The Current World Status of Bluetongue

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Introduction

Bluetongue (BT) is an infectious disease of ruminants caused by viruses of the genus orbivirus. Currently there are 24 known serotypes of bluetongue virus worldwide. These viruses have been recognized on six continents, Africa, North America, South America, Australia, Asia and Europe, and currently five continents (all but Europe) have infection. South Africa has the greatest number of serotypes, followed by Australia and the United States.

BTV is a double stranded RNA virus. There are 10 strands of RNA which code for the 7 structural and 3 non-structural proteins. Gene segments 2 and 5 code for viral proteins 2 and 5. These proteins make up the outer coat and VP2 is responsible for neutralizing antigens. VP3 and 7 are the major proteins that make up the core. The core proteins, particularly VP7, is important for bluetongue group specificity.

The Disease

BT causes infections in ruminants. Sheep, cattle, goats, and wild ruminants have been reported to be infected with BTV. The infection rate varies with species. The limiting factor in distribution rests with the feeding habits of the culicoides vectors. Some species of culicoides favor feeding on cattle rather than sheep. The highest percentage of infection occurs in cattle, followed by sheep, goats, and other domestic ruminants. There is little or no information on culicoides feeding habits on wild ruminants. Morbidity including the expression of disease occurs in 0 to 50% of infected sheep with the mortality ranging from 0% to 30%. Epidemiologic surveys have indicated that infection in sheep with no clinical evidence of disease is more common than previously recognized. The infection rate in cattle ranges from 35% to 100%. Morbidity defined as clinical disease expression is .001% in cattle and mortality rarely occurs. Rarely, an infected herd may have morbidity rates as high as 15% to 20%. Mortality in white-tailed deer and American antelope varies but it can be as high as 60% to 70% in experimental cases.

Congenital infections have been reported in both sheep and cattle. Although there are reports of these infections, it is uncommon. Affected newborn lambs and calves may have hydranencephaly. Embryonic mortalities and abortions have also been reported. In one epidemiologic study of dairy cattle, there was evidence of early embryonic deaths associated with seroconversion to BTV. The estimated loses for California were $5 million.

The pathogenesis of bluetongue disease differs in cattle and sheep. In sheep, the virus has a predilection for endothelial cells resulting in microthromni. These lesions are the basis for focal necrosis along mucous membranes and in striated muscles of the skeletal and cardiac systems. These lesions are associated with cardiac failure and muscle weakness. Hemorrhage at the base of the pulmonary artery is pathognomonic for bluetongue in sheep. In contrast, the expression of clinical disease in cattle has been associated with an immune mediated (IgE) allergic hypersensitivity. This occurs rarely in cattle. In fetal animals infected during the second 1/3 of gestation, the virus has a predilection for undifferentiated cells in the developing brain.

The length of viremias in cattle differs from that in sheep. Viral replication takes place primarily in macrophages in the lymphoid system. Virus can be isolated from buffy coat cells only through 11 to 14 days after infection. After that time, virus is isolated only from red blood cells. Viremias in cattle may last 50–60 days after infection—in contrast, viremias in sheep seldom last longer than 21 days post infection.

BTV can also be shed into the semen of bulls and rams with viremias. This is a transient phenomena associated with vascular lesions in the epididymis. Although there have been two reports of bulls with persistent viremias and immune tolerance, numerous studies have failed to reproduce or confirm these findings. At the National Veterinary Services Laboratory/Animal and Plant Health Inspection Services of USDA, over 15,000 semen straws have been tested and BTV was recovered from two straws. In a study of over 300 semen collections from bulls serologically positive by bluetongue virus group antibodies, virus was not isolated from either blood or semen of these bulls. These studies indicate that shedding of BTV into semen occurs rarely (in 2 of 15,000 semen specimens) in bulls. The conclusions that can be drawn from these observations is that dissemination of BTV through semen of bulls is not a significant factor.

The principal means of transmission of BTV is by insect vectors. The principal vectors are small flies of the *Culicoides* genus. The distribution of BTV is limited by the distribution of these vectors. The major vectors are *C. imicola, C. variipennis, C. insignis, C. brevatarsis, C. wadi,*

and possibly *C. fulvis*. These vectors remain active year around in tropical areas. In temperate regions of the world, the vectors are active only during the summer and fall months. Vector activity and the spread of BTV stops abruptly with the first frost in the fall. These vectors tend to breed in animal waste matter. Each female may take five different blood meals during her life span. The biological vectors and virus multiplies to high titers, making them effective agents for transmitting virus.

Recent evidence suggests that the distribution of the viral serotype may be limited by the genus and species of vector. For instance, *Culicoides insignis* appears to transmit BTV 2, 3, 6 and 12. However, these serotypes are not observed in areas inhabited by *C. variipennis* which readily transmits BTV 10, 11, 13 and 17. There is evidence that BTV-2 is not readily reproduced in *C. variipennis*.

Vertical transmission of BT has been reported. Congenital infections were first reported following administration of a modified live virus vaccine to BTV-10 in 1953. Large numbers of lambs with hydranencephaly and cerebral cysts were observed. There have been sporadic reports of abortion and fetal infections resulting in the birth of lambs with neurological lesions. A few sporadic reports of newborn calves with neurological lesions and associated clinical deficits have been reported.

The report of BTV being shed in semen in the mid 1970s led to considerable concern on the part of countries importing semen. There have been two reports of two different bulls which shed virus in semen. One bull was reported to shed virus sporadically for up to eight years. These bulls were also reported to be immunologically tolerant to BTV. Immune tolerance was not confirmed in this particular bull, nor has it ever been experimentally confirmed. BTV is very rarely shed in semen of bulls or rams. If it occurs, it is only during the time of viremias. In epidemiologic studies of large numbers of animals, it appears that persistent viremias in cattle and sheep are nonexistent or rare. Similar observations have been reported in viremic cows which have been superovulated for embryo transfer. Vigorous washing of embryos has been shown to be very effective in limiting the spread of BTV to susceptible recipients. Germplasm does not appear to be a significant factor in the transmission of BTV.

Fomites, such as needles, are an effective means of transmitting BTV. This is particularly important when animals are viremic and the same needles are used on a number of different animals.

Epidemiology

BTV has worldwide distribution in temperate and tropical areas of the world. The virus is endemic in tropical and subtropical areas where the virus-vector-ruminant hosts appear to maintain the cycle. In the temperate climates, the virus is active only during the vector season. The seasonal activity is most apparent in the summer and fall months when the vectors are most active. Ruminants in countries or areas within countries which do not have vectors remain free of infection.

BTV can be introduced into areas with susceptible vector populations by the transport of viremic animals. These animals will serve as the source of virus for vectors which will in turn spread the infection to animals in the vicinity over the next two to four weeks. There have also been reports that vectors may be carried on cyclonic winds. In these instances the vectors may travel long distances and infect new susceptible animal populations. If the vector is capable of adapting to the new regions, BT could become endemic. In light of the global warning which has been suggested to be taking place, there is concern that the culicoides vectors may become established in new areas.

Epidemiological studies in the United States indicates that multiple serotype infections occur on approximately 30% of all farms from which BTV were isolated. Two and sometimes three different serotypes of infection occurred. In some instances two different serotypes of virus were isolated from the same blood samples from one animal. A genetic analysis of the individual virus isolates indicated that as many as six genotypic variants of the same BTV serotype were recovered from one blood sample. These studies indicate that this is a very heterogenous group of viruses that are continuing to evolve. A major genetic shift has recently been recognized. Gene segment 5 from a strain of BTV-11 designated as UC-8 appears to have been derived from BTV-10. Approximately 15% of BTV-11 field virus isolates have this gene, whereas 80% of the BTV-10 isolates contain this gene. These results indicate that a new subtype of BTV-11 occurs in nature. This virus has greater virulence characteristics than other strains of the BTV-11 virus. The biological significance of these genetic changes remains to be determined.

Import-Export Considerations

One of the major concerns with BTV in a country is the impact that the virus has on international trade. Countries with no evidence of BTV do not want to be put at risk and as a consequence, they place restrictions on importation of ruminants and germplasm from countries with BTV. Exporting countries with BTV need to 1) identify areas free of BT infection within the country, and 2) develop programs/protocols which certify germplasm and/or animals free of BTV infection. Vector monitoring and serological surveys are the two means of identifying areas of countries free of BTV. Serologic tests such as the competitive ELISA and agar gel immunodiffusion test identifies antibodies to BTV group specific antigens. Serological surveys which demonstrated less than 2% positive reactors are considered free of BTV infection by most importing countries. Monitoring for vectors to demonstrate their absence in an area can also be used to demonstrate that vectors capable of transmitting the virus

are not present in designated regions.

It is possible to certify animals and germplasm free of BTV. The two ways which establish animals free of BTV are 1) to collect germplasm from serologically negative animals and 2) by virus isolation. Serological tests may be at the time of collection of germplasm and then 3 weeks later. If the tests remain negative or if there is less than a 4-fold increase in titer, the animals are considered negative for BTV.

Control

Vaccines are available as a means of control for BTV in some countries. Most commercial vaccines are modified live virus vaccines. Experimental inactivated vaccines have been reported, however, these are not currently in use. In South Africa, multiserotype vaccines containing 5 or more serotypes are in use for disease control. A total of 15 to 17 different serotypes are administered in 3 different vaccines. In the United States, the only vaccine sold nationwide is a MLV vaccine for BTV-10. In California, MLV vaccines are available to BTV 10, 11 and 17. These are distributed as individual serotype specific vaccines. The need for the three serotypes was based upon epidemiological studies which indicated that BTV-10 accounted for 10% of the virus isolates, whereas BTV-11 and BTV-17 accounted for 55% and 25% of the isolates respectively. In addition, it is recommended that these 3 vaccines be administered separately and at 2 week intervals before the vector season. This recommendation is based upon research and field data which indicates that BTV's have a tendency to reassort and make genetically new progeny. The separate administration of the vaccines at 2 week intervals greatly reduces the chance for new types of viruses to arise. These vaccines are recommended only for sheep at this time. There has not been a demonstrated benefit for vaccinating cattle. In fact, the use of inactivated vaccines in cattle resulted in clinical expression of disease when the cattle were exposed to live virus. Recently a successful genetically engineered vaccine has been reported for use in sheep. This vaccine utilized subunit viral proteins which precluded problems that are associated with modified live virus vaccines. This product was used only in sheep.

References

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