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HEALTH IMPACTS AND CONTROL MEASURES IN INFECTIOUS BOVINE RHINOTRACHEITIS – A REVIEW

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Abstract

Infectious bovine rhinotracheitis is a viral, endemic, specific bovine, goat and swine (genital) disease with acute evolution, clinically characterized by hyperthermia and respiratory involvement, inflammation of the anterior respiratory tract (rhinitis, tracheitis) or genital disorders (abortions, infertility, balanopostitis), often accompanied by conjunctivitis. This entity is globally spread and is considered to be one of the most costly diseases affecting bovine livestock, and can have major economic consequences by decreasing productivity (milk production, low yield on fattening, animal culling), high morbidity, lethality, which can reach 12% for youth, as well as by restrictions in trade between countries. The review examined the impact of the infection on health status of affected bovine and possibilities to control the disease based on general and specific measures.

Key words: *bovine, IBR, clinical outcome, reproductive problems, prevention.*

INTRODUCTION

Bovines have a particular socio-economic importance in the economy as a whole and in agriculture. This results from the fact that they provide an increased and varied volume of products of primary importance for the consumption of the population, and raw materials for the processing industries. At the same time cattle breeding is an intensive agricultural production, a market for production means and industrial products, a source of income for the economy and a means of capitalizing on natural resources (Georgescu, 1995).

The main purpose of cattle breeding is to provide some of the necessary means of subsistence for humans. Thus, cattle provide 96% of the world's total milk production, 33% of the world's meat and 90% of the total weight of leathers processed in the world's tannery industry. In human food, bovine account for about 12% of their energy intake, ie 56% of all animal protein in ration (Morar et al., 2005).

Each mammal lives in its living environment alongside a multitude of microorganisms that occupy every ecological niche. To maintain animal integrity against aggressors' pathogenic effects, there is a wide range of defense mechanisms, from simple barriers that protect against insect attack and complex immune responses directed against viruses and bacteria.

When the aggressor is a virus, the immune defense mechanism protects the recipient host against the initial attack, especially when the animal has been previously specifically immunized. For the synthesis of antibodies and, implicitly, long-term protection, the presence of the micro-organism or their fragments is required. In such cases, the survival of a small viable population is beneficial, a condition called pre-immunity, a type of non-sterile immunity that is necessary to prevent reinfection.

Infectious bovine rhinotracheitis is a viral, endemic, specific bovine, goat and swine (genital) disease with acute evolution, clinically characterized by hyperthermia and respiratory involvement, inflammation of the anterior respiratory tract (rhinitis, tracheitis) or genital disorders (abortions, infertility, balanopostitis), often accompanied by conjunctivitis. This entity is globally spread and is considered to be

one of the most costly diseases affecting bovine livestock, and can have major economic consequences by decreasing productivity (milk production, low yield on fattening, animal culling), high morbidity, lethality, which can reach 12% for youth, as well as by restrictions in trade between countries.

1. ETIOLOGY

Bovine herpesvirus 1 (Bovine herpesvirus - 1; BHV-1), belonging to the family *Herpesviridae*, the subfamily *Alphaherpesvirinae*, Varicellovirus genus, is incriminated in the etiology of bovine infectious rhinotracheitis. The viral genome consists of double strained DNA, and the viral particle presents a capsid with icosahedral symmetry, surrounded by a pericapsid. Glycoproteins (gB-gE, gG-gI, gK-gM) have been identified at the level of the viral envelope having a primary role in interacting with host cells and the humoral and cellular immune system of the host. Some glycoproteins, such as especially gE, but also gC, gG and gI, are not essential and as such, deletion of the gene encoding these glycoproteins only affects viral multiplication to a small extent. The absence of a serological response to gE allows the differentiation of vaccinated animals (gE-deleted vaccines) from naturally infected animals.

Genetic research has revealed the existence of two distinct subtypes: the respiratory subtype (BHV-1.1) and the genital subtype (BHV-1.2), the latter with two variants: BHV-1.2a in Europe and BHV-1.2b in Australia. All BHV-1 strains are very similar in both genomic and antigenic terms, so a BHV-1 subtype 1 vaccine confers immune protection against both subtype 2 infection and inverse (cross-immunity).

Regarding BHV-1 virulence, hypervirulent, virulent and hypovirusemic strains are distinguished.

2. EPIDEMIOLOGY

Only cattle, especially young and adult animals in large herds (intensive system), are susceptible to the natural infection.

2.1. Susceptibility and risk factors

There are authors who consider that receptivity is not influenced by age, breed, and sex. However, various epidemiological studies indicate that clinical symptoms in young cattle include severe forms of development (oculo-respiratory syndrome, gastroenteropathy, meningoencephalitis, etc.).

Certain risk factors for the installment of BHV-1 infection also highlight the high importance of the animal exploitation system. Thus, the disease expresses itself exclusively on large farms, being virtually unknown in extensive raising, this situation being correlated with the inappropriate carrier state; the severe progression of the disease may be due either to the increase in virulence of the virus through repeated passages or to greater probability of direct transmission between susceptible individuals (Solis-Calderon et al., 2003; Boelaert et al., 2005). The size of the flock is therefore a risk factor.

2.2. Sources of infection and transmission pathways

The main infectious source is represented by the infected animals showing or not clinical signs, which eliminate the virus through respiratory, genital and ocular secretions. Nasal discharge is the major source of the virus, the BHV-1 virus being present in the nasal mucus at 24 hours post-infection, at a sometimes very high titer. The primary excretion period, corresponding to an intense dissemination of the virus in the external environment, ranges from 10 to 16 days, with a peak between the 4th and 6th day post-infection.

Due to the immune response installed immediately after the infection, the animal is able to control the infection and stop primary viral excretion, but becomes a latent, asymptomatic, virus. The virus is no longer detected in the nasal mucus, being present in neurons of the regional ganglion as a non-integrated viral genome. Under the influence of various factors: transport, parturition, glucocorticoid administration, secondary infection with other viruses, bacteria and parasites, latency can be annulled and the virus resumes the multiplication cycle in the body. Viral reactivation results in a re-expression of BHV-1, with or without symptoms of disease, with an increase in the circulating specific antibody titer, depending on the degree of immunization of the animal.

The presence of latent carriers is the essential element of the persistence of the virus in flocks.

Epidemiological research indicates that in some high-prevalence populations of BHV-1 infection, some latent carriers do not have a detectable antibody titer, being classified as false and which, being undetectable, are the source of infection for the rest of the flock. The unresponsive state of latency was observed in calves infected but benefiting of colostrum immunity or in virulent strain infection (Bradshaw and Edwards ,1996). This category of animals (seronegative and latent carriers of the virus) is a major draw-back in controlling the disease (Ackermann and Engels, 2006; Mollema et al., 2005, Anita, 2008, Anita et al., 2008).

Disease transmission is achieved either by direct, nose to nose contact or indirectly through secondary sources. The infection is possible by respiratory route, by inhalation of virulent aerosols from the nasal and ocular secretions of diseased animals. Caretakers may intervene in spreading the virus to other susceptible cattle through various objects or clothing contaminated by nasal secretions. Transmission through artificial insemination or mounting is also frequent, the virus being isolated from serum positive serum bulls. The risk of transmission of the infection by embryo transfer is very low, although BHV-1 is able to adhere to the oviduct or embryo pellucid membrane after *in vitro* infection.

2.3. Evolutionary dynamics

Infectious bovine rhino-tracheitis is of an endemic character, with high outbreak spreading, affecting all susceptible animals within the infected herd. The maximum number of sick animals is recorded 2-3 weeks after the first case occurred, and the duration of endemic is generally of 2-6 weeks, up to several months. Although the morbidity is high (20-100%), mortality does not exceed 10-12%. In fattening units, however, the disease becomes stationary, appearing 10-15 days after the introduction of a new batch of calves (Noordegraaf et al., 1998; Mollema et al., 2005).

3. IMMUNITY

Immune protection against BHV-1 involves various mechanisms, both specific and non-specific. It is also considered that bovine, either naturally infected or vaccinated, develop an immune response primarily focused on the synthesis of specific neutralizing antibodies and lymphocyte proliferation (Loehr et al., 2000; Van Drunen et al., 2006 and 1994). In the natural infection, by passing through the disease, the healed animals become resistant to the pathogenic action of the virus. However, the immunity in this disease is somewhat relative, because despite a pronounced immune response, the virus does not disappear, so the healed animal remains a latent carrier of the virus and potentially shedding. The presence of neutralizing antibodies in the serum does not exclude the possibility of virus removal and their absence does not indicate that the animal is not a carrier (Ackermann and Engels, 2006). Thus, immunity in infectious bovine rhinotracheitis is not sterilizing, in the cured animals the infection and immunity persist simultaneously.

3.1. Specific immune response (cellular and humoral)

BHV-1 infection stimulates a specific response, provided by B lymphocytes and T lymphocytes, which have receptors for this virus (Babiuk et al., 1996, Platt et al., 2006). T lymphocytes respond to BHV-1 infection by recognizing the specific antigens presented in connection with the major histocompatibility complex and B lymphocytes by producing specific neutralizing antibodies. The primary neutralizing antibodies in cattle are directed against gB and gD. These antibodies also participate in complement-dependent complement activation mechanisms or cytotoxicity, to lysis of infected cells. In the antiviral immune response, it is important to involve cytotoxic T lymphocytes, which, given the "spectrum" of their immune activity, can contribute to limiting viral spread.

Conventional anti-BHV-1 vaccines usually induce a strong humoral response but no cytotoxicity. In contrast, a marker vaccine resulting from DNA techniques was able to induce moderate antibody synthesis to gB, but the cellular response was very intense (Huang et al., 2005). The augmentation of the cellular immune response to BHV-1 was also observed in the testing of a plasmid encoding gD but without providing protection against clinical signs (Pontarollo et al., 2002).

Concerning the category of infected animals and latent carriers, serological positivity (especially to gE) is mentioned for a period of 2-3 years.
Also, Lemaire et al. (2001) have shown that negative gE calves which have benefited of passive immunity from vaccinated negative gE mother can produce antibodies to this glycoprotein after infection with a natural strain of BHV-1.

3.2. Non-specific immune response

In addition to the specific immune response, bovine herpesvirus infection 1 also stimulates a non-specific immune response characterized by the secretion of type 1 interferon (IFNα and IFNβ)(Woolums et al., 2003). This non-specific response is mediated by polymorphonuclear leukocytes (neutrophils), macrophages and natural killer lymphocytes. The moment of intervention of these immune cells coincides with the early phase of the infection because, unlike B and T lymphocytes, they do not have antigenic memory.
The onset of BHV-1 infection is also dependent on the activity of non-specific defense mechanisms that provide a first line of defense against viral extension. The more nonspecific the immune response is, the easier the role assigned to the specific immune component represented by the B and T lymphocytes is. Activation of systems involved in non-specific defense can occur under natural conditions (natural infection or body-virus contact) or may be induced artificially by administration of so-called non-specific inducers, "NSD inducers" or immunomodulators. Thus, there are authors who consider it appropriate in the case of IBR to administer an immunomodulator, eg Baypamun (Bayer), in an *in vivo* study demonstrating the following effects: reducing the gravity of the clinical picture, reducing the susceptibility of animals to the virus, significantly reducing the level of elimination viral (Castrucci et al., 2000).

3.3. Disturbing factors of immune reactivity in IBR

Vitamin - mineral deficiencies, especially vitamins B (vitamin B6, pantothenic acid, vitamin B12), vitamin C (Dubeski et al., 1996) and vitamin E (Cusack et al., 2005) have negative consequences on the immune status of calves, disturbing the immune response to vaccination and natural infection. In the Hereford x Angus crossbreeds, experimentally induced with Cu deficiency by molybdenum administration, it was found that this mineral deficiency causes in BHV-1 infected animals the alteration of acute phase protein concentrations during the acute phase protein response to viral infection and can also affect lymphocyte response to mitogen stimulation (Arthington et al., 1996).
Starting from the consideration that water and feed deprivation during commercial operations and transport may adversely affect the ruminant synthesis of vitamin B at the time of maximum susceptibility to infectious agents, the effect of parenteral vitamin B administration on infection and immune status in restricted calves. The parenteral intake of vitamins did not significantly affect viral concentration, interferon titer in nasal secretions, and blastogenic lymphocyte activity, however, the post-infective IgG titer tended to increase. In conclusion, it is argued that the immune response of stressed cows at the time of vaccination can be favorably influenced by the vitamin B level in the body.
Due to the fact that in monogastric species, stress and disease cause the increase of the need for vitamin B6, folic acid, pantothenic acid and ascorbic acid, thus the effects of food restriction, of the herpesvirus infection, as well as the effects of vitamins on the vitamin B plasma are critical to the immune response.
It appears that the levels of vitamin B6, B12, pantothenic acid and ascorbic acid influence the immune response to infection or vaccination in stressed cows.
Since there is a close relationship between stress, nutritional status and thyroid status, the effects of thyroid hormone administration on immune and metabolic response are dependent on the nutritional status of the animal (Cole et al., 1994).

4. CLINICAL PICTURE

The incubation period is 4-7 days. Clinically, depending on strain tropism and age of infected animals, evolutionary forms with respiratory, conjunctival, encephalic, cutaneous, genital and abortions may occur.

4.1. Respiratory form (infectious bovine rhinotracheitis)
This IBR form is the most common and affects bovines of all ages. Calves become sensitive at age 3-4 months when protection from colostrum antibodies disappears. The disease begins with hyperthermia, numbness, diminished appetite, sudden decrease in milk production, than the respiratory changes become obvious: nasal discharge, initially serous, then mucopurulent, while breathing becomes accelerated and superficial, hyperemia and ulcers in the nasal mucosa appear.
Sometimes, due to secondary bacterial infections, the process may expand to the posterior respiratory tract, clinical manifestation being bronchitis and pneumonia.
At the level of the nipple there is an initial erythema, followed by the formation of crusts which, by detachment, leaves ulcerated areas of red color. In the absence of bacterial complications, healing occurs after 15 days. Some very virulent strains of BHV-1 can induce a high mortality rate. During the development of this form, embryo mortality in early pregnancy or in heifers after mating, repeated heat and abortion between months 4-7 of gestation were noticed.
4.2. Conjunctival form may sometimes develop in the absence of other signs, usually in benign form, but following secondary infections with *Moraxella bovis* or other bacteria, it can lead to irreversible lesions of the eyeball, including panophthalmia.
4.3. The encephalitic form may occur in calves below the age of 5 months. It starts with hyperthermia (40ºC), nasal and mucous membrane hyperemia, lacrimation, nasal discharge and foamy saliva, but without respiratory symptoms. After 1-2 days from onset, nervous signs appear in the form of seizures, which occur at at shortening intervals. Death occurs within 6-7 days in all cases with nervous signs.
4.4. The cutaneous form is localized at the interdigital space as a round ulcer with smooth edges and healing tendency within the next 4-5 days. Frequently, by the intervention of the secondary bacterial flora, an ulcerative lesion healing very slowly is produced. Sometimes skin lesions also occur in the perineum as a decuamative dermatitis that extends to the scrotum.
4.5. The genital form (infectious pustular vulvovaginitis - IPV) develops sporadically and is sexually transmitted by artificial insemination with BHV contaminated sperm. It is the most benign form and is expressed by hyperthermia (up to 41.5 ° C), pustular vulvovaginitis and balanopostitis. Females are anxious, look stunned, frequently urinate, the vulva is swollen with a yellowish secretion present. In males, especially the gland and foreskin, initially pustules are formed, which turn to erosions. The passage areas from the foreskin to the gland are edematous and subsequent necrosis of the gland can occur. Symptoms persist for 1-2 weeks, depending on their severity and the disease ends with healing. Prolapse of the uterus can sometimes occur due to the efforts of females following pain caused by lesions, and in males, adhesions and fibrosis accompanied by phimosis or paraphimosis.
4.6. *Generalized form* is often found in newborn calves if they are not protected by colostrum or active immunity, induced by vaccination.
The disease usually occurs at the age of 3-4 days, with the following clinical picture: severe hyperthermia, severe botulism (red muzzle disease), anorexia, lacrimation, nasal discharge, coughing, laryngeal ulcers, exceeding salivation, bronchopneumonia and diarrhea, followed by death in 3-4 days.

5. PATHOLOGY

At the necropsy, besides the injuries observed at the clinical examination, exsudation with fibrin and puss, petechiae, necrosis and ulcers in the anterior respiratory tract mucosa, the presence of false membranes in the larynx, erosive-ulcerative foci in the pharynx, esophagus, abomasum and gut mucosa chosen in generalized forms, serous or mucopurulent exudates in the sinuses, edema of regional lymph nodes. In the case of bacterial complications, bronchopneumonia can be observed at various development stages.
Fetuses have subcutaneous and pulmonary edema, hemorrhagic liquid in the cavities, small hemorrhages in the epicardium, endocardium, pleura and lungs, and small, point-like necroses in the liver and other organs, destruction of the renal cortex.

The histological examination reveals congestive-hemorrhagic, necrotic, ulcerative and infiltrative processes, meningoencephalitis with lympho-monocytes and acidophilic intranuclear inclusions in the respiratory and vaginal epithelium.

6. DIAGNOSIS

For the diagnosis, epidemiological, clinical and pathological data are corroborated with the laboratory ones (histological, virological and serological examination) (OIE Manual of Diagnostic, 2004).
For virus isolation, testicular or renal cell cultures of calf, primary or secondary cells obtained from bovine pulmonary cells or bovine kidney cell lines are used. In 3 days after inoculation cytopathic effect appears (rounding of cells and their clustering, the occurrence of dropsy, intranuclear oxyphilic inclusions).
BHV-1 can be identified by SN, IF, ELISA (very sensitive) (Rosskopf et al., 1994, Perrin et al., 1996), immune peroxidase test, electron microscopy, PCR. Viral antigen research can be performed on frozen tissue sections (mucous membranes and organs) and on cell smears (nasal swabs or tracheobronchial washings) with IF. By the avidin-biotin complex method, the viral antigen appears localized intra- and perinuclear in the epithelial cells.
The indirect, retrospective diagnosis, based on the detection of specific antibodies, includes as most important, SN methods and different ELISA techniques. Of these, the blocking allows the differentiation of naturally infected animals from those vaccinated with marker vaccines.

7. DIFFERENTIAL DIAGNOSIS

The differential diagnosis of infectious bovine rhinotracheitis is related to a wide range of diseases, most notably:
• Viral diarrhea - mucosal disease in which diarrhea is usually present and development is more severe - the laboratory exam is used;
• Malignant catarrh fever, which occurs sporadically, the symptoms are more polymorphic, mortality is high;
• Rinderpest, which is enzootic-epizootic, the progress of the disease is severe, with high mortality;
• Allergic rhinitis, which occurs during grazing, no temperature increase, the animals sneeze, show inspiratory dyspnea, greenish-orange, caseous nasal discharge.
Consideration will also be given to: pasteurellosis, calf diphtheria, viral pneumonias.

8. TREATMENT

At present, there is no specific treatment against bovine infectious rhinotracheitis. The usefulness of a mixed antipasturelic and a bivalent bovine antiviral serum (anti-IBR-IPV and PI-3) in the dose of 0.5-0.6ml / kg is quoted. Also, in the event of an IBR outbreak, antibiotic therapy is recommended to minimize the risk of bacterial secondary infections, accompanied by symptomatic and dietary therapy and good hygiene. Vaccination of bovine during the outbrake, in the early phase of BHV-1 infection with a live attenuated vaccine by intranasal administration has been observed to reduce the number of clinical illnesses. However, this measure does not influence the development of clinical cases.

9. PREVENTION AND CONTROL

9.1. Prophylaxis

Prophylaxis is achieved through general and specific measures.
9.1.1. General measures: the general measures concern: the purchase of animals only from vaccinated flocks, the establishment of prophylactic quarantine, the supervision of the breeding and exploitation technologies, the avoidance of stress factors, serological surveillance, the use of the serologically negative bulls, current disinfection.
9.1.2. Specific measures (immune prophylaxis). In specific IBR prophylaxis, various inactivated or attenuated, monovalent or polyvalent vaccines have been used with definite effectiveness only in preventing clinical signs associated with bhv-1. To date, no vaccine is capable of providing complete protection against BHV-1, so it is necessary to establish a repeat vaccination protocol supplemented by

strict sanitary and hygienic measures to reduce the risk of contamination (Ackermann and Engels, 2006). An alternative to conventional vaccines are those designated as marked or marker vaccines, consisting of viral strains from which genes encoding glycoprotein gE or gC were deleted. They immunize the animals against all bhv-1 antigens, except for gE (gC), thus allowing seronegative animals to be distinguished from gE (animals vaccinated with marker vaccines) from naturally infected seropositive bovine animals. in perspective, it is hoped that recombinant subunit vaccines or those made up of plasmid DNA, will provide improved protection. The benefits of the latest generation vaccines are: superior levels of seroconversion, reduction of viral excretion, booster effect from a third administration, possibility of differentiation between diseased and vaccinated animals.

Live modified, inactivated, conventional or modern generation IBR (subunit, marker deleted) vaccines reduce only the gravity of clinical symptoms, viral replication and viral transmission but are not capable of preventing BVH-1 infection. From this point of view some authors argue that there are no differences between conventional and marker vaccines (Lemaire et al., 2000a and b, Ellis et al., 2005, Gogev et al., 2004). However, it has been observed that the transmission of the virus via the marker vaccines was minimal (Mars et al., 2000). The problem is the possibility of inducing the latency status, sometimes associated with reactivation and elimination of the virus in the herd, following the use of attenuated preparations (Castrucci et al., 2002). It has also been demonstrated, though experimental studies, the possibility of combining a deleted gE vaccine strain with a wild-type strain in the vaccinated herds (Schynts et al., 2003). However, the time interval between two successive infections has a major influence on this recombination (Meurens et al., 2004).

Although the protective effect against viral infection cannot be guaranteed and there are also other inconveniences, of which the induction of latency was quoted above, vaccination represents a choice since it was found that the presence and spread of the virus in the herd is thus significantly diminished (Trapp et al. , 2003; Bowland et al., 2000).

In IBR eradication programs, marker vaccines are recommended, given the two characteristics: they protect against the viral pathogenic effect and offer the possibility of differentiation between vaccinated animals and diseased ones (Bosch et al., 1998, 1997, 1996). Detection of infected animals is based on the assumption that all wild-type viruses express glycoprotein gE and that all these animals will produce anti-gE antibodies (Egyed et al., 2000). Different combined live vaccines (IBR-IPV; IBR-IPV, PI-3; PI3-IBR-BVD), inactivated monovalent vaccines or others, depending on the country or producer, are available on the market (Fulton et al., 1995, 2003, 2004, Kerkhofs et al., 2004, Kujik, 2002, Silva et al., 2006).

The administration protocols depend on the vaccine type. The IBR-IPV vaccine is administered at a dose of 2 ml, irrespective of age, boosted after 21 days in the previously unvaccinated breeding herds and after 7 days in the other age groups, when the first vaccination was by aerosol or nasal instillation. Immunity is maintained through annual vaccinations, i.m., at the same dose.

Bi- and trivalent vaccines are applied to calves under the same conditions as the trivalent vaccine against BVD-MD (Gogev et al., 2002, 2004, Gupta et al., 2001). Thus, the vaccine is administered by intranasal route (1 ml in each nostril) starting with the first few days of life, with repeat after 15-20 days (im, 2ml) or from 2-3 weeks (im, 2ml) and repeat after 15-20 days.

The inactivated vaccine is applied to cows and bulls on breeding farms, 5-ml, s.c. injection, repeated after 15-20 days and then every 6 months.

9.2. Control

On farms with disease outbreaks, the diseased animals are isolated and treated symptomatically and the healthy ones, depending on the epizootiological situation, are serum treated using the mixed serum (0.3-0.4 ml / kg, s.c.) or vaccinated by emergency procedure. For the genital form, reproduction is discontinued throughout the course of the disease, the artificial insemination is carried out

with the semen from non-infected bulls. The diseased animals are isolated and treated symptomatically with antiseptics or antibiotics, in the form of sprays or ointments. Since the healed animals become latent carriers of the virus, the most drastical method to eradicate the disease is by eliminating the seropositive animals (Ackermann and Engels, 2006). A very strict monitoring procedure should be in place, ie, in Romania, in the strategic disease control program includes in the case of IBR, active surveillance by serological screening (ELISA), only upon request, for bulls and breeding buffaloes (2 times a year, sem. I and II); mothers of bulls, on licensing, and candidate bulls mothers (once a year); breeders, after the age of 6 months.

10. ERADICATION

BHV-1 infection is highly contagious and causes important economic losses. In numerous European countries, there are programs to control and / or eradicate IBR. Disease free countries or those where the disease was eradicated impose restrictions on the import of bovines and their products from countries where the virus is present, since the (re)introduction of this herpesvirus in free herds leads to a rapid spread of the disease. Therefore, EU directives also include special conditions for the import of bovine, semen and embryos.

IBR / IPV eradication refers to the eradication of BHV-1 virus in bovine populations. Bovine herpes virus becomes latent due to infection, so all seropositive animals are considered to be carriers and permanent viral shedders. In order to eradicate BHV-1 from a bovine herd, it is necessary to identify and eliminate all seropositive animals.

This approach has been used in countries with low prevalence of infection, namely in the Scandinavian countries, Austria and Switzerland.

In high-prevalence countries the elimination of all HIV-positive animals is not an economically feasible solution; the only viable solution for eradicating this disease is to reduce the incidence of seropositive animals at national level and to use marker vaccines to differentiate between infected and vaccinated animals. The IBR eradication program is based on vaccination of cattle with marker vaccines, controlled bovine movement, stock monitoring and rigorous bio-security measures. In order to follow progress in the eradication of rhinotracheitis, permanent sampling of cattle belonging to several age categories is recommended, as follows: - two years after the start of vaccination, samples are taken from animals between 6-24 months of age, including bovine no longer having maternal antibodies, non-pregnant heifers as well as pregnant heifers. A negative result in this age group (6-24 months) suggests the absence of the virus from the herd.

In the subsequent years, the same age category (6-24 months) will be monitored along with the surveillance of the previously monitored groups from the herd.

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REFERENCES

Ackermann M., Engels M., (2006): Pro and contra IBR-eradication, *Vet. Microbiol.*, 113:293-302

Aniţă D.C., (2008) Seroepidemiological investigations regarding infectious bovine rhinotracheitis in farms from Suceava aria, *Buletin USAMV Iaşi, vol.51/2008 IM/PRESS*

Aniţă D.C., Merticariu Ş., Savuţa Gh., (2008): Observations from an aut break of Infectious Bovine Rhinotracheitis in Iaşi county, *Buletin USAMV Iaşi, vol.51/2008 IM/PRESS*

Arthington JD, Corah LR, Blecha F., (1996): The effect of molybdenum-induced copper deficiency on acute-phase protein concentrations, superoxide dismutase activity, leukocyte numbers, and lymphocyte proliferation in beef heifers inoculated with bovine herpesvirus-1, *J Anim Sci.*, 74(1):211-7.

Babiuk L.A., van Drunen Littel-van den Hurk S., Tikoo S.K., (1996): Immunology of bovine herpesvirus 1 infection, *Vet. Microbiol.,* 53:31-42

Beer M., Konig P., Schielke G., Trapp S., (2003): Diagnostic markers in the prevention of bovine herpesvirus type 1: possibilities and limitations, *Berl. Munch. Tierarztl. Wochenschr* 116:183-191

Boelaert F., Speybroeck N., de Kruif A., Aerts M., Burzykowski T., Molenberghs G., Berkvens D.L., (2005): Risk factors for bovine herpesvirus-1 seropositivity, *Prev. Vet. Med*. 69:285-295

Bosch J.C., De Jong M.C.M., Franken P., Frankena K., Hage J.J., Kaashoek M.J., Maris-Veldhuis M.A., Noordhuizen J.P.T.M., Van der Poel W.H.M.,

Verhoeff J., Weerdmeester K., Zimmer G.M., Van Oirschot J.T., (1998) An inactivated gE-negative marker vaccine and an experimental gD-subunit vaccine reduce the incidence of bovine herpesvirus 1 infections in the field, *Vaccine* 16:265-271

Bosch J.C., Kaashoek M.J., Kroese A.H., Van Oirschot J.T. (1996): An attenuated bovine herpesvirus 1 marker vaccine induces a better protection than two inactivated marker vaccines, *Vet. Microbiol.* 52:223-234

Bosch J.C., Kaashoek M.J., van Oirschot J.T. (1997): Inactivated bovine herpesvirus 1 marker vaccines are more efficacious in reducing virus excretion after reactivation than a live marker vaccine, *Vaccine* 15:1512-1517

Bowland S.L., Shewen P.E. (2000): Bovine respiratory disease: commercial vaccines currently available in Canada, *Can. Vet.* J. 41:33-48

Bradshaw B.J., Edwards S. (1996): Antibody isotype responses to experimental infection with bovine herpesvirus 1 in calves with colostrally derived antibody, *Vet. Microbiol.* 53:143-151

Castrucci G, Frigeri F, Salvatori D, Ferrari M, Dico ML, Rotola A, Sardonini Q, Petrini S, Cassai E., (2002): A study on latency in calves by five vaccines against bovine herpesvirus-1 infection, *Comp Immunol Microbiol Infect Dis.*, 25(4):205-15

Castrucci G, Frigeri F, Salvatori D, Ferrari M, Sardonini Q, Cassai E, Lo DM, Rotola A, Angelini R, (2002): Vaccination of calves against bovine herpesvirus-1: assessment of the protective value of eight vaccines, *Comp Immunol Microbiol Infect Dis.*, 25(1):29

Cole NA, Gallavan RH, Rodriguez SL, Purdy CW. (1994): Influence of triiodothyronine injections on calf immune response to an infectious bovine rhinotracheitis virus challenge and nitrogen balance of lambs, *J Anim Sci.* 72(5):1263-73.

Cusack PM, McMeniman NP, Lean IJ., (2005) The physiological and production effects of increased dietary intake of vitamins E and C in feedlot cattle challenged with bovine herpesvirus 1, *J Anim Sci.* 83(10):2423-33.

Dubeski PL, d'Offay JM, Owens FN, Gill DR., (1996): Effects of B vitamin injection on bovine herpesvirus-1 infection and immunity in feed-restricted beef calves, *J Anim Sci.*, 74(6):1367-74.

Dubeski PL, Owens FN, Song WO, Coburn SP, Mahuren JD, (1996): Effects of B vitamin injections on plasma B vitamin concentrations of feed-restricted beef calves infected with bovine herpesvirus-1, *J Anim Sci. Jun*;74(6):1358-66.

Egyed L., Ros C., Belak S., (2000): Genomic and pathogenic studies on a glycoprotein E variant field isolate of bovine herpesvirus 1, *Vet. Res. Comm.*, pp. 423–431

Ellis J, Waldner C, Rhodes C, Ricketts V, (2005): Longevity of protective immunity to experimental bovine herpesvirus-1 infection following inoculation with a combination modified-live virus vaccine in beef calves, *J Am Vet Med Assoc.* 1;227(1):123-8.

Fulton RW, Briggs RE, Payton ME, Confer AW, Saliki JT, Ridpath JF, Burge LJ, Duff GC. (2004): Maternally derived humoral immunity to bovine viral diarrhea virus (BVDV) 1a, BVDV1b, BVDV2, bovine herpesvirus-1, parainfluenza-3 virus bovine respiratory syncytial virus, Mannheimia haemolytica and Pasteurella multocida in beef calves, antibody decline by half-life studies and effect on response to vaccination, *Vaccine*. 26;22(5-6):643-9.

Fulton RW, Confer AW, Burge LJ, Perino LJ, d'Offay JM, Payton ME, Mock RE., (1995): Antibody responses by cattle after vaccination with commercial viral vaccines containing bovine herpesvirus-1, bovine viral diarrhea virus, parainfluenza-3 virus, and bovine respiratory syncytial virus immunogens and subsequent revaccination at day 140, *Vaccine.* 13(8):725-33.

Fulton RW, Saliki JT, Burge LJ, Payton ME. (2003): Humoral immune response and assessment of vaccine virus shedding in calves receiving modified live virus vaccines containing bovine herpesvirus-1 and bovine viral diarrhoea virus 1a., *J Vet Med B Infect Dis Vet Public Health.*; 50(1):31-7

Gogev S., de Fays K., Versali M.F., Gautier S., Thiry E., (2004) Glycol chitosan improves the efficacy of intranasally administrated replication defective human adenovirus type 5 expressing glycoprotein D of bovine herpesvirus 1, *Vaccine* 22:1946-1953

Gogev S., Georgin J.P., Schynts F., Vanderplasschen A., Thiry E., (2004) Bovine herpesvirus 1 glycoprotein D expression in bovine upper respiratory tract mediated by a human adenovirus type 5, *Vet. Res*. 35:715-721

Gogev S., Vanderheijden N., Lemaire M., Schynts F., D'Offay J., Deprez I., Adam M., Eloit M., Thiry E., (2002) Induction of protective immunity to bovine herpesvirus type 1 in cattle by intranasal administration of replication-defective human adenovirus type 5 expressing glycoprotein gC or gD, *Vaccine* 20:1451-1465 .

Gupta PK, Saini M, Gupta LK, Rao VD, Bandyopadhyay SK, Butchaiah G, Garg GK, Garg SK., (2001): Induction of immune responses in cattle with a DNA vaccine encoding glycoprotein C of bovine herpesvirus-1, *Vet Microbiol.* 26;78(4):293-305.

Huang Y, Babiuk LA, van Drunen Littel-van den Hurk S., (2005): Immunization with a bovine herpesvirus 1 glycoprotein B DNA vaccine induces cytotoxic T-lymphocyte responses in mice and cattle, *J Gen Virol.*, 86(Pt 4):887-98.

Kaashoek M.J., Van Oirschot J.T., (1996) Early immunity induced by a live gE-negative strain of bovine herpesvirus 1 marker vaccine, *Vet. Microbiol.,* pp. 191–197

Kerkhofs P, Renjifo X, Toussaint JF, Letellier C, Vanopdenbosch E, Wellemans G. (2003): Enhancement of the immune response and virological protection of calves against bovine herpesvirus type 1 with an inactivated gE-deleted vaccine. *Vet Rec.* 31;152(22):681-6.

Kujik HA. (2002): Experiences of selection eradication, based on IBR-marker vaccine in the Netherlands, *Magyar Allatorvosok Lapja.*;124(7):398–408.

Lemaire M., Meyer G., Baranowski E., Schynts F., Wellemans G., Kerkhofs P., Thiry E., (2000a): Production of bovine herpesvirus type 1-seronegative latent carriers by administration of a live-attenuated

vaccine in passively immunized calves, *J. Clin. Microbiol.* 38:4233-4238 .

Lemaire M., Schynts F., Meyer G., Georgin J.P., Baranowski E., Gabriel A., Ros C., Belak S., Thiry E. (2001): Latency and reactivation of a glycoprotein E negative bovine herpesvirus type 1 vaccine: influence of virus load and effect of specific maternal antibodies, *Vaccine* 19:4795-4804

Lemaire M., Weynants V., Godfroid J., Schynts F., Meyer G., Letesson J.J., Thiry E., (2000b): Effects of bovine herpesvirus type 1 infection in calves with maternal antibodies on immune response and virus latency, *J. Clin. Microbiol.* 38:1885-1894.

Loehr B.I., Willson P., Babiuk L.A., van Drunen Littel-van den Hurk S., (2000): Gene gun-mediated DNA immunization primes development of mucosal immunity against bovine herpesvirus 1 in cattle, *J. Virol.* 74:6077-6086

Mars M.H., M.C.M. de Jong, Van Oirschot J.T., (2000): A gE-negative BHV1 vaccine virus strain cannot perpetuate in cattle populations, *Vaccine*, pp. 2120–2124.

Meurens F., Schynts F., Keil G.M., Muylkens B., Vanderplasschen A., Gallego P., Thiry E., (2004): Superinfection prevents recombination of the alphaherpesvirus bovine herpesvirus 1, *J. Virol.*, pp. 3872–3879.

Moga- Mânzat R. (editor) (2005): *Boli virotice şi prionice ale animalelor,* Edit. Brumar, Timişoara, 67-73

Mollema L, De Jong MCM, Van Boven M., (2005): Prolonged persistence of bovine herpesvirus in small cattle herds: a model-based analysis. *Epidemiol Infect.*;133:137–148.

Morar R., Pusta D. (2005): *Ghidul crescatorului de vaci cu lapte,*Editura Risoprint, Cluj-Napoca

Noordegraaf AV, Buijtels JAAM, Dijkhuizen AA, Franken P, Stegeman JA, Verhoeff J., (1998), An epidemiological and economic simulation model to evaluate the spread and control of infectious bovine rhinotracheitis in the Netherlands, *Prev Vet Med.*;36:219–238.

OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals (2004): http://www.oie.int/eng/normes/mmanual/A_summry.htm

Perrin B., Perrin M., Moussa A., Coudert M. (1996): Evaluation of a commercial gE blocking ELISA test for detection of antibodies to infectious bovine rhinotracheitis virus, *Vet. Rec*. 138:520.

Platt R, Burdett W, Roth JA.(2006): Induction of antigen-specific T-cell subset activation to bovine respiratory disease viruses by a modified-live virus vaccine, *Am J Vet Res.*, 67(7):1179-84.

Pontarollo RA, Babiuk LA, Hecker R, Van Drunen Littel-Van Den Hurk S. (2002): Augmentation of cellular immune responses to bovine herpesvirus-1 glycoprotein D by vaccination with CpG-enhanced plasmid vectors, *J Gen Virol.*, 83(Pt 12):2973-81

Schynts F., Meurens F., Detry B., Vanderplasschen A., Thiry E. (2003): Rise and survival of bovine herpesvirus 1 recombinants after primary infection and reactivation from latency, *J. Virol.* 77, pp. 12535–12542.

Silva AD, Spilki FR, Franco AC, Esteves PA, Hübner SO, Driemeier D, Oliveira AP, Rijsewijk F, Roehe PM., (2006): Vaccination with a gE-negative bovine herpesvirus type 1 vaccine confers insufficient protection to a bovine herpesvirus type 5 challenge, *Vaccine*. 12;24(16):3313-20.

Solis-Calderon J.J., Segura-Correa V.M., Segura-Correa J.C., Alvarado-Islas A., (2003) Seroprevalence of and risk factors for infectious bovine rhinotracheitis in beef cattle herds of Yucatan, Mexico, *Prev. Vet. Med.* 57:199-208

Trapp S., König P., Beer M., (2003): Conventional and marked BHV-1 vaccines in Germany A brief review, *Berl. Münch. Tierärztli. Wschr.* 116, pp. 208–215.

Van Drunen Littel-van den Hurk S., (2006): Rationale and perspectives on the success of vaccination against bovine herpesvirus-1, *Vet. Microbiol.* 113:275-282

Van Drunen Littel-van den Hurk S., Garzon S., van den Hurk J.V., Babiuk L.A., Tijssen P., (1995): The role of the major tegument protein VP8 of bovine herpesvirus-1 in infection and immunity, *Virology* 206:413-425

Van Drunen Littel-van den Hurk S., Van Donkersgoed J., Kowalski J., van den Hurk J.V., Harland R., Babiuk L.A., Zamb T.J., (1994): A subunit gIV vaccine, produced by transfected mammalian cells in culture, induces mucosal immunity against bovine herpesvirus-1 in cattle, *Vaccine* 12:1295-1302

Van Engelenburg F.A., Kaashoek M.J., van Oirschot J.T., Rijsewijk F.A., (1995): A glycoprotein E deletion mutant of bovine herpesvirus 1 infects the same limited number of tissues in calves as wild-type virus, but for a shorter period, *J. Gen. Virol.* 76:2387-2392

Van Oirschot J.T., Kaashoek M.J., MarisVeldhuis M.A., Weerdmeester K., Rijsewijk F.A.M., (1997): An enzyme-linked immunosorbent assay to detect antibodies against glycoprotein gE of bovine herpesvirus 1 allows differentiation between infected and vaccinated cattle, *J. Virol. Methods* 67:23-34

Woolums AR, Siger L, Johnson S, Gallo G, Conlon J. (2003): Rapid onset of protection following vaccination of calves with multivalent vaccines containing modified-live or modified-live and killed BHV-1 is associated with virus-specific interferon gamma production, *Vaccine*. 7;21(11-12):1158-64.