the virus spreads from cell to cell across the mucosal surface, either in the respiratory or reproductive tract mucosa. It has proved difficult to demonstrate systemic spread by viraemia (Muylkens et al, 2007); however, evidence from other herpesviruses suggests that systemic spread occurs by the invasion of lymph nodes and the lymphatic system (Engels and Ackermann, 1996). Indeed, previous difficulties in demonstrating viraemia may have been due to insensitive virus detection methods, as 92% of samples of peripheral blood leukocytes from suspected BoHV-1 positive animals were positive for the presence of the virus when polymerase chain reaction (PCR) testing of peripheral blood leukocytes was conducted (Fuchs et al, 1999). Given that abortion is considered to occur following respiratory infection (Nettleton and Russell, 2017) and the virus can be detected by PCR in the foetus (Crook et al, 2012), it would appear that viraemia does occur in natural infection.

The high prevalence and widespread distribution of BoHV-1 is partly due to the high viral loads shed during the initial infection, but also due to the ability of the virus to establish lifelong latency in sensory ganglia or tonsils (Muylkens et al, 2007). All animals that experience a primary infection become latently infected and the infection can reactivate and lead to infection of other animals within the herd. It has been suggested that possible causes of reactivation of the virus include transport, parturition, infection with lungworm or bovine parainfluenza-3 virus, administration of corticosteroids and ingestion of 3-methylindole (Thiry et al, 1985). A further characteristic of importance consequent to the carrier state is the creation of seronegative carriers when calves with maternally derived antibodies are exposed to infection. These animals become latently infected and yet do not seroconvert at the time, ultimately becoming seronegative as maternally derived antibodies decline to undetectable levels. This offers a way in which latently infected animals that are negative for antibody to BoHV1 at purchase can introduce BoHV1 infection to the herd (Lemaire et al, 2000).

The clinical syndromes associated with BoHV-1 are well documented, and the strain of the virus, the route of exposure, the viral load and the immune response of the host are all believed to be important factors in determining the progression to clinical disease. However, in many endemically infected herds infection is subclinical (Pritchard et al, 2003), but nevertheless has been shown to have a significant negative impact on milk yield and fertility with a consequent increase in culling rates within a herd (Pritchard et al, 2003).

The impact of BoHV-1 on bull fertility

If BoHV1 infection is acquired by the genital route, infectious balanoposthitis can be the consequence. The pain caused by this condition may result in a reluctance to mate, and adhesions between the prepuce and penis (Lawrence, 2012). Previously it has been understood that preputial infection results in multiplication of the virus in the mucosa, leading to spread of infection from preputial contamination of the penis rather than directly from the semen. However, the virus has been isolated from the distal urethra, and from the testes of a bull with orchitis (van Oirschot, 1995) and, more recently, BoHV-1 was demonstrated in situ and detected by PCR in the testicular tissue and epididymis of unvaccinated seropositive bulls (Dias Queiroz-Castro et al, 2021), indicating that semen can become contaminated with the virus from several different sources.

Abnormal motility and morphology of sperm has been reported following acute genital infection (White and Snowdon, 1973); however, this may be due to systemic illness rather than a direct effect on the reproductive tract, as other studies have demonstrated normal motility and morphology in acutely affected animals (White and Snowdon, 1973).

The duration of virus contamination in the semen can vary markedly between individual bulls, with the initial period of detection lasting up to several weeks and the virus may be detected in semen samples intermittently thereafter. Reactivation following the establishment of latency in the sacral ganglia can result in shedding of the virus in the semen again (Bitsch, 1973) and therefore bulls that have been infected with BoHV-1 are always at risk of producing ejaculates infected with the virus (van Oirschot, 1995).

The impact of BoHV-1 on female fertility

The effects of BoHV-1 infection on female fertility can be divided into those affecting conception, early gestation or the later stages of pregnancy.

Impact on fertility around the time of conception

Both artificial insemination and natural service can result in transmission of BoHV-1, and both can result in infectious pustular vulvovaginitis. This is painful and can lead to suppression of oestrous behaviour. It can also result in adhesions (Lawrence, 2012), which may subsequently affect fertility. However, the impact of BoHV-1 transmitted directly from bull to cow via natural service is limited. Deposition of infected semen in the vagina during natural service produced a localised infection that resolved with no apparent impact on fertility, while in contrast when the semen and virus were deposited in the uterus by artificial insemination, reduced conception rate and shortened oestrous cycles were observed (Parsonson and Snowdon, 1975). The subsequent reduction in conception rate was marked, with 40% of animals served with infected semen pregnant after two oestrus cycles, compared to 90% of control animals served with uninfected semen. The virus induced a chronic endometritis, which was evident on histopathological examination. Although the semen used was experimentally infected, the virus inoculum was equivalent to the peak titres detected in semen during natural infection of bulls (Nettleton and Russell, 2017).

The strain of BoHV-1 infection also influences the impact of the infection. The intra-uterine introduction of BoHV-1.1 to heifers resulted in cystic corpora lutea in all inoculated animals, with varying severities of endometritis or metritis and some had areas of ovarian necrosis or oophoritis. In contrast, intra-uterine infection with BoHV-1.2a produced no lesions in the reproductive tract (Miller and Van der Maaten, 1984).

Intra-venous administration of BoHV-1 has been found to adversely affect the function of the corpus luteum (Miller and Van der Maaten, 1985) and both intra-venous and intra-muscular inoculation has induced ovarian necrosis (Van der Maaten and Miller, 1985). However, neither of these are naturally occurring routes of infection and virus was not isolated from the ovaries of heifers inoculated intra-nasally, and these animals had no evidence of ovarian pathology.

Intra-venous inoculation of BoHV-1 1–4 weeks after service has been shown to result in early embryonic death (Miller and Van der Maaten, 1986; Miller and Van der Maaten, 1987), but an adverse effect of BoHV-1 in early gestation following a naturally occurring route of infection has not been demonstrated.

Impact of BoHV-1 in later pregnancy

Most BoHV-1-associated abortions are detected in the last trimester, but earlier infection is possible (Saunders et al, 1972). The length of time between infection of the dam and expulsion of the foetus may be between 15 and 64 days (Crook et al, 2012). Abortion has followed experimental and natural infection with BoHV-1 both with and without clinical signs of disease. Abortion can also occur during an acute clinical outbreak, due to pyrexia (Crook et al, 2012).

Abortion has been demonstrated experimentally following inoculation by the aerosol route (Saunders et al, 1972; Miller and Van der Maaten, 1987). Abortion rates following experimental infection have been high, with six of sixteen cattle aborting in one study (Miller et al, 1978) and ten of sixteen in another (Saunders et al, 1972). In this latter study a further three calves from 16 pregnancies died of disease consistent with BoHV-1 infection before 12 days of age. Experimental infections are likely to offer a more severe challenge than occurs in natural infection, nevertheless these studies have shown the lethal potential of BoHV-1 infection for the foetus following incursion into a group of susceptible pregnant animals.

The different subtypes of BoHV-1 appear to vary in their ability to cause abortion (Miller et al, 1991). While the intravenous inoculation of subtype 1.1 and 1.2a at 25–27 weeks post breeding reliably caused the loss of the foetus, all five heifers inoculated with type 1.2b delivered full term viable calves, albeit with type 1.2b virus detected in each of the four associated placentae that were available for examination.

Diagnosis of an abortion due to BoHV-1 can be challenging; however, focal necrotic lesions can be observed in the chorionic villi of the placenta and in the foetus, particularly in the liver, and can be stained to confirm the presence of BoHV-1 antigen while PCR can be used to detect BoHV-1 in the placenta (Mahajan et al, 2013). These tests for this virus are readily available in diagnostic laboratories in Great Britain, but they are seldom included in the routine abortion screening package and must be specifically requested. Furthermore, the placenta is often in an advanced state of autolytic change, limiting its value or it simply cannot be found once abortion has been recognised. Further it is to be expected that, if the abortion results from maternal pyrexia rather than foetal infection, the virus may not be present in the foetus or placenta. As a consequence of the time lag of at least 15 days between infection of the dam and expulsion of the foetus (Crook et al, 2012), no rise in antibody titre occurs between expulsion of the conceptus and convalescent sampling, precluding the option of using serology to associate time of infection with abortion.

The impact of BoHV-1 on fertility at a herd level

While there is experimental evidence linking BoHV-1 infection to reduced conception rates, embryonic death and abortion in individual animals, the literature addressing infection at a herd level is less definitive. Some authors have linked adverse reproductive events to seropositivity to BoHV-1 (Ayahan et al, 2006; Ata et al, 2012; Sibhat et al, 2018). Seropositivity has been associated with an increased odds of having a high abortion rate and increased number of services per conception (Raaperi et al, 2012a); however, none of these studies proved a direct causal link between seropositivity to BoHV-1 and a poor reproductive performance, and other potential abortion agents were not investigated.

While reports of endemic BoHV-1 infection in herds with poor reproductive performance can be found in the literature (e.g. Elazhary et al, 1980), the clinical signs and reproductive failures described are not consistent with the disease processes identified in experimental infection. Therefore, case reports associating chronic herd problems of postpartum metritis or repeat breeders with endemic BoHV-1 infection may be discounted both because of an absence of corroborating diagnostic information for the case and a lack of biological rationale.

The impact of vaccination for BoHV-1 on herd level fertility

The BoHV-1 vaccines available in Great Britain include modified live or inactivated and conventional or marker vaccines. Both modified live and inactivated vaccines have been shown to be effective in preventing clinical signs and reducing the spread of the virus (van Drunen Littel-van den Hurk, 2006).

In the absence of control measures, the basic reproduction ratio (R0) of BoHV-1 has been found to be 2.8–7 (Hage et al, 1996; Mars et al, 2001), whereas R0 for a population vaccinated with an inactivated marker vaccine was 2.28–2.6 and for a live marker vaccine, 0.92–1.5 (Bosch et al, 1998; Mars et al, 2001). This indicates that new infections can still occur in vaccinated herds. Nevertheless, the reduction in spread of infection in vaccinated herds has been well described by a number of authors (Ackerman and Engels, 2006; Raaperi et al, 2012b; Alkan et al, 2018) and vaccination has been shown to reduce the duration and magnitude of virus shedding in acutely and latently infected animals (Patel, 2005; Raaperi et al, 2012b).

Vaccination also reduces the risk of abortion associated with BoHV-1 infection. A meta-analysis that examined 15 pertinent studies (Newcomer et al, 2017) found that in an experimental situation vaccination could be expected to reduce the risk of abortion by 60% with no significant difference between the use of a modified live vaccine (relative risk 0.42; 95% confidence interval 0.26–0.68) and an inactivated vaccine (relative risk 0.38; 95% confidence interval 0.21–0.67). A protective effect was also observed in the field evaluation of vaccines, but at the lower level of 35%. This difference was considered to be consistent with the less uniform viral challenge that occurs in the naturally infected herd.

There is a lack of studies examining the effect of vaccination against BoHV-1 on conception rates. This may reflect the fact that, with the exception of artificial insemination, the impact of naturally occurring routes of infection on the conception rates has not been established as the studies have not included intra-nasal inoculation. The ability of intra-nasal infection with BoHV-1 to cause abortions is well established, and thus the ability of vaccination to control intranasal infection is of advantage in reducing the risk of abortion.

Factors to consider when using modified live vaccines

Although vaccination for BoHV-1 is considered safe and effective, there are a few factors that need to be considered when using modified live vaccinations.

In north America, some modified live vaccines have been associated with reduction in conception rates and abortions (Perry et al, 2013; Chase et al, 2017). However, in some of these cases (Perry et al, 2013), the vaccine had been used much closer to the date of service than the data sheet advises. Additionally, the non-gE-deleted live vaccines available in Great Britain are temperature sensitive, inducing a lower level of viraemia and so have a reduced risk of affecting reproduction or causing foetal loss (Caldow et al, 2018). Vaccination with live vaccines does result in latent infection, creating the possibility of reversion to virulence. The live gE-deleted vaccine viruses have a reduced ability to move from cell to cell, because of the absence of glycoprotein-E, and so these are also licensed for use in pregnant animals. No difference has been found to occur in the shedding and subsequent transmission of vaccine virus following the use of conventional or marker live vaccines (Ackermann and Engels, 2006). It has been shown that recombination between a gE deleted vaccine and wild-type virus can occur experimentally (Schynts et al, 2003) but this has not been documented in the field (Ackermann and Engels, 2006). Nor is it likely that such a recombination could lead to increased virulence.

There are no reports in the literature of adverse effects of vaccination with temperature sensitive strains of the virus or for gE-deleted vaccines.

Conclusions

The impact of infection with BoHV-1 on fertility has been established experimentally. BoHV-1 infection of naïve animals via semen at the time of artificial insemination can have a significant effect on conception rate. The potential for this to occur is limited, as artificial insemination centres producing semen for export will require that bulls entering the stud are seronegative for BoHV-1. Seropositive bulls may be used in domestic semen collection centres, providing samples of each ejaculate are screened for BoHV-1 (Department for Environment, Food and Rural Affairs, 2007; Balsom, 2009). The possibility of seronegative, latently infected bulls remains, although these can be expected to seroconvert once infection is reactivated. Additionally, the artificial insemination regulations do not cover semen taken to inseminate cows on the same holding as the bull (Department for Environment, Food and Rural Affairs, 2012). Artificial insemination therefore remains a potential route for transmission while genital transmission by natural service appears to present a lower risk (Parsonson and Snowdon, 1975).

There does not appear to be an impact on conception rates following intra-nasal infection, and there is no information available on the effect of BoHV-1 on early pregnancy after natural infection. Abortion due to infection with BoHV-1 is well documented, both experimentally and in natural infection, and has been demonstrated following intra-nasal inoculation, which may be the most important reproductive sequelae to incursion of the virus to a herd.

KEY POINTS

- The clinical presentations associated with BoHV-1 are well-documented but much of the impact of infection with BoHV-1 will not be clinically apparent, particularly in endemically infected herds. Subclinical infection can have an effect on milk yield, fertility and culling rates.
- Infectious pustular vulvovaginitis and infectious pustular balanoposthitis can occur after genital infection with BoHV-1 and may have an effect on herd level fertility as a result of an unwillingness to mate and the formation of adhesions.
- Transmission of the virus by natural service does not appear to have an impact on conception, while inoculation of the virus into the uterus during artificial insemination with contaminated semen results in a reduction in conception rate.
- Neither a decrease in conception rates nor early embryonic loss have been documented following aerosol spread of the virus.
- Abortion has been documented following aerosol spread, both experimentally and during the course of natural infection.
- Because BoHV-1 infection is endemic in the UK, eradication programmes based solely on testing and culling are unlikely to be economically viable in most herds. Vaccination is, therefore, critical in herd level control.
- Vaccination has been shown to decrease the spread of infection within a herd and the duration and magnitude of shedding by latently infected animals. A reduction in the odds of vaccinated cattle aborting has been demonstrated.

The differences in BoHV-1 subtypes, individual and herd immunities and transmission pathways make it difficult to predict the impact of infection on fertility at the herd level. Most of the literature fails to demonstrate causality between BoHV-1 infection as indicated by seropositivity and a particular episode of reduced fertility. This is partly unavoidable, as by the time a failure to conceive or early embryonic loss is evident, seroconversion will already have taken place. There is clearly a difference in the response of herds to the incursion of BoHV-1, with some exhibiting only mild clinical signs of infectious bovine rhinotracheitis or infectious pustular vulvovaginitis, and others experiencing outbreaks of severe clinical disease. It can therefore be expected that the impact of BoHV-1 on fertility will be similarly variable.

The efficacy of live and inactivated vaccines in reducing the spread and clinical impact of BoHV-1 is well established. Given the endemic nature of BoHV-1 in the UK, vaccines form an important part of reducing the impact of this virus. Furthermore, experience elsewhere has shown that gE-deleted vaccines supported by a gE antibody enzyme-linked immunosorbent assay (ELISA) can provide tools to use to achieve eradication of the virus from herds that have an initial high seroprevalence (Raaperi et al, 2014). While the impact of vaccination on conception has not been thoroughly examined through experimental challenge, the ability of vaccines to reduce abortion associated with BoHV-1 infection has been established. Although abortion due to BoHV-1 is not a common diagnosis in the UK, it may well be underdiagnosed, as the most useful diagnostic tests for this agent are not used routinely. The cost of an abortion within any herd is related to the gestational age at which abortion occurs, the milk yield at the time of abortion, the parity of the cow, value of the milk, cost of feed and replacement, and consequently can be highly variable across different production systems and regions, but it is rarely without financial significance to the herd. Taken with the profoundly negative impact of an outbreak of infectious bovine rhinotracheitis on milk production (Hage et al, 1998) and the health and welfare of cattle, vaccination is likely to provide a cost-effective mitigation for most UK herds. LS

Conflicts of interest

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References

Ackermann M, Engels M. Pro and contra IBR-eradication. Vet Microbiol. 2006;113(3-4):293–302. https://doi.org/10.1016/j.vetmic.2005.11.043

Alkan F, Bilge-Dagalp S, Karapınar Z, Timurkan MO, Coskun N, Burgu I. Long-term study (2005–2010) on the vaccination with BoHV-1 glycoprotein E-deleted marker vaccine in selected two dairy herds in Turkey. Trop Anim Health Prod. 2018;50(2):353–363. https://doi.org/10.1007/s11250-017-1440-3

Ayahan A, Kale M, Yavru S, Bulut O, Buyukyoruk U. The effect of subclinical bovine herpesvirus 1 infection on fertility of cows and heifers. Acta Vet (Beogr). 2006;56(2-3):267–273. https://doi.org/10.2298/AVB0603267A

Ata A, Kocamüftüoğlu M, Hasircioğlu S, Kale M, Gülay MŞ. Investigation of relationship between bovine herpesvirus-1 (BHV-1) infection and fertility in repeat breeding dairy cows in family-type small dairy farms. Kafkas Univ Vet Fak Derg. 2012;18(4):579–583. https://doi.org/10.9775/kvfd.2011.5893

Balsom A. Genus bulls found with infectious bovine rhinotracheitis [Internet] Surrey: Farmers Weekly International. 2009. https://www.fwi.co.uk/livestock/livestock-breeding/genus-bulls-found-with-infectious-bovine-rhinotracheitis (accessed 2 October 2023)

Bitsch V. Infectious bovine rhinotracheitis virus infection in bulls, with special reference to preputial infection. Appl Microbiol. 1973;26(3):337–343. https://doi.org/10.1128/am.26.3.337-343.1973

Bosch JC, De Jong MCM, Franken P et al. An inactivated gE-negative marker vaccine and an experimental gD-subunit vaccine reduce the incidence of bovine herpesvirus 1 infections in the field. Vaccine. 1998;16(2-3):265–271. https://doi.org/10.1016/S0264-410X(97)00166-7

Caldow G, Geraghty T, Mason C, Carty H, Wilson D. Bovine herpesvirus 1 infection in cattle: a discussion on vaccination and control. Livestock (Lond). 2018;23(3):110–115. https://doi.org/10.12968/live.2018.23.3.110

Chase CCL, Fulton RW, O'Toole D et al. Bovine herpesvirus 1 modified live virus vaccines for cattle reproduction: balancing protection with undesired effects. Vet Microbiol. 2017;206:69–77. https://doi.org/10.1016/j.vetmic.2017.03.016

Cattle Health Certification Standards. Setting Industry Standards in Cattle Disease Control. 2023. https://checs.co.uk/ (accessed 2 October 2023)

Crook T, Benavides J, Russell G, Gilray J, Maley M, Willoughby K. Bovine herpesvirus 1 abortion. J Vet Diagn Invest. 2012;24(4):662–670. https://doi.org/10.1177/1040638712448187

Department for Environment, Food and Rural Affairs. Explanatory memorandum to the bovine semen (England) regulations. 2007. http://www.legislation.gov.uk/uksi/2007/1319/pdfs/uksiem_20071319_en.pdf (accessed 2 October 2023)

Department for Environment, Food and Rural Affairs. Artificial insemination of cattle (Animal Health) (Scotland) Regulation. 2012. http://adlib.everysite.co.uk/adlib/defra/content.aspx?doc=18833&id=18835 (accessed 2 October 2023)

Dias Queiroz-Castro VL, Santos MR, Augusto de Azevedo-Júnior M et al. Bovine alphaherpesvirus 1 (BHV1) infection in testes and epididymis from bulls from a slaughterhouse. Theriogenology. 2021;159:1–6. https://doi.org/10.1016/j.theriogenology.2020.10.001

Edwards S. Changing trends in infectious bovine rhinotracheitis in Great Britain. Vet Rec. 1988;123(24):614–618

Elazhary MA, Lamothe P, Silim A, Roy RS. Bovine herpesvirus type 1 in the sperm of a bull from a herd with fertility problems. Can Vet J. 1980;21(12):336–339

Engels M, Ackermann M. Pathogenesis of ruminant herpesvirus infections. Vet Microbiol. 1996;53(1-2):3–15. https://doi.org/10.1016/S0378-1135(96)01230-8

Fuchs M, Hübert P, Detterer J, Rziha HJ. Detection of bovine herpesvirus type 1 in blood from naturally infected cattle by using a sensitive PCR that discriminates between wild-type virus and virus lacking glycoprotein E. J Clin Microbiol. 1999;37(8):2498–2507. https://doi.org/10.1128/JCM.37.8.2498-2507.1999

Hage JJ, Schukken YH, Barkema HW, Benedictus G, Rijsewijk FAM, Wentink GH. Population dynamics of bovine herpesvirus 1 infection in a dairy herd. Vet Microbiol. 1996;53(1-2):169–180. https://doi.org/10.1016/S0378-1135(96)01245-X

Hage JJ, Schukken YH, Dijkstra T, Barkema HW, van Valkengoed PHR, Wentink GH. Milk production and reproduction during a subclinical bovine herpesvirus 1 infection on a dairy farm. Prev Vet Med. 1998;34(2-3):97–106. https://doi.org/10.1016/S0167-5877(97)00088-3

Hodnik JJ, Acinger-Rogić Ž, Alishani M et al. Overview of cattle diseases listed under category C, D or E in the Animal Health Law for which control programmes are in place within Europe. Front Vet Sci. 2021;8:688078. https://doi.org/10.3389/fvets.2021.688078

Lawrence L. An overview of bovine herpesvirus 1. 2012. https://agrihealth.co.nz/uploads/c9b4f7bb6a2c4b37b3292951ae68f9ef.pdf (accessed 2 October 2023)

Lemaire M, Meyer G, Baranowski E et al. Production of bovine herpesvirus type 1-seronegative latent carriers by administration of a live-attenuated vaccine in passively immunized calves. J Clin Microbiol. 2000;38(11):4233–4238. https://doi.org/10.1128/JCM.38.11.4233-4238.2000

Mahajan V, Banga HS, Deka D, Filia G, Gupta A. Comparison of diagnostic tests for diagnosis of infectious bovine rhinotracheitis in natural cases of bovine abortion. J Comp Pathol. 2013;149(4):391–401. https://doi.org/10.1016/j.jcpa.2013.05.002

Mars MH, de Jong MCM, Franken P, van Oirschot JT. Efficacy of a live glycoprotein E-negative bovine herpesvirus 1 vaccine in cattle in the field. Vaccine. 2001;19(15-16):1924–1930. https://doi.org/10.1016/S0264-410X(00)00435-7

Miller RB, Smith MW, Lawson KF. Some lesions observed in calves born to cows exposed to the virus of infectious bovine rhinotracheitis in the last trimester of gestation. Can J Comp Med. 1978;42(4):438–445

Miller JM, van der Maaten MJ. Reproductive tract lesions in heifers after intrauterine inoculation with infectious bovine rhinotracheitis virus. Am J Vet Res. 1984;45(4):790–794

Miller JM, Van der Maaten MJ. Effect of primary and recurrent infections bovine rhinotracheitis virus infection on the bovine ovary. Am J Vet Res. 1985;46(7):1434–1437

Miller JM, Van der Maaten MJ. Experimentally induced infectious bovine rhinotracheitis virus infection during early pregnancy: effect on the bovine corpus luteum and conceptus. Am J Vet Res. 1986;47(2):223–228

Miller JM, Van der Maaten MJ. Early embryonic death in heifers after inoculation with bovine herpesvirus-1 and reactivation of latent virus in reproductive tissues. Am J Vet Res. 1987;48(11):1555–1558

Miller JM, Whetstone CA, Van der Maaten MJ. Abortifacient property of bovine herpesvirus type 1 isolates that represent three subtypes determined by restriction endonuclease analysis of viral DNA. Am J Vet Res. 1991;52(3):458–461

Muylkens B, Thiry J, Kirten P, Schynts F, Thiry E. Bovine herpesvirus 1 infection and infectious bovine rhinotracheitis. Vet Res. 2007;38(2):181–209. https://doi.org/10.1051/vetres:2006059

Nettleton P, Russell G. Update on infectious bovine rhinotracheitis. In Pract. 2017;39(6):255–272. https://doi.org/10.1136/inp.j2226

Newcomer BW, Cofield LG, Walz PH, Givens MD. Prevention of abortion in cattle following vaccination against bovine herpesvirus 1: A meta-analysis. Prev Vet Med. 2017;138:1–8. https://doi.org/10.1016/j.prevetmed.2017.01.005

Parsonson IM, Snowdon WA. The effect of natural and artificial breeding using bulls infected with, or semen contaminated with, infectious bovine rhinotracheitis virus. Aust Vet J. 1975;51(8):365–369. https://doi.org/10.1111/j.1751-0813.1975.tb15595.x

Patel JR. Characteristics of live bovine herpesvirus-1 vaccines. Vet J. 2005;169(3):404–416. https://doi.org/10.1016/j.tvjl.2004.03.005

Paton DJ, Christiansen K, Alenius S, Cranwell MP, Pritchard GC, Drew TW. Prevalence of antibodies to bovine virus diarrhoea virus and other viruses in bulk tank milk in England and Wales. Vet Rec. 1998;142(15):385–391. https://doi.org/10.1136/vr.142.15.385

Perry GA, Zimmerman AD, Daly RF et al. The effects of vaccination on serum hormone concentrations and conception rates in synchronized naive beef heifers. Theriogenology. 2013;79(1):200–205. https://doi.org/10.1016/j.theriogenology.2012.10.005

Pritchard GC, Banks M, Vernon RE. Subclinical breakdown with infectious bovine rhinotracheitis virus infection in dairy herd of high health status. Vet Rec. 2003;153(4):113–117. https://doi.org/10.1136/vr.153.4.113

Raaperi K, Bougeard S, Aleksejev A, Orro T, Viltrop A. Association of herd BRSV and BHV-1 seroprevalence with respiratory disease and reproductive performance in adult dairy cattle. Acta Vet Scand. 2012a;54(1):4. https://doi.org/10.1186/1751-0147-54-4

Raaperi K, Aleksejev A, Orro T, Viltrop A. Dynamics of bovine herpesvirus type 1 infection in Estonian dairy herds with and without a control programme. Vet Rec. 2012b;171(4):99. https://doi.org/10.1136/vr.100253

Raaperi K, Orro T, Viltrop A. Epidemiology and control of bovine herpesvirus 1 infection in Europe. Vet J. 2014;201(3):249–256. https://doi.org/10.1016/j.tvjl.2014.05.040

Saunders JR, Olson SM, Radostits OM. Efficacy of an intramuscular infectious bovine rhinotraceitis vaccine against abortion due to the virus. Can Vet J. 1972;13(12):273–278

Schynts F, Meurens F, Detry B, Vanderplasschen A, Thiry E. Rise and survival of bovine herpesvirus 1 recombinants after primary infection and reactivation from latency. J Virol. 2003;77(23):12535–12542. https://doi.org/10.1128/JVI.77.23.12535-12542.2003

Sibhat B, Ayelet G, Skjerve E, Gebremedhin EZ, Asmare K. Bovine herpesvirus-1 in three major milk sheds of Ethiopia: serostatus and association with reproductive disorders in dairy cattle. Prev Vet Med. 2018;150:126–132. https://doi.org/10.1016/j.prevetmed.2017.12.019

Thiry E, Saliki J, Schwers A, Pastoret P. Parturition as a stimulus of IBR virus reactivation. Vet Rec. 1985;116(22):599–600. https://doi.org/10.1136/vr.116.22.599

Van Der Maaten MJ, Miller JM. Ovarian lesions in heifers exposed to infectious bovine rhinotracheitis virus by non-genital routes on the day after breeding. Vet Microbiol. 1985;10(2):155–163. https://doi.org/10.1016/0378-1135(85)90017-3

van Drunen Littel-van den Hurk S. Rationale and perspectives on the success of vaccination against bovine herpesvirus-1. Vet Microbiol. 2006;113(3-4):275–282. https://doi.org/10.1016/j.vetmic.2005.11.002

van Oirschot JT. Bovine herpesvirus 1 in semen of bulls and the risk of transmission: A brief review. Vet Q. 1995;17(1):29–33. https://doi.org/10.1080/01652176.1995.9694526

Velasova M, Damaso A, Prakashbabu BC et al. Herd-level prevalence of selected endemic infectious diseases of dairy cows in Great Britain. J Dairy Sci. 2017;100(11):9215–9233. https://doi.org/10.3168/jds.2016-11863

White MB, Snowdon WA. The breeding record of cows inseminated with a batch of semen contaminated with infectious bovine rhinotracheitis virus. Aust Vet J. 1973;49(11):501–506. https://doi.org/10.1111/j.1751-0813.1973.tb02332.x

Woodbine KA, Medley GF, Moore SJ, Ramirez-Villaescusa AM, Mason S, Green LE. A four year longitudinal sero-epidemiological study of bovine herpesvirus type-1 (BHV-1) in adult cattle in 107 unvaccinated herds in south west England. BMC Vet Res. 2009;5(1):5. https://doi.org/10.1186/1746-6148-5-5