Viral Respiratory Infections of Cattle

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Introduction

Respiratory and digestive tracts are the most common entrances for the majority of viruses which are the causative agents for the most devastating diseases in cattle. Some viruses which are responsible for the lesions causing disease in the digestive tract enter the body frequently through the upper respiratory tract, such as foot and mouth disease virus. It is also of importance to differentiate between those viruses which cause a severe disease by themselves and those which open pathways for the infection by secondary agents, mostly bacteria. And, finally it is possible that different viruses cause concurrent infections.

Viruses Causing Respiratory Diseases by Themselves

In Table 1 a summary of viruses is given that have been identified as causing disease primarily in the respiratory tract without any additional environmental or microbiological factors.

Table 1. Classification of viruses causing primary disease in the respiratory tract and availability of vaccines.

Name	Family	Subfamily or Genus	Occurrence	Vaccines available
BHV1	Herpes-viridae	Alphaherpes-virinae	world wide	Yes
AHC1	Herpes-viridae	Gammaherpes-virinae	world-wide?	no
OHV2	Herpes-viridae	Gammaherpes-virinae	world-wide?	no
SHV1	Herpes-viridae	Alphaherpes-virinae	world-wide	yes
Rinder-pestvirus	Paramyxo-viridae	Morbillivirus	Africa, Asia	yes
Peste-des-Petits-Rumi-nants Virus	Paramyxo-viridae	Morbillivirus	Africa, Asia	yes
Breda Virus	Torro-viridae		USA, Belgium, The Netherlands	no

Bovine Herpesvirus 1 (BHV1)

Originally this virus was isolated and identified as a causative agent of genital diseases in male and female cattle. In the fifties, it was first described in the USA as the causative agent of the then new "infectious bovine rhinotracheitis- IBR", and later in many countries.[24] Nowadays BHVI is also known to cause conjunctivitis, abortions, mastitis, dermatitis, enteritis, metritis, lesions in the interdigital space and encephalitis. Some strains isolated from cases of encephalitis in Australia and South America are now classified as BHV5.[17]

BHV1 is, among this group, perhaps the best known cattle virus. Numerous vaccines - live attenuated, temperature sensitive and inactivated - are available in many countries, and more recently also marker vaccines, both live and inactivated. At this point it must be stressed that all vaccines are able to prevent outbreaks of clinical disease, but none of them can prevent infection and establishment of latency, the most important and characteristic property of herpesviruses. That means that the genome of the virus persists in the ganglia of the tract of the original infection. Latency in genital and respiratory tracts occurs only if the infection was an experimental intravenous one.[4,28,33] Following stress and/or application of immunosuppressive compounds, infectious virus is assembled and shed. A single injection of an immunosuppressive drug such as dexamethasone or prednisolone, however, in cases of emergency, is usually tolerable.[6]

Alcelaphine Herpesvirus 1 (AHC1)

Until recently this virus had the designation BHV3, but the International Committee for the Taxonomy of Viruses Herpes Virus Study Group decided to name it AHC1 because the natural virus carrier is the wildebeest in Africa.[17] But the disease occurs in cattle, and not in the wildebeest, known as wildebeest associated bovine malignant catarrhal fever. The clinical picture is the same as the one of the sheep associated malignant catarrhal fever, but the infectious agent got the designation.

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Ovine Herpesvirus 2 (OHV2)

Numerous investigations tried to isolate the agent responsible for the sheep associated disease. AHV1 has spread from captive ruminants of African origin in the USA to neighboring cattle herds. The Scottish group[2] found common sequences between AHV1 and material from diseased animals and named the agent caprine herpesvirus 3 (CHV3). Finally, in Austria a close relationship if not identity between AHV1 and OHV2 was postulated.[19,20,21] The question may be raised whether or not it would have been better to maintain the original designation BHV3 for the disease called bovine malignant catarrhal fever, because the clinical features of the disease(s) are identical and invariably leading to the death of the animal. The so-called head-eye form is the one that closely resembles severe cases of infectious bovine rhinotracheitis, but in contrast IBR there are usually additional symptoms that facilitate a differential diagnosis easily, such as a continuous high body temperature which cannot be influenced by treatments, changes in both eyes starting with a keratitis near the limbus followed by an iridocyclitis and photophobia. In general, only individual animals are affected and some contact with sheep has taken place. In rare instances, high numbers of cattle were involved.

Suid Herpesvirus 1 (SHV1)

Synonyms for this important virus are Aujeszky's disease virus (ADV) and pseudorabies virus (PRV). Usually SHV1 is spread from infected pigs to cattle, but also to dogs, cats, sheep and goats. Frequently a dead dog or cat on the premises is the first indicator of the viral presence. Until recently, cattle were considered to be always dead end hosts in that after infection they develop clinical symptoms that may be mistaken for IBR but never shed enough virus necessary to infect neighboring cattle. Sometimes they die before persistent itching points to pseudorabies. Recently, however, strains were detected that pass from cattle to cattle.[16] They also lead to death of the recipient unless it has been vaccinated a few times intranasally against BHV1. Commercial inactivated SHV1 vaccines lead to no protection, live attenuated SHV1 vaccines to protection in some, but not all, animals.[28] It has, however, been demonstrated that a protection with an inactivated SHV1 vaccine can be achieved, if 200 mg of zinc aspartate is included in the vaccine.[26] Also in acute outbreaks of Aujeszky's disease, it is possible to protect the still non-infected animals by immediate intranasal application of a live BHV1 vaccine.

Rinderpest and Peste-des-Petits-Ruminants Virus

Devastating diseases caused by these viruses are still a problem in a number of African and Asian countries. From a recent conference in India, it could be learned that the role sheep play is not fully understood, because it is quite difficult to differentiate the two agents unless modern diagnostic laboratory tools such as PCR are employed. Both agents are able to cause disease in both species.

Vaccines are readily available but it is very difficult to carry out country-wide vaccinations when funds are limited. The use of recombinant vaccines on the basis of vaccinia virus is also of questionable value, because firstly humans may be infected and secondly a revaccination does not lead to a booster effect against the rinderpest virus because the antigenic stimulus of the vaccinia virus is too strong. But conventional vaccines can successfully be used and revaccinations lead to increases in specific antibody levels.

Breda Virus

This virus has been associated with calf diarrhoea but already in 1982 it was reported to cause hyperpnoea and ocular discharge following experimental infection.[37] When sero-conversions were found in four out of ten calves suffering from respiratory disease it was suggested that this agent may play a role.[8] Direct proof came in 1991 when severe respiratory symptoms occurred in two day old calves. The causative virus was identified as Breda virus serotype 2.[31] Time will tell whether or not this virus will play a major or minor role in respiratory disease.

Viruses Involved in Respiratory Diseases

In Table 2 viruses are listed which have been isolated from cases of respiratory disease where they may play a predesposing role for secondary infections, sometimes in connection with environmental factors and viruses that, dependent on the strain, may be responsible for other clinical symptoms but to a certain extent also for respiratory disease.

Table 2. Other viruses that play a role in respiratory diseases.

Name	Family	Subfamily	Occurrence or Genus	Vaccines available
BVD virus	Flaviviridae	Pestivirus	world-wide	yes
BHV4	Herpesviridae	Gammavirinae	world-wide	no
BRSV	Paramyxoviridae	Pneumovirus	possibly worldwide	yes
PI3 virus	Paramyxoviridae	Paramyxovirus	world-wide	yes
Bovine Parvovirus	Parvoviridae	Parvovirus	possibly world-wide	yes
Bovine Rhino viruses	Picornaviridae	Rhinovirus	possibly world-wide	no
Bovine Coronavirus	Coronaviridae	Coronavirus	possibly world-wide	yes (x)
Adenoviruses	Adenoviridae	Mastadenovirus	world-wide	yes
Reoviruses	Reoviridae	Reoviruss	world-wide	yes

(x) generally recommended for vaccination of pregnant cattle in order to increase the antibody titre in colostrum

Bovine Virus Diarrhoea Virus (BVDV)

Although many questions this virus poses have been answered in recent years, there are still problems left. Originally it was thought that the virus causing diarrhoea was different from the one causing mucosal disease. Next it was found that the virus was the same. Then came the differentiation between strains that induced cytopathogenicity in tissue cultures and strains that replicated in the same culture without a cytopathogenic effect. Now we know that the noncytopathogenic virus transmitted during certain stages of pregnancy leads to a persistent infection of the fetus, and mucosal disease breaks out when a persistent infected animal at any age is infected by a homologous cytopathogenic virus. If immunocompetent cattle are infected by any of the two strains, the majority develop clinical symptoms involving the digestive tract but a certain percentage succumb to respiratory disease. Since BVD virus acts like an immunosuppressive compound, secondary infections frequently follow. It is also possible that latently BHV1 infected cattle start to shed infectious BHV1. Live attenuated as well as inactivated vaccines based on cytopathogenic BVDV leave, as far as inducing immunity, something to be desired. They also have an immunosuppressive effect as experienced in the author's own experiments. The live vaccines can also infect the fetus.

The latest development is an inactivated vaccine containing two noncytopathogenic American strains.

Bovine Herpesvirus 4 (BHV4)

In addition to cases of respiratory disease in which the clinical picture looked like mild cases of IBR it was possible to isolate this virus in cases of conjunctivitis, genital tract diseases, abortion, skin lesions and enteric diseases. In the authors's own experiments, six (3 x 2) cattle were intranasally inoculated with three different strains of BHV4 in isolation units. None of them developed any sign of a respiratory disease and the humoral antibody response was rather weak. Next, an intradermal test was carried out to determine whether or not the cell mediated immunity gave better results, but the response was also rather weak, however, detectable. It must therefore be concluded that this virus may function as a precursor, yet being unable to induce clinical disease by itself.

Bovine Respiratory Syncytial Virus (BRSV)

This agent has lately drawn much attention, because it seems to spread to geographic areas that are quite different from the ones were the first isolations were achieved. Originally a maritime climate and the winter season appeared to be the main environmental factors that led together with BRSV to the most dramatic clinical symptoms leading frequently to the death of the patient. But more recently respiratory disease in continental climate areas influenced by BRSV seems in increasing tendency to affect calves and young cattle. The most prominent symptoms resemble those of an allergic reaction and anaphylactic shock syndrome. It is not fully understood which role IgE class antibodies play in this connection. All vaccine producers for live and inactivated vaccines recommend therefore a parenteral vaccination. They want also to be on the safe side because BRSV is closely related if not identical to human strains affecting babies and young children. On the other hand, it has been shown that intranasal application leads rather to better than to adverse results. If seronegative healthy cattle in isolation units are intranasally inoculated with BRSV they do not develop any distinct clinical respiratory disease as demonstrated in two of the author's own experiments. It must therefore be concluded that the environmental factors are responsible for the induction of disease by BRSV. There are, on the other hand, reports from other countries where severe disease is attributed solely to BRSV following experimental infections by intranasal and intratracheal route. If only intranasally inoculated, the symptoms were minor.[3] Possible environmental factors are not mentioned. In another report,[36] BRSV is described as acting immunosuppressively. Also passively acquired colostral antibodies are supposed to offer no protection.[5,13]

Parainfluenza 3 Virus (PI3V)

There is no question that this virus is the typical precursor of secondary respiratory infections because destruction and loss of cilia and of ciliated cells follow after the virus penetrated the protective mucus layer in upper and lower respiratory tracts. The virus is so widely spread that it is almost impossible to find seronegative adult cattle. As a consequence, it has to be assumed that all neonatals receive sufficient maternal antibodies provided proper quantities of colostrum are fed.[23] The best time for vaccination is therefore the period following the disappearance of the passively acquired antibodies, usually around the third and fourth month. It is advisable to use live vaccines for intranasal application available in most countries. Although a second vaccination four to six weeks later does not lead to a booster effect if the calves were seronegative at the time of the first vaccination,[1] it is recommended to carry it out because the serological status at the time of the first vaccination is as a rule unknown and still present passively acquired in some animals may have prevented an active immune response.

Bovine Parvovirus (BPV)

It is not known how widespread this agent is, because in most countries other viruses are of more

importance and therefore it receives relatively little attention. But there are exceptions. Other members of the family paroviridae such as the canine, feline and swine parvovirus play an important role. The bovine parvovirus is mostly isolated from the digestive tract and in some instances mentioned in connection with the respiratory disease complex.[32] Bovine parvovirus is only included in one inactivated vaccine combination recommended for application in pregnant cattle.[27]

Bovine Rhinoviruses

Three serotypes are known and isolations were achieved from healthy animals and calves suffering from respiratory disease.[12] If inoculated intranasally into calves, no clinical symptoms follow but if rhinovirus is instilled into the mammary gland, a catarrhal mastitis develops.[22] Bovine rhinoviruses are certainly not of any relevance in the respiratory disease complex. It is therefore no surprise that no vaccine is available.

Bovine Coronavirus

Coronaviruses are usually associated with neonatal calf diarrhoea but there are reports that they also can play a role in respiratory infections. One detailed report comes from Austria[14] where two outbreaks of respiratory disease are considered to be caused by coronavirus. It was isolated from nasal swabs of sick cattle up to an age of 13 weeks and from cattle without clinical symptoms up to an age of 17 months. Young calves were obviously protected by maternally derived antibodies.

Bovine Adenoviruses (BAV)

Many serotypes and strains of bovine adenoviruses exist[18] and their role is certainly a pathmaking one for other microbes. Contrary to other viral serotypes, those of the adenovirus change their geographic occurrence and distribution from year to year. This property causes problems for the commercial vaccine producer. To overcome this problems most adenovirus vaccines - there are only a few inactivated ones on the market - contain a number of serotypes supposedly most common.[27]

Bovine Reoviruses

The role reoviruses - three serotypes are known - play as precursors and this is the only one possible, is a matter of discussion. The fact that not one American vaccine contains a reovirus component leads to the assumption that reoviruses do not deserve special attention in the respiratory disease complex. This is actually surprising because there are some reports from the USA and elsewhere that make reovirus responsible for the induction of respiratory disease.[9,30,35]

Concurrent Viral Infections

Most papers - predominantly the older ones (for example 25,34) - base their results concerning concurrent viral infections on serological data, but newer papers - and they are more reliable - report concurrent isolations. A summary of reports of concurrent isolations is presented in Table 3.

Table 3. Proven concurrent viral isolations from cases of respiratory infections in cattle[7,10,14,15,29,32]

Viral agents identified	year	author (s)
PI3V + enterovirus + rhinovirus	1979	Moreno-López
PI3V + parvovirus	1983	Weiblen
PI3V + BRSV	1987	Gabathuler *et al.*
PI3V + Parvovirus	1988	Möstl u. Bürki
PI3V + BRSV + BVDV	1988	Steinhagen u. Heckert
PI3V + BRSV + BAV + Coronavirus + BVDV	1990	Läuchli *et al.*

It becomes obvious that PI3V as mentioned before is the typical precursor and therefore justifies prophylactic vaccinations. The same is true for BRSV depending on proven evidence and not only on serological data. It is out of the question that vaccination against BVDV is a must in herds involved.

Discussion

It is out of question that diseases of the respiratory tract are no problem for the clinical diagnosis, because the symptoms are easy to recognize, but it takes knowledge and experience to make a diagnosis without laboratory tests. In many countries, kits are available that can prove or disprove a diagnosis within hours. But a few important steps when examining a herd should be pointed out. Whenever an obviously sick animal is supposedly suffering from an infectious disease of unknown etiology, neighboring animals or lots have to be examined. In young animals off feed the body temperature is often almost normal when infections with the viruses listed in Table 2 are involved. Temperatures in neighboring cattle or cattle in neighboring lots are frequently strongly elevated, but otherwise no sign of disease present. Cattle eat and drink normally. If viruses listed in Table 1 hit cattle, they immediately go off their feed, show very high temperatures and cattle of all ages are involved. Milk production drops to almost nil.

Gauze, not cotton swabs and blood samples - one for serum and a second one of heparinized blood if a test for BVDV is asked for - should be taken from the obviously sick and contact animals that run an elevated body temperature. For the confirmation of a diagnosis based on serology, a second blood sample should be taken

four to six weeks later from the same animals.

Vaccinations as an emergency measure are possible with live vaccines; inactivated vaccines may have a detrimental effect. Paramuninizing products, various in their nature, can also be administered. **It is also of upmost importance to check the parameters responsible for a hygienic environment.**[11]

Summary

The viruses isolated from respiratory diseases of cattle can be classified as to their virulence. One group consists of viruses that, after infection without any environmental influences, lead to severe clinical disease. Viruses of the other group act mostly as precursors for other agents, sometimes also viruses, the best example being parainfluenza 3 virus. A number of vaccines are available for prophylactic and emergency vaccinations against most of the severe and, to a lesser extent, for the other viruses.

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Abstract

Effect of fertirelin acetate (GnRH Agonist) on postpartum ovarian dysfunction

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During the regular reproductive check at a two weeks interval, 35.5% of 470 cows examined at about one month postpartum were diagnosed as having ovarian dysfunction. Eighty-five of the 167 cows with postpartum ovarian dysfunction were treated with an intramuscular injection of 100 μg fertirelin acetate. Other 82 cows were not treated and served as controls. About 93% of the cows treated responded to fertirelin with the ovulation and corpus luteum formation as indicated by the increase of milk progesterone level, while only 11% of the control cows showed an increase of milk progesterone level. The difference in the percentages between the two groups was statistically significant ($P < 0.001$). Cows in the fertirelin-treated group required a shorter interval between parturition and first insemination, showed a higher first insemination conception rate, and required a shorter interval from parturition to conception than the non-treated controls. It may be concluded that the early diagnosis of postpartum ovarian dysfunction and treatment with GnRH or its analogs are useful for improving reproductive performance in dairy herds.