

## LENTIVIRUSES IN UNGULATES. I. GENERAL FEATURES, HISTORY AND PREVALENCE

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The Russian Veterinary Journal

### Summary

Shuljak, B. F., 2006. Lentiviruses in ungulates. I. General features, history and prevalence. *Bulg. J. Vet. Med.*, **9**, No 3, 175–181.

In this part of the review the history of studies and information about the prevalence of five lentivirus infections (equine infectious anaemia, maedi-visna disease, caprine arthritis-encephalitis, bovine immunodeficiency and Jembrana disease) is provided.

**Key words:** cattle, goat, horse, lentiviruses, sheep

### INTRODUCTION

Lentiviruses (LV) are nononcogenic viruses, belonging to the Lentivirinae subfamily. The name comes from the Latin word “lenti”, meaning “slow”. According to the definition of B. Sigurdsson, they are causing infections in a limited number of hosts with a long incubation period (months and years) and progressive course, accompanied by damage in definite organs/tissues and a lethal outcome (Sigurdsson, 1954).

Initially, the Lentivirinae subfamily comprised only the maedi-visna virus (MVV) and the caprine arthritis encephalitis (CEA) virus as well as human and simian immunodeficiency viruses (HIV, SIV). Investigation of the genetic structure of retroviruses shows that there are many phylogenetically similar agents, but not all of them caused slow infections. That is why, the Lentivirinae family includes (with the exception of human and simian retroviruses), six animal lentiviruses: the maedi-visna virus (MVV), the caprine arthritis encephalitis (CEA) virus, equine infectious anemia (EIA) virus, the

Jembrana disease (JD) virus, the bovine immunodeficiency virus (BIV) and the feline immunodeficiency virus (FIV).

### HISTORY

*EIA.* The equine infectious anaemia was observed for the first time in France in 1843 (Ligné, 1843). In 1903, Torrance described the disease in the USA and called it “swamp fever”. Its viral etiology was supposed in 1904 (Vallé & Carré, 1904) but the pathogenesis of EIA and the features of its agent were a mystery for more than 50 years as the attempts to select a culture, sensitive to it were not successful until 1964.

*Maedi-visna.* The first data about ovine progressive pneumonia (OPP, “zwoegerziekte”) are reported by the Dutch veterinarian Loman D.C. in 1862. After a quarter century, the disease was mentioned also by South-African, American, French and Dutch specialists that called it Graaf Reynet disease (Mitchel,

1915), Montana<sup>1</sup> disease (Marsh, 1923) and la bouchite (Lucam, 1942), respectively. The most extensive studies were however performed by G. Gislason, G. Sigurdsson and other Islander researchers who called the respiratory form of the disease “maedi” or dyspnea (Sigurdsson, 1954) and the neuroparalytical form – “visna” or wasting (Sigurdsson & Palsson, 1958). The agent was introduced in Iceland with some asymptotic infected rams originating from Germany. After several years, the infection spread over 70% of Iceland territory and caused enormous economical losses. For its eradication, a stamping-out and a complete replacement of affected sheep flocks with unaffected sheep was necessitated. The infection was eradicated only in 1965<sup>2</sup>. During this unique combat, about 105 thousands of sheep died and another 650 thousands were culled (Palsson, 1976). Possibly, these huge losses could be avoided and the eradication of MV in Iceland should occurred in shorter terms if serological methods of diagnostics were available. They were however applied only in the 60-ties of the last century.

In Kirgizia, the pathomorphology of ovine progressive pneumonia was described by V. M. Mitrofanov in 1976. The lack of specific diagnostic means did not allow him to tell the precise diagnosis. In 1984 we tested in the reaction of diffuse precipitation of about 300 sera from 6 farms in this republic. Two farms were affected, with seropositivity to OPP agent between 9 and 14%.

By the end of the 70-s and the early

80-s of the last century, in farms from the non-chernozem zone of the Russian Federation, specialized in the rearing Romanov breed of sheep, a neurological disease had appeared. We also participated in the determination of its aetiology. Through serological analysis, isolation and identification of the agent as well as its reproduction in sheep in experimental condition, it was found out that the disease was caused by the MVV (Karavaev *et al.*, 1983; Shuljak, 1985)<sup>3</sup>.

*Caprine arthritis encephalitis.* One of the first diseases in goats, resembling the OPP was described by Indian researchers in 1964 (Rajya & Singh, 1964). Later, similar cases were reported in Germany (Stavrou *et al.*, 1969). Viral leukoencephalomyelitis was detected in goat kids from the USA in the middle 70-s of the 20th century (Cork L.C. *et al.*, 1974). The disease was called caprine arthritis encephalitis because of the fact that both syndromes were caused by the same agent (Crawford *et al.*, 1980).

*Jembrana disease.* For the first time it was recognized in 1964 in Bali cattle (*Bos sondaicus*) in the Indonesian province Jembrana. The first outbreak was characterized by a high morbidity rate and mortality (Ramachandran, 1997). With time, the disease involved the entire island and caused losses of about 10% (26 thousands of animals) of Bali cattle population. Afterwards the disease became endemic for Indonesia accompanied by considerably reduced morbidity and mortality rates. In 1993, the viral aetiology of the disease was established (Kertayadnya *et al.*, 1993).

Later, the infection was spread to Sumatra, Java and Kalimantan (Soeharsono,

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<sup>1</sup> Named upon the American state where it was widely distributed.

<sup>2</sup> Formally, it is considered that eradication occurred in 1952, but single episodes of the disease were observed in 1954 and 1965.

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<sup>3</sup> In some farms, scrapie was simultaneously diagnosed.

1997). For now, it was not reported in other regions around the world.

*Bovine immunodeficiency.* By the end of the 60-s of the 20th century, investigators from many countries have tried to determine the aetiology of leukaemia lymphosarcoma of cattle. During these studies, American researchers (van der Maaten *et al.*, 1972) have discovered in animals affected from this neoplastic disease, a retrovirus that was morphologically similar to MVV. When it was established that the MVV and the agent of bovine immunodeficiency were different viruses, the last one was called BIV (Gonda *et al.*, 1987).

#### DISTRIBUTION

EIA and lentiviral infections of small ruminants are widely distributed. The countries, members of the Office International des Epizooties are regularly reporting on their absence. It should however distinguish the true absence of these infections and the observable absence due to the lack of regular screening of these infections, because they could remain undetectable in affected herds for a long time. Unfortunately, there is no a country around the world that performs diagnostic screening of all herds of animal species, susceptible to lentiviral infections.

*EIA.* In the period 1928–2004, EIA was observed in the following regions of the world (the year in brackets designates the last outbreak of the infection): Australia (2004), Austria (2003), Albania (1983), the Antilles (1985), Argentina (2004), Beliz (2001), Bolivia (2004), Bosnia and Herzegovina (2004), Bulgaria (1962), Brazil (2004), Great Britain (1976), Hungary (1965), Venezuela (2004), Haiti (2004), Guatemala (2004), Germany (2002), Honduras (2004), Hong

Kong (1976), Greece (2003), Denmark (1028), the Dominican Republic (1988), Italy (2004), India (1996), Spain (1983), Cameroon (2004), Kirgizia (1989), Columbia (2004), Costa Rica (2004), Latvia (2002), Lithuania (2002), Macedonia (2004), Mexico (2004), Moldova (1946), Mongolia (2004), Nicaragua (2004), New Zealand (1999), Norway (2004), Panama (2004), Paraguay (2004), Peru (1988), Poland (1960), Belarus (2001), The Republic of Korea (1995), Russia (2004), Romania (2004), Salvador (2004), Saudi Arabia (1998), Serbia (2004), Slovenia (2004), the USA (2004), Thailand (1996), Turkey (2004), Uzbekistan (1996), Ukraine (2003), Uruguay (1995), the Philippines (2004), Finland (1953), France (2001), French Guiana (1999), Croatia (2004), Chile (1988), Sweden (1989), Ecuador (2004), Estonia (1997), Ethiopia (1966), The Republic of South Africa (1995) and Japan (1993).

In Russia, 286 outbreaks of EIA were observed between 1996 and 2004 with a total of 6223 horses affected.

*Maedi-visna.* For the last 45 years, the infection was diagnosed as follows (the year in brackets shows the last registered): Austria (1996), Andorra (2004), Argentina (2004), Belgium (2004), Bulgaria (2001), Brazil (1997), Great Britain (2004), Germany (2004), Greece (2004), Denmark (2004), Israel (1991), India (1996), Iraq (2004), Ireland (1986), Iceland (1965), Spain (2004), Canada (2004), Cyprus (2002), Latvia (2004), Luxemburg (2004), Namibia (1998), The Netherlands (2004), Norway (2004), Poland (1997), Portugal (2004), Romania (2004), Senegal (1997), Slovakia (2004), the USA (2004), Finland (2002), France (2004), The Czech Republic (2003), Chile (2004), Switzerland (2004), Sweden (2004), Estonia (2003), Ethiopia (2002)

and The Republic of South Africa (2004).

The respiratory form of the disease is predominating. Visna is observed considerably more rarely. The sheep from the Iceland (Sigurdsson & Palsson, 1958) and Romanov (Karavaev *et al.*, 1983; Koromislov *et al.*, 1984) breeds are the most susceptible.

The serological methods of diagnostics of the infection showed that the level of infection of flocks affected by MVV could vary within a wide range – from 1 to 90% (Cutlip *et al.*, 1977). According to our observations, the level of infection of 40% in Romanov sheep flocks is critical – higher morbidity rates are a sign for the transition from sporadic cases to mass morbidity. It is beyond any doubt that the distribution of the infection in affected farms depends on the rearing technology of sheep. In many farms of the sheep complex “Mariy El” (where tremendous amounts of sheep were rearing in a stable), the MVV seropositivity level between ewes reached 60% (personal observations). The infection rate of young ewes and lambs was significantly lower, that was indicative for the horizontal distribution of the infection.

*CAE.* Officially, the infection was registered during the last 35 years in 51 regions of the world (year of last outbreak given in brackets): Australia (2004), Algeria (1998), the Antilles (1996), Barbados (2002), Belgium (2004), Bulgaria (2001), Bolivia (1996), Brazil (1996), Great Britain (2004), Hungary (2004), Venezuela (1960), the Virgin Islands (1995), Haiti (1996), Germany (2004), Greece (2002), Denmark (2004), Jamaica (1987), the Dominican Republic (2003), Zimbabwe (1987), Israel (2002), Ireland (2004), Spain (2004), Italy (1996), Canada (2004), Kenya (2003), Columbia (1993), Costa Rica (1998), Latvia (2004), Leba-

non (1994), Liechtenstein (2000), Morocco (2002), Mexico (2004), Mozambique (1998), the Netherlands (2004), New Zealand (2004), New Caledonia (2004), Norway (2004), Panama (2004), Peru (2004), Romania (2004), Singapore (1989), Slovakia (2004), the USA (2004), Taipei (2004), Trinidad & Tobago (1996), Tunisia (2000), France (2004), French Guiana (1999), the Czech Republic (2003), Switzerland (2004), Sweden and Japan (2004).

CEA is especially prevalent among the dairy goat herds in Europe, the USA and Canada.

By the end of the 80-s of the 20th century, we studied sera from Saanen dairy goats in a private farm in Tverskoy district, where an outbreak of mastitis and neurological disease in goat kids was observed. In the reaction of diffuse precipitation performed with non-purified antigen of MVV, about 7% of samples were found positive. There is no information about other serological investigations performed in Russia with regard to this infection.

*Jembrana disease.* This infectious disease in cattle was described only in Indonesia. Due to the illegal export of cattle from the country, the infection was spread to Sumatra, Java and Kalimantan (Soeharsono, 1954). For now, the disease was not registered in other regions of the world.

*Bovine immunodeficiency.* Through serological studies, a wide distribution of BIV was detected all over the world. The infection was observed in Australia, Argentina, Brazil, Great Britain, Germany, Denmark, Zambia, Italy, Canada, Korea, Costa Rica, The Netherlands, Pakistan, the USA, Turkey, France, Japan. In most cases the seropositivity percentage varies between 1.5 and 15%. An exception is the Republic of Korea, where specific anti-

bodies against BIV were observed in 33–35% of meat cattle (Cho *et al.*, 1999). It should be however acknowledged that the performed studies used non-standard diagnostic reagents, various serological tests and tested animals were at a different age, thus impeding the assessment of obtained results.

#### DAMAGES

The literature data on this subject are contradictory. This is not surprising taking into consideration that in field conditions, it is very difficult to determine precisely the cause of reduced productivity, culling and death of animals mainly because of the fact that affected herds are never free of other pathogenic or conditionally pathogenic agents, that are more easily recognized. Depending on the genetic and immune status of herds, the rearing technology and a number of other factors, slow infections could not provoke a special concern or on the contrary could make the further breeding of animals non-profitable. The factors contributing to the intense circulation of retroviruses among animals (prolonged rearing in stables, high concentration of animals etc.) render the lentivirus infections in ungulates economically important. Yet, there are several characteristic features. For instance, the primary importance in Maedi-visna disease has the clinical form of the disease. In most regions of the world, the respiratory form is prevalent that is characterized with lower death rate (and consequently, with longer disease course) compared to the nervous form. An extensive visna morbidity occurred only in Iceland and the Non-Chernozem Zones of Russia, where the death rate reached 20–30% (Karavaev *et al.*, 1983; Ramachandran, 1997). In CAE, young

animals die more frequently (Crawford *et al.*, 1980). In EIA, the lethality is the highest during the first attack of the disease, so the surviving horses die because of this infection considerably rarely. In the Jembrana disease, the death rate could reach 17% (Soesanto *et al.*, 1990). During the first outbreak of this disease, Indonesia lost about 10% of its cattle population (26000 cattle). Subsequently, the disease became endemic for Indonesia that was accompanied by a significant reduction of morbidity and mortality rates (Ramachandran, 1997). BIV is causing lethal oncological disease only in few cases but the immunodeficiency that develops throughout this infection makes the animals more susceptible to other infectious and parasitic agents and bring to the related consequences.

For prevention of the dissemination of lentiviruses, affected cattle and horse herds should be isolated. The possibility of persistence of lentiviruses when infected animals are a source of infection but remain clinically healthy make lentivirus infections particularly dangerous. They could be imperceptibly transmitted from herd to herd, from one region to another, crossing state boundaries too. The history of transmission of the MVV in Iceland was already mentioned. In a similar fashion, this agent was imported in Denmark from Norway, from Scotland to Canada, from England to Hungary, from Holland to France, from Sweden to Finland (Suveges & Szeky, 1973; Dukes *et al.*, 1979). Affected farms lose its breeding status for a long time (and sometimes, until the complete replacement of the population). Animals from such farms should not be traded, used for artificial insemination, collection of embryos, transplants and other biological products. The animal production from this farms is

generally used without restrictions because there is not a background to considered that the agents of lentivirus infections in ungulates have a zoonthropogenic potential. Nevertheless, in the Jembrana disease and lentivirus infections in sheep and goats, a considerable reduction in milk production and the weight gain of animals occurs. The testicular form of Maedi-visna is causing loss of fertility in rams (Palfi *et al.*, 1989).

*To be continued...*

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