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EUROPEAN COMMUNITY PREVIEW ARTICLE

CONTROL OF ACUTE VIRUS DISEASES OF CALVES IN THE FEDERAL REPUBLIC OF GERMANY*

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ABSTRACT

Mayr, A., 1979. Control of acute virus diseases of calves in the Federal Republic of Germany. Vet. Sci. Commun., 3: 3-19.

The most important acute viral diseases of calves in the Federal Republic of Germany (FRG) are:
1. Enzootic bronchopneumonia
2. Bovine viral diarrhoea - mucosal disease (BVD-MD)
3. Infectious bovine rhinotracheitis - infectious pustular vulvovaginitis (IBR-IPV)
4. Rota- and Coronavirus infections

The incidence, diagnosis and control of these infections in the FRG are discussed. Stomatitis papulosa and malignant catarrhal fever are also briefly mentioned.

INTRODUCTION

In the Federal Republic of Germany there are at present 14.5 million cattle, of which 2.8 million are calves up to 6 months of age. Annual production from these cattle exceeds 21 billion DM and satisfies about 95% of the FRG's total beef consumption and 60% of its veal consumption. These figures emphasize the enormous economic importance of cattle breeding and production in the FRG, and the great responsibility of veterinary medicine in establishing and maintaining a healthy and productive cattle population.

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* This article was originally written in German. Copies of the German version may be obtained free of charge by writing to: Mr. J. Rodesch, Commission of the European Communities, DG XIII, Bâtiment Jean Monnet, Rue Alcide de Casperi, Kirchberg, Luxembourg.

Calf losses are about 12% in the FRG, depending upon husbandry conditions and area, (Senft and Mayr, 1977), and the most frequent causes for these losses are infections:

1. During the first few days of life
2. During the period when passive maternal immunity is fading and before active immunity has been established
3. Shortly after crowding calves together for veal production
4. At the beginning of the cold season (common cold).

Apart from the diseases caused by E. coli, Salmonellae and parasites the acute viral infections of calves are of greatest importance. Two groups of these viral diseases can be differentiated:

1. Specific infectious diseases with a single cause
2. Multifactorial infectious diseases which develop through the interaction of many different microbial and non-microbial factors.

The latter diseases develop by the synergistic interaction of a variety of agents especially shortly after calves are crowded together for veal production and at the beginning of the cold season. The acute viral diseases of calves which are of most importance in the Federal Republic of Germany are summarized in Table 1.

Calf rearing and fattening is mainly plagued by Enzootic Bronchopneumonia, Mucosal Disease, IBR-IPV and Rota- and Coronavirus infections. During recent years we have worked particularly on the incidence of these acute calf diseases, and developed diagnostic and control measures.

Rota/Coronaviruses

During recent years two viruses have been demonstrated to play a role in the complex diarrhoeal diseases of newborn calves. First is the so-called Nebraska calf diarrhoea virus, a non-enveloped, RNA containing, reo-like virus, which is now called Rotavirus, and secondly a Coronavirus, which also contains RNA, and has an envelope with clublike projections (Table 2). Although the two viruses are very different in their properties they have many similarities with respect to their pathogenesis. The bovine rotaviruses and coronaviruses both have a strong affinity for epithelial cells of the small intestine, and the coronaviruses also have an affinity for the epithelium of the colon. Infection with these viruses rapidly leads to a loss of function of the

TABLE I

Survey of the most important acute virus diseases of calves in the Federal Republic of Germany

Disease	Viruses involved	Percentage of animals with antibodies
Bovine enzootic pneumonia		
(a) season dependent	Adenoviruses (types 1 - 8)	30 - 85%
(b) crowding-associated	Reoviruses (types 1 - 3)	27 - 38%
	Rhinovirus	74%
	Parainfluenza 3 virus	89%
	Respir. Syncyt. virus	57%
Bovine virus diarrhoea-mucosal disease	BVD-MD virus	27%
Infectious bovine rhino-tracheitis - Infectious pustular vulvovaginitis	IBR-IPV virus	3 - 40%
Neonatal calf diarrhoea	Rotavirus	95%
	Coronavirus	?
Bovine papular stomatitis	Pseudocowpox virus	sporadic
	Milker's nodules virus?	sporadic
	Orf virus?	sporadic
Malignant catarrhal fever	Malignant catarrh virus	sporadic
Foot and mouth disease	FMD virus, types O, A, C	annual vaccin-ation

TABLE II

Properties of bovine rota - and coronaviruses

	Rotavirus	Coronavirus
Nucleic acid	RNA	RNA
Size	55 - 65 nm	120 nm
Envelope	no	yes, with club-like projections
Stability		
$CHCl_3$	resistant	sensitive
pH_3	resistant	resistant
Heat 56°C, 30 min	resistant	sensitive
Hemagglutination activity (type RBC)	probably not	yes, (hamster, mice, rats)
Replication	fetal bovine kidney cell cultures (difficult)	fetal bovine kidney cell cultures (difficult)
Demonstration	EM, FAT	EM, FAT
Classification	Reoviridae	Coronaviridae
Control	live vaccine	live vaccine

epithelial cells in the gut, caused by intensive viral replication and detachment of villous epithelium. These changes are accompanied by villous atrophy and failure of absorption, which favour secondary bacterial infections, especially with E. coli.

Both virus infections cause similar clinical signs. After an incubation period of 13 to 24 hours calves develop diarrhoea with watery, yellowish faeces. This diarrhoea may stop very rapidly, or may be complicated by secondary infections. In complicated

outbreaks a morbidity of around 90-100% and a mortality of up to 50% are not uncommon. We know that bovine rotavirus and bovine coronavirus infections occur in many countries, and we have demonstrated that they occur in the Federal Republic of Germany.

The methods used were electron microscopy, using faecal filtrates, and immunofluorescence to demonstrate antigen-containing cells in the faeces (Bachmann, 1977). According to preliminary serological investigations the incidence of rotavirus infections in Germany is very high (up to 95%), and therefore comparable to the incidence in the United States and England. Unfortunately we do not know very much about the role of bovine coronaviruses.

Diagnosis of rota- or coronavirus infections is difficult. Three methods are used at present:

1. Direct electron microscopical demonstration of viral particles in faecal filtrates: Faeces have to be collected during the first 6-10 hours after the onset of diarrhoea. Electron microscopy is still the best method for diagnosis of the two infections.
2. Immunofluorescence: Two techniques can be employed. The better method is to use frozen sections of small intestine, where antigen can be demonstrated by the direct or indirect technique in the intestinal epithelium. This method is especially useful for the diagnosis of coronavirus. Rotaviruses can also be demonstrated in monkey kidney cell line cultures (e.g. Vero) after inoculation with faecal filtrates or intestinal suspensions and incubation for 18-24 hours. Rotaviruses undergo an abortive cycle of replication in these cells, and single antigen-containing cells can be demonstrated in positive cases. It is also possible to demonstrate antigen with the fluorescent antibody test in epithelial cells present in diarrhoeal faeces.
3. Serological investigation is possible for both agents using either the neutralization test or indirect immunofluoresence.

In differential diagnosis other infections such as E. coli, Chlamydiae, Salmonellae, yeasts, the BVD-virus and also non-infectious factors such as hygiene and diet have to be considered. At present control measures in the FRG consist of diagnosis and epidemiological investigations on the role and incidence of these infections. Uncomplicated infections improve rapidly after the administration of electrolytes and/or the replacement of milk by water or glucose and water. A second method of treatment depends on the control of secondary infections.

Although most cows have humoral antibodies, the passive transfer of maternal antibodies has no practical importance. Milk antibodies decrease rapidly 24-72 hours after birth and do not protect the calf adequately. An active immune prophylaxis against corona- and rotavirus diarrhoea has been developed in the United States, using an attenuated live virus and, if the US experience can be confirmed, it may be an answer to these infections.

At present experiments are in progress to combine rota- and coronaviruses in one vaccine, and we have started investigations to test the effect of adding the E. coli vaccine that has been developed in our Institute to these viral components. Unfortunately results are not available yet (Bachmann, 1977).

IBR-IPV

The IBR-IPV infection has been known in Germany for decades. Until recently the infection produced mostly genital lesions (infectious pustular vulvovaginitis; infectious balanoposthitis; IPB; IBP) but during the last two years a respiratory form has been observed to increase. Other diseases due to the IBR-IPV virus, such as encephalitis and abortion, do not play a role according to our experiences.

The epizootiology of IBR-IPV in the FRG is variable. The virus is much more common in Northern than Southern Germany, and much more common in bulls on artificial insemination stations than in animals on ordinary farms.

IBR-IPV viral infections can be diagnosed from clinical signs, but diagnosis is mainly performed by the isolation of virus and the demonstration of neutralizing antibodies. We regard the antibody test as the most reliable method.

The control of IBR-IPV in the FRG is regulated partly by law (especially by the use of vaccines), but further measures depend on the current disease situation, for example on the incidence in an infected population (region and herd) and on the nature of the disease (respiratory or genital form; acute or persistent). Control can be difficult because IBR-IPV virus infections tend to become persistent, (when virus can be excreted intermittently for years), and also because of the common occurrence of infections without clinical signs.

Only one vaccine type is used for immune prophylaxis against IBR-IPV in the FRG. It is an inactivated vaccine which contains

four other antigens in addition to IBR-IPV virus. An attenuated live virus is being tested at present, but it can be used only with special government permission. Vaccines made from inactivated IBR-IPV virus are less effective than vaccines made with live virus. However, inactivated vaccines are completely safe and prevent the spread of vaccine virus into populations free from infection or with a low incidence of infection. Live virus vaccines are usually used only when the genital form of the disease occurs in valuable animals, for example at insemination stations, or when breeding damage may be expected.

A vaccination campaign has to be supplemented by organizational and preventive measures (e.g. quarantine; hygiene; slaughter etc.), whether inactivated or live virus vaccines are used, and such measures have to be adjusted to the conditions on each farm, according to the epidemiological situation and husbandry methods (Straub, 1976; 1977; Straub and Wizigmann, 1968).

BVD-MD

Bovine viral diarrhoea- mucosal disease (BVD-MD) was observed in the FRG for the first time in 1957. Today the virus is widespread throughout the country and increasingly causes disease in calves and young cattle. During the first few years the mucosal form of the disease ("mucosal disease") was most commonly diagnosed, but now the enteritic form ("viral diarrhoea") predominates. BVD-MD may generally be diagnosed by clinical and pathological investigation in addition to the isolation of the agent in secretions and excretions, the intestinal mucosa, lymph nodes, spleen and blood. The demonstration of virus neutralising antibodies in paired sera is of little importance because of time reasons. A survey of the methods for diagnosing BVD-MD is shown in Table III.

Effective control of BVD-MD is possible only by active immunization combined when necessary with hygienic measures such as isolation and quarantine, and disinfection. No treatment for the disease is known, and the success of symptomatic therapy is limited (Table IV).

For immune prophylaxis of BVD-MD in the FRG a combination vaccine made from inactivated agents is commercially available and there is also a live vaccine developed at our Institute. The live virus vaccine is produced in cell culture with an attenuated

TABLE III

Diagnosis of bovine viral diarrhoea - mucosal disease

Disease status	Clinical and pathological diagnosis	Demonstration of agent
Incubation	-	?
Acute phase (febrile phase)	-	Blood
Subacute phase	Enteritis Erosion in buccal mucosa	Nasal mucus Tears Saliva Buccal mucosa Blood Faeces
Post mortem	Erosions in intestinal tract	Altered mucosa of intestinal tract Intestinal lymph nodes Spleen and other organs
Serological diagnosis:	investigation of paired sera: demonstration of neutralizing antibody formation or rise	

virus strain. The vaccine is safe and effective and has the advantage that freshly infected populations can be vaccinated ("emergency vaccinations") without harmful side effects. Prophylactic vaccinations are carried out according to the following schedule:

1. Vaccination of all farm animals by subcutaneous administration.
2. Second vaccination of animals that were younger than 3 months at time of first vaccination; this booster vaccination is carried out at least four weeks after the first vaccination, and not before the age of 3 months.

The efficacy is demonstrated very clearly from the results of emergency vaccination. We have data on such vaccinations from 101 farms where animals had died from BVD-MD or had been slaughtered because of the disease before vaccinations were started. The observations were made on 2,994 young animals, and at the time of vaccination:-

13% of them had died from or been slaughtered because of BVD-MD or had recovered.

2% were clinically ill and

85% were without symptoms.

In evaluating the pattern of disease after vaccination it is necessary to take into account the fact that already infected populations were vaccinated and that further cases or losses decreased only gradually in parallel with the development of active immunity. After vaccination 15 of the clinically ill animals died, and all the others recovered. Of 2,502 healthy animals 21 (0.8%) became ill, and the others remained healthy. The results of these trials are summarized in Table V.

They show clearly that the vaccinations were effective and rapidly and completely stopped the disease in infected populations.

Enzootic Bronchopneumonia

Enzootic bovine bronchopneumonia, which is also often called "cattle flu", "viral pneumonia", or "enzootic bronchitis" has a complex etiology and may be classified as a multifactorial infectious disease. At present the disease is thought to be caused primarily by viruses, but the "triggers" that convert an infection into disease may be non-microbial factors. The disease is also complicated by bacterial infections (Wizigmann, 1974; Wizigmann et al. 1976). Among the participating viruses the

TABLE IV

Control measures for bovine viral diarrhoea - mucosal disease

Control method	Details
Causal therapy	none known
Immune prophylaxis	1. Combination vaccine made from inactivated agents (PI-3, BAV-3, Reo-1, IBR, BVD-MD). 2. BVD-MD vaccine made from living, attenuated virus.
Symptomatic therapy	Administration of electrolytes to prevent fluid imbalance. Support of circulation. Control of secondary infections.
Hygienic measures	Isolation Disinfection
State control measures	None

TABLE V

Efficacy of emergency vaccinations against BVD-MD in 101 cattle herds after onset of BVD-MD cases

Total observed:	2,944 young cattle in 101 herds	
Disease situation at time of vaccination:		
Diseased and recovered	36 animals	1%
Died or slaughtered	352 animals	12%
Clinically ill	54 animals	2%
Clinically healthy	2,502 animals	85%
Disease course after vaccination of 54 diseased animals vaccinated:		
Died	15 animals	
Recovered	39 animals	
Disease course after vaccination of 2,502 clinically healthy recipients:		
Stayed healthy	2,481 animals	(99.2%)
Became ill	21 animals	(0.8%)
Recovered	12 animals	

adenoviruses (at least 8 serotypes) and reoviruses (at least 3 serotypes) are particularly important. The most important bacteria associated with the disease are Pasteurellae. The most common factors which reduce resistance are colds, inadequate and faulty environmental conditions, transport stress, unfavourable husbandry and nutrition. These "trigger" factors - microbial and non-microbial - can vary in different cases and frequently several factors co-operate (Fig. 1).

The complex etiology of enzootic bovine pneumonia must always be taken into account when designing a programme for the control of the disease. Only an optimal combination of measures which supplement and support each other will lead to consistent and lasting success. Both prophylactic and therapeutic measures may be used.

Prophylactic measures include:

a. Organisational preventive measures such as good husbandry, the all in-all out-method, quarantine, good environmental conditions and surveillance of food.
b. Hygienic measures such as cleaning and disinfection and good hygiene of people in contact with the animal.
c. Preventive measures with suitably medicated food.
d. Appropriate immunoprophylaxis.

For effective and safe immunoprophylaxis two epidemiologically different forms of bovine enzootic bronchopneumonia must be considered:

1. A form which occurs only during the cold season.
2. A form associated with crowding of livestock which is observed in beef production farms. This form may occur at any season but is always associated with "Crowding".

Attention must also be paid to the method of husbandry, the age of the animals, the time of vaccination, the kind of vaccines and/or drugs used and the form in which they are administered (Wizigmann et al. 1976).

In the season-dependent form of enzootic bronchopneumonia vaccination with an agent-specific vaccine is most important. We have had success with a combination vaccine derived from inactivated agents (bovine adenoviruses type 1, 3 and 5-reoviruses type 1 and 3 and parainfluenza 3-virus) which has been developed on the basis of investigations of the epidemiology and pathogenesis of bovine enzootic bronchopneumonia (Wizigmann, 1974; Wizigmann,

et al. 1976).

We have data from the vaccination of more than 70,000 animals in problem herds during four vaccination campaigns. After vaccination the morbidity in these herds decreased from 72% to 6.8% and mortality decreased from 5.1% to 1%. 86-89% of the animal's owners were satisfied with the vaccination results, and veterinarians evaluated the efficacy of the vaccines as "very good" or "good" in 89-94% of the herds (Wizigmann et al. 1976).

In enzootic bovine bronchopneumonia associated with crowding it seems that prophylactic measures should at first be non-specific, using so called paramunity-inducers, (Mayr, 1976; Mayr et al. 1976). These should be followed and supplemented by agent-specific vaccines.

The paramunity-inducers increase non-specific resistance to infection in the short term, induce interferon production and activate the lymphopoietic cell system (Mayr, 1976; Mayr et al. 1976). Paramunity inducers of very different natures are known (Mayr, 1976); the most useful in bovine practice are biological inducers or safe living vaccines (e.g. PI-3; BVD-MD). These have the advantage of combining non-specific and specific effects. In practice the inducer and vaccine should preferably be administered together.

So far we have obtained good results with a preparation (PIND-AVI) which is produced from an inactivated avipoxvirus which is heterologous for mammals, (Mayr et al. 1976; Wizigmann, unpublished observations).

When administering a combination vaccine derived from inactivated agents one must consider the age of the animal and the danger of vaccination provocation, for example by vaccinations during the incubation period. Animals bought at 1-3 weeks of age should be vaccinated first with a paramunity inducer which should be followed by the "cattle flue vaccine" 2-4 weeks later, but not before 5 weeks of age. By this means the danger of provoking the disease by the vaccination is reduced. Such provocation of disease can always occur when the first vaccination, (using vaccines made from inactivated agents), is done either during the incubation of infectious disease or when the animal is infected but shows no clinical signs.

When animals are brought together at 2-3 months of age, vaccination with "Cattle flu vaccine" should be performed on their

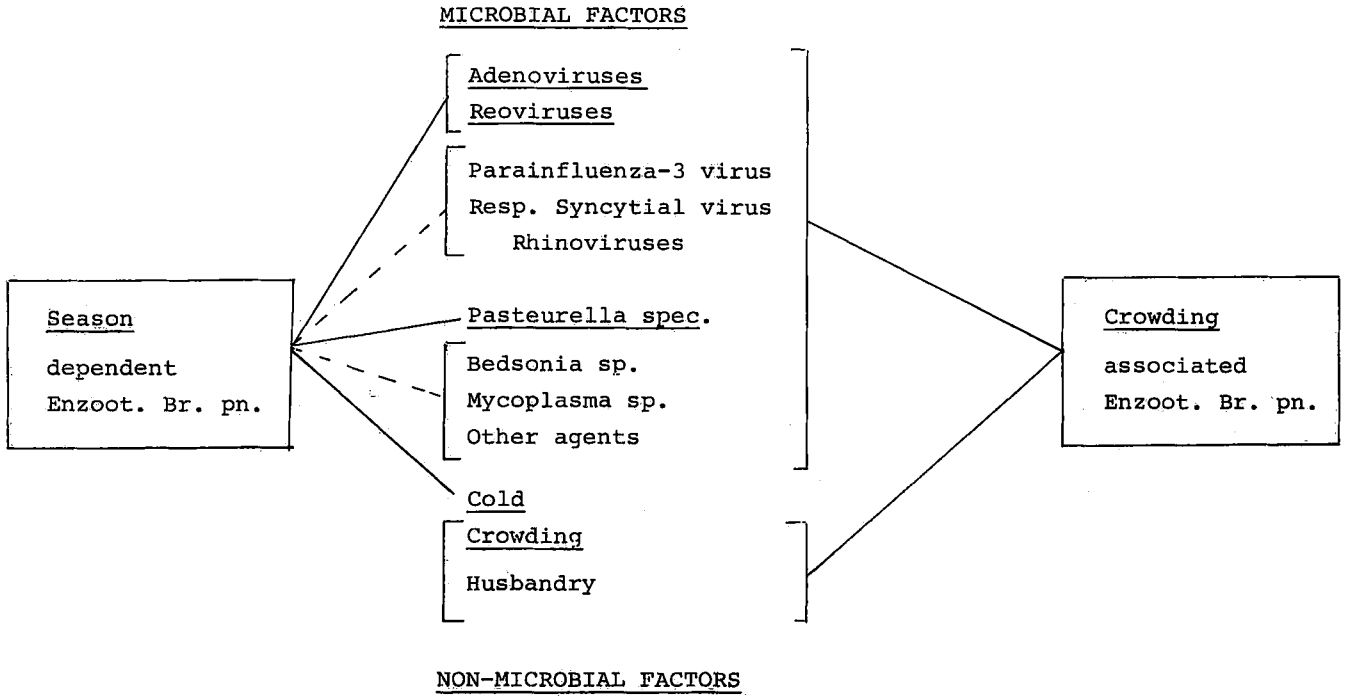

Fig. 1. Cause-effect relationships in the development of bovine enzootic bronchopneumonia.

farm of origin, although not earlier than 5 weeks of age. Ideally booster vaccinations should also be carried out there. The animals then already have a developing or formed immunity against the most important viral agents when they are crowded together. If necessary revaccination has to be done after they are crowded together. If vaccination with "Cattle flu vaccine" is not possible on the animal's farm of origin, it should be carried out as in younger calves; that is paramunization followed by vaccination with "cattle flu vaccine".

Depending on the method of husbandry, the age of the animals and the disease problem in a population the following vaccination schedules are suggested:

Closed herds

All animals more than 6 weeks and up to 18 months old should be vaccinated twice with an interval of 4-6 weeks between vaccinations; the first vaccination should be at the end of August/beginning of September. Calves born later should also be vaccinated twice with the first vaccination at 5-6 weeks of age and revaccination at the end of August/beginning of September. In grazing animals the double vaccination should be completed before the animals are stabled in the autumn.

Herds which buy in calves

1. Animals bought at 1-3 weeks old: these animals should receive a paramunity inducer and be vaccinated with a suitable living vaccine before or immediately after being crowded together. They should be vaccinated with "cattle flu vaccine" about 3-4 weeks after being crowded together, again 4-6 weeks later and, if necessary, revaccinated at the end of August/beginning of September.
2. Animals bought at over 2 months of age: these animals should be vaccinated with a "cattle flu vaccine" at the farm of origin, the first administration being at 5 weeks of age. They should be revaccinated at the farm of origin or from the 3rd week after crowding together. Herds with a severe disease problem should also receive paramunity inducers or suitable live vaccines as soon as they are crowded together and a further vaccination with "cattle flu vaccine" at the end of August/beginning of September.

If vaccination is not possible at the farm of origin, the schedule should be similar to that in younger animals.

Stomatitis papulosa and Malignant Catarrhal fever

Stomatitis papulosa and Bovine malignant catarrhal fever are also acute viral diseases which are important in calves. Stomatitis papulosa infections spread enzootically. They are usually subclinical or they may occur as "teat pox" in dairy cows. In veal production farms stress and synergistic interactions with other mixed infections may activate these infections and cause clinical disease. In these cases they may be confused with mucosal disease and other mucosal infections. Stomatitis papulosa became apparent in the FRG mainly because of pustular lesions on the hands, arms and legs of persons working with the animals. These lesions have become more common during the last two years. Diagnosis may easily be made by means of the electron microscope and by isolation of the virus in secondary bovine fetal lung cell cultures. No specific control has been carried out in practice, but experimental studies have been performed on the virus in connection with the Orf virus infection of sheep. We have shown, by means of quantitative cross neutralization tests, that there is a close antigenic and immunologic relationship between Orf and Stomatitis papulosa viruses, although the agents can be differentiated on the basis of their nucleic acid structure, by analysis with restriction enzymes. The close immunologic relationship is important because calves can be vaccinated against Stomatitis papulosa with a live Orf virus vaccine. Recently, we have developed an Orf virus cell culture vaccine from an attenuated virus strain (140 alternate passages in secondary cultures from fetal ovine and bovine lungs), which is safe for lambs and calves and has good immunogenic properties. It also has the advantage that, in contrast to other Orf virus vaccines, it can be given subcutaneously without loss of immunogenicity.

Bovine malignant catarrhal fever is also enzootic in the FRG. In differential diagnosis it can be confused with mucosal disease and IBR-IPV, especially when it occurs in calves. The exotic diseases Rinderpest and blue tongue also have to be excluded. The disease is diagnosed on the basis of clinical signs and pathological changes. We have not been able to isolate a virus in thyroid cell cultures.

Effective control is difficult, because the disease occurs only sporadically. Both diseased and suspected cases are slaughtered immediately because of the unfavourable prognosis. Specific prophylaxis or therapy will not be possible until we know more about the properties of the virus that causes bovine malignant catarrhal fever in the FRG. Isolates from other countries have proved to be herpesviruses (Plowright, 1968).

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KURZFASSUNG

Mayr, A., 1979. Kontrolle über akute Viruserkrankungen bei Kälbern in der Bundesrepublik Deutschland. Vet. Sci. Commun.,3: 3-19 (in Englisch).

Zu den wichtigsten akuten Viruserkrankungen bei Kälbern in der Bundesrepublik Deutschland zählen:
1. Rinderbronchopneumonie
2. BVD-MD
3. IBR-IPV
4. Rota-coronainfektion

Auftreten, Diagnose und Kontrolle über diese Infektionskrankheiten in der BRD werden erörtert. Stomatitis papulosa und bösartiges Katarrhalfieber werden kurz angesprochen.

RESUME

Mayr, A., 1979. Contrôle des maladies virales aiguës des veaux en république fédérale d'Allemagne. Vet. Sci. Commun.,3: 3-19 (en anglais).

Les principales maladies virales aiguës des veaux en republique fédérale d'Allemagne sont les suivantes:
1. Bronchopneumonie enzootique
2. Diarrhées à virus des bovine - maladie des muqueuses
3. Rhino-trachéite infectieuse des bovins - vaginite pustuleuse infectieuse
4. Infections rotavirales et coronavirales

La fréquence, le diagnostic et le contrôle de ces infections en république fédérale d'Allemagne sont examinés. La stomatite papuleuse et la fièvre catarrhale maligne sont mentionnées brièvement.

RIASSUNTO

Mayr, A., 1979. Controllo delle affezioni virali acute dei vitelli nella Repubblica Federale Tedesca. Vet. Sci. Commun.,3: 3-19 (in Inglese).

Le principali affezioni virali acute dei vitelli nella Repubblica Federale Tedesca sono le seguenti:
1. Broncopolmonite enzootica
2. Complesso Diarrea Virale del Bovino-Malattia delle Mucose (Bovine Virus Diarrhoea-Mucosal Disease - BVD-MD)
3. Rinotracheite Infettiva Bovina-Vaginite Pustulare Infettiva (Infectious Bovine Rhinotracheitis-Infectious Pustular Vaginitis - IBR-IPV)
4. Infezioni da Rotavirus e da Coronavirus

Vengono esaminati l'incidenza, la diagnosi e il controllo di queste infezioni nella Repubblica Federale Tedesca, e si dà un breve cenno anche sulla Stomatite papulosa e la Febbre catarrale maligna.