Bluetongue

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Bluetongue

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Summary

Bluetongue (BT) is an arthropod-transmitted viral disease of non-African ungulates, principally sheep. The disease results from vascular injury analogous to that of human haemorrhagic viral fevers, with characteristic tissue infarction, haemorrhage, vascular leakage, oedema, and hypovolaemic shock. Importantly, BT is not zoonotic. Bluetongue virus (BTV) infection of ruminants and vector *Culicoides* midges is endemic throughout many tropical and temperate regions of the world; however, within this global range the virus exists within relatively discrete ecosystems (syn. episystems) where specific constellations of BTV serotypes are spread by different species of biting *Culicoides* midges. Recently discovered goat-associated BTVs, notably BTV serotype 25 (BTV-25) in central Europe, appear to have distinctive biological properties and an epidemiology that is not reliant on *Culicoides* midges as vectors for virus transmission. Bluetongue virus infection of ruminants is often subclinical, but outbreaks of severe disease occur regularly at the upper and lower limits of the virus's global range, where infection is distinctly seasonal. There have been recent regional alterations in the global distribution of BTV infection, particularly in Europe. It is proposed that climate change is responsible for these events through its impact on vector midges. However, the role of anthropogenic factors in mediating emergence of BTV into new areas remains poorly defined; for example, it is not clear to what extent anthropogenic factors were responsible for the recent translocation to northern and eastern Europe of live attenuated vaccine viruses and an especially virulent strain of BTV-8 with distinctive properties. Without thorough characterisation of all environmental and anthropogenic drivers of the recent emergence of BT in northern Europe and elsewhere, it is difficult to predict what the future holds in terms of global emergence of BTV infection. Accurate and convenient laboratory tests are available for the sensitive and specific serological and virological diagnosis of BTV infection and confirmation of BT in animals. Prevention and control strategies for BT are largely reactive in nature, and typically are reliant on vaccination of susceptible livestock and restrictions on animal trade and movement.

Keywords

Bluetongue – Bluetongue virus – Climate change – *Culicoides* midges – Haemorrhagic fever.

Introduction

Bluetongue (BT) is an insect-transmitted, viral haemorrhagic fever of non-African ungulates (1, 2). Descriptions of BT in sheep were first published in South Africa in 1876, although the disease likely had occurred there since the late 18th Century, when European sheep were first introduced and intensive farming of sheep was undertaken in the region (3, 4). Spreull published a remarkable description of BT and its epidemiology in 1905, along with the first BT vaccination strategy (5). Theiler confirmed that the causative agent of BT was a virus (bluetongue virus [BTV]) in 1905, and he then developed a sheep-adapted vaccine that was used extensively in South Africa from approximately 1906 to 1943 (3, 4). Early research in South Africa also confirmed that BT was an insect-transmitted disease, with haematophagous *Culicoides* midges being the essential vector (5, 6, 7).

Bluetongue was considered initially to be exclusively an African disease, although outbreaks were described among sheep on Cyprus from 1924, and anecdotal reports suggest that outbreaks may have occurred even earlier than that (3, 8). Bluetongue was first recognised beyond Africa and the Mediterranean Basin in approximately 1950, when the disease was confirmed in sheep in the United States (9). The subsequent identification of BTV and/or BT in much of Asia, including the Indian subcontinent, the Middle East, southern Europe, Australia, Central and South America, and the Caribbean Basin, led to the dogma of the mid-20th Century, which said that BT was an emerging disease that had recently spread beyond Africa as a result of the movement and trade of ruminant livestock (10, 11, 12). As a consequence, BT was included in the former World Organisation for Animal Health (OIE) List A of high-consequence 'transboundary' diseases. However, information presented at OIE-sponsored international symposia in 1984 (Asilomar, California) and 1991 (Paris, France), and in other venues, confirmed infection of livestock with divergent BTV serotypes and strains throughout many temperate and tropical regions of the world, often in the absence of obvious BT disease (10, 13, 14, 15). Indeed, in several countries, BT was first recognised as a disease problem only after susceptible livestock were introduced into an area already endemic for the virus (12, 16).

Ongoing research, coupled with the occurrence of natural events such as recent epidemics in Europe, has profoundly changed scientific opinion and international attitudes towards BT. Notably, the chapters of the OIE *Terrestrial Animal Health Code* pertaining to BT (17) were substantially revised and rationalised following the incursion of BTV into Europe and after the 3rd OIE BT Symposium, which was held in Taormina, Sicily, in 2003 (18). Since that symposium, however, the ongoing emergence of BT and/or BTV infection in multiple areas of the world has raised significant questions regarding both anthropogenic and environmental influences on the global distribution of BTV. There is particular concern for what the future might hold for ruminant livestock production given the impact of climate change on the vectorial capacity of the populations of vector *Culicoides* midges that reside in different regions of the world (19, 20, 21, 22, 23, 24, 25).

Aetiological agent

Bluetongue virus is the prototype virus in the genus *Orbivirus,* family *Reoviridae*. Other closely related viruses in the genus *Orbivirus* include the viruses responsible for epizootic haemorrhagic disease of deer, African horse sickness, and equine encephalosis. The genome of BTV consists of ten distinct segments of double-stranded RNA, and each gene segment encodes at least one protein (26). The unenveloped and icosahedral BTV virion includes seven proteins (VP 1–7), and at least five additional non-structural (NS 1, 2, 3/3A, 4) proteins are produced in virus-infected cells (26, 27). The structural protein VP7 expresses group antigens common to all BTV strains and serotypes, whereas segregation of BTV into serotypes is largely determined by the VP2 outer capsid protein (28, 29, 30).

The occurrence of multiple antigenically distinct serotypes of BTV was first established by Neitz after it became apparent that Theiler's original vaccine did not uniformly protect sheep against BT (31). There are currently 26, likely 27, serotypes of BTV (30, 32, 33). The global distribution of these serotypes is not uniform, rather, different constellations of BTV serotypes are disseminated by different species of *Culicoides* vector in relatively distinct global ecosystems (11, 14, 34, 35). Bluetongue virus serotypes 25 to 27 have been identified only recently as infections of small ruminants in Europe and the Middle East, and serotype 25 (BTV-25; also known as Toggenburg orbivirus) has yet to be isolated, although it has been sequenced (32, 33, 36). The epidemiological features of infection with BTV serotypes 1 to 24 are similar, in that they are all spread predominantly by biting *Culicoides* midges, but there is uncertainty regarding the exclusive role of *Culicoides* midges in the transmission of BTV-25 and BTV-26 (37, 38). Duration of viraemia in BTV-25-infected goats is also markedly more prolonged than that in livestock infected with other BTV serotypes (1, 2, 17, 38, 39).

Bluetongue virus infects its insect and mammalian hosts in alternating cycles, which gives the virus the opportunity to genetically diversify (40, 41, 42). Thus, there is marked genetic variation among field strains of BTV in historically endemic regions, even among viruses of the same serotype from the same region (43, 44, 45, 46, 47, 48). The genetic diversity and heterogeneity of field strains of BTV arise as a consequence of both genetic shift and drift (40, 42). Specifically, genetic

shift occurs by reassortment of individual viral gene segments during infections of cells with more than one virus serotype or strain (49, 50) or by intragenic recombination (42). In contrast, individual genes evolve by genetic drift as a consequence of quasispecies (a swarm of genetic viral variants all related to a common consensus sequence) evolution and founder effect during alternating cycles of virus replication in insect and mammalian hosts (51). Importantly, however, there is currently some uncertainty about the genetic basis of virulence and other important biological characteristics of individual BTV strains, e.g. the potential role of quasispecies (population) diversity in determining these characteristics is not yet known (1, 41, 42).

Epidemiology and modes of transmission

Bluetongue virus infection occurs throughout tropical and temperate regions of the world, coincident with the distribution of competent vector *Culicoides* midges (10, 11, 14, 19, 52). The global distribution of BTV is limited to a band between approximately 50°N and 35°S; however, *Culicoides* midges, including known BTV-vector competent species, occur beyond this global range (52, 53). Thus, climate and other environmental factors potentially limit the global distribution of BTV, even in the presence of appropriate vectors. The global range of BTV has expanded recently, especially in the Northern Hemisphere (10, 20, 22, 24, 54, 55, 56, 57).

Bluetongue virus infection of wild and domestic ungulates occurs in distinct global ecosystems (syn. episystems) in which different species of *Culicoides* midges transmit different constellations of BTV serotypes (11, 14, 16, 34, 35). Each incursion of BTV into a new region represents a 'founder event' and negative (purifying) selection of certain BTV genes (those encoding the VP3 and NS3/3A proteins in particular) leads to the emergence of geographically specific 'genetic BTV topotypes' over time (43, 47, 48, 58). The presence of multiple serotypes and strains of BTV in an area appears important for regional persistence of the virus over many years, such that there is no clear example of eradication of BTV from a historically 'long-term' endemic region (10). Specifically, BTV persists long term only in regions of the world where more than one virus serotype circulates. Incursions of single BTV serotypes into the Iberian Peninsula, the Okanagan Valley of Canada, Greece (repeatedly), northern Europe and portions of the British Isles and Scandinavia, among other examples, were transient and the invading virus soon disappeared with or without vaccination of livestock. In contrast, BTV has persisted in other recently invaded areas, such as in much of Italy since 1999, where multiple serotypes now circulate despite intensive vaccination of livestock (46, 59). The mechanism determining this phenomenon remains poorly understood, however, it is clear that whereas incursions of BTV into a previously free region involve a genetically distinct virus strain, the strains of BTV that circulate in endemic regions become genetically heterogeneous over time.

With the possible exception of BTV-25 and BTV-26, the usual route of BTV transmission to its animal (ruminant) hosts is via the bites of virus-infected haematophagous *Culicoides* midges that serve as biological vectors of the virus (7, 14, 19, 52). *Culicoides* midges only become infectious after an incubation period of approximately ten days (depending on ambient temperature) after taking a BTV-infected blood meal from an animal host, which is required for the virus to disseminate from the gut to the salivary glands of the vector (60, 61). Once infected with BTV, female midges remain persistently infected for the remainder of their lives. Other important aspects of the role of vector midges in the natural epidemiology and spread of BTV include:

– Long-distance spread of BTV from endemic regions to adjacent uninfected areas can occur via the windborne dissemination of virus-infected midges, especially over water (62, 63, 64). Thus, novel strains of BTV are regularly introduced by windborne midges from Indonesia to the 'Top End' of Australia, and into Mediterranean Europe from North Africa (46, 59, 65). Similarly, recent incursions of novel serotypes of BTV into the south-eastern United States are perhaps the result of spread by windborne midges carrying viruses that circulate in the Caribbean Basin (10, 20, 55).

– Whereas BTV infection can occur year-round in tropical areas, it is distinctly seasonal in temperate zones, where it occurs during the later summer and autumn (approximately July through November in the Northern Hemisphere). Vector midges appear to be central to the interseasonal maintenance of BTV in temperate regions, so-called virus 'over-wintering' (7, 66). Recent studies in California have confirmed the presence in mid-winter of BTV-infected parous female *Culicoides* midges without concurrent infection of adjacent sentinel cattle, suggesting that long-lived vectors infected in the prior seasonal period of transmission might sustain BTV throughout the over-wintering period in seasonally endemic areas (67).

Vector-independent transmission of BTV clearly can occur, although its significance is largely unknown. The epidemiology of BTV-25 infection of goats in Europe appears to be different than that of the other serotypes (BTV 1 to 24) and may not involve *Culicoides* midges (38). Recent studies also suggest direct contact transmission of BTV-26, likely by aerosol, between livestock (37). Oral BTV infection of both ruminant livestock and wild and zoo carnivores has been described, including infection of calves via the feeding

of infective colostrum (68, 69, 70, 71). Contamination of biological products, notably those that utilise fetal bovine serum, is also well described, for example, contaminated canine vaccines (72). Lastly, vertical transmission of BTV in animals certainly does occur, notably with live attenuated vaccine strains of BTV and European BTV-8, but this route is considered unlikely to be important to the epidemiology of natural BTV infections (1, 2, 73, 74).

The movement of BTV-infected animals can be responsible for translocation of BTV, however, such occurrences are only important if the local vector population within the receiving region is able to efficiently acquire and transmit the introduced virus. For example, a novel strain of BTV-2 that recently appeared in California is closely related to viruses from Florida, suggesting this virus was translocated across the continental United States by animal movement and then spread by vectors in California (75). In a related but different context, the role of live attenuated vaccines in the spread of BTV, whether by vectors or other routes, awaits thorough characterisation (43). For example, the recent appearance of at least three (BTV-6, BTV-11, BTV-14) different South African live attenuated BTV vaccine strains among livestock in Europe (most recently BTV-14 in western Russia, Poland and Lithuania) suggests a direct human role in mediating the introduction of these viruses, rather than animal movement (76, 77). Interestingly, live attenuated vaccine strains of BTV-6 and BTV-11 first appeared in the same general region of northern Europe as did BTV-8 in 2006 (54), again suggesting an as-yet unexplained anthropogenic phenomenon. Without question, climate change alone cannot explain the recent introduction of multiple serotypes of BTV into northern and eastern Europe, however, environmental factors were clearly conducive to spread of these viruses by resident vectors after their introduction. Similarly, in India, strains of BTV that are genetically similar or identical to live attenuated vaccine viruses used elsewhere in the world have also been identified as infecting local livestock, raising further concerns regarding the unauthorised international movement of vaccine viruses (78).

In summary, the emergence of BTV from historically endemic to previously unaffected regions, or between different episystems, reflects the complex interplay of environmental and anthropogenic drivers/factors, critical aspects of which remain poorly defined.

Clinical signs

Bluetongue is a systemic haemorrhagic viral fever that results from vascular injury that affects multiple organs and tissues, notably the upper gastrointestinal tract, skin, and lungs (1, 2). Injury to small vessels is likely a consequence of both direct virus-mediated endothelial injury as well as the effects of vasoactive and proinflammatory mediators produced by a variety of host cells in response to the infection (1, 79). Sheep are the animals most commonly affected, particularly European fine-wool breeds such as the Merino and crosses thereof. Bluetongue also occurs in cattle, goats and South American camelids, but less commonly than in sheep and only after infection with especially virulent virus strains (2).

In susceptible sheep, the first clinical signs of BT appear after an incubation period of about a week or sometimes longer (2, 3, 5). These signs include fever; oedema of the face, lips, muzzle, and ears; excessive salivation; hyperaemia of the oral mucosa; and profuse serous nasal discharge that becomes mucopurulent after a few days, leaving crusts around the nostrils and muzzle. Infrequently, cyanosis of the tongue and oral mucous membranes imparts a purple/dirty blue discoloration. Severely affected sheep develop focal haemorrhages and ulcers in the oral cavity that are especially prominent on the dental pad. The oral lesions can be sufficiently painful that animals will not eat, and severely affected sheep will stand over water without drinking. Lameness and stiffness caused by coronitis and myopathy can be severe, and the coronary band characteristically shows haemorrhages and hyperaemia. Haemorrhages also may be evident in the subcutis of non-haired skin such as the inguinal region, and breaks in the wool are common. Diarrhoea, with or without blood, can occur. Many sheep become depressed, are unable to rise, and die, but some severely affected sheep make a full recovery. Pulmonary oedema is often marked, especially in fatal cases. Acute secondary bacterial bronchopneumonia may be present in addition to the characteristic pulmonary oedema of BT. Cardiac necrosis may result in sudden death at any time, even in an animal that appears to be recovering. Clinical disease is uncommon among cattle infected with most virus strains, particularly in BTV-endemic areas. However, as evidenced emphatically by the recent BTV-8 epidemic in northern Europe, disease certainly can occur in BTV-infected cattle and affected cattle can exhibit many of the same signs and lesions as those that occur in sheep (80, 81, 82).

The reproductive and teratogenic brain defects (cavitating encephalopathy leading to hydranencephaly or porencephaly) that result from BTV infection of pregnant sheep and cattle vary depending on the virus strain, the gestational stage at infection, and other factors (1). Reproductive effects, including abortions, stillbirths, and weak but live 'dummy lamb' births, were recognised after live attenuated vaccine was administered to pregnant ewes in California in the 1950s. Teratogenic brain defects have not been commonly linked to BTV infection in South Africa despite the widespread use of polyvalent live attenuated vaccines in sheep. However, fetal infections were clearly documented in livestock after these same vaccines were introduced into Europe recently, and it was also established that these vaccine viruses also circulated naturally (and

reassorted genes with other viruses) after they were used in Italy (83, 84, 85, 86). Abortion and teratogenic defects have been associated with live attenuated vaccine viruses, but were historically uncommonly associated with natural BTV infection of livestock in endemic areas (1, 2). However, the strain of BTV serotype 8 (BTV-8) that was responsible for the recent epidemic in northern Europe crossed the placenta in a substantial proportion of pregnant ruminants, including cattle, resulting in a large number of abortions and fetal malformations (73, 74, 80, 81, 82, 87). This latter observation raises questions as to the natural history of BTV-8 prior to its emergence in Europe, specifically whether or not it had previously been passaged in embryonated eggs or cell culture, or was a reassortant that contained genes of a laboratory-adapted virus (88).

Ocular lesions sometimes occur in BTV-infected ruminants. The syndrome was well characterised during the BTV-8 epidemic in northern Europe when calves infected transplacentally in late gestation developed transient corneal opacity (blue-eye) following ingestion of colostrum that contained BTV-8-specific antibody (89). Non-African ungulates, such as European bison at the Berlin Zoo, also developed this same ocular lesion following BTV-8 infection (82). These lesions potentially result from deposition of complexes of viral antigen and specific antibody in the eye, leading to immune complex-mediated uveitis.

Intimate association of BTV with circulating erythrocytes can produce a prolonged (<60 days), but not persistent, infection of livestock (1, 17, 39, 90, 91, 92); however, BTV-25 infection of goats is clearly an exception to this general property, because viraemia in BTV-25-infected goats can persist for several years and is potentially lifelong (38). If it occurs, the phenomenon of immune tolerance to BTV (*in utero* infection producing antibody-negative, virus-positive ruminants) is now regarded as unimportant to the natural epidemiology of BTV infection, although controversy persists, specifically with European BTV-8 and perhaps BTV-25 (1, 38, 93). It should be stressed that fetuses infected with BTV in early gestation are typically aborted or born with teratogenic brain defects (hydranencephaly), and they have high titres of BTV-specific serum antibody. In contrast, fetuses infected in late gestation are born viraemic and, potentially, before they have had the time necessary to develop an immune response; the fact that these animals are born viraemic (virus positive) and antibody negative should not erroneously be interpreted to mean that they are immunologically tolerant (1, 88).

Diagnosis

Serological diagnosis of previous BTV infection of livestock is now usually done by competitive enzyme-linked immunosorbent assay (cELISA) that detects antibodies to the BTV VP7 core protein (94). When properly validated, the test is highly sensitive and specific, and detects antibodies to most, if not all, serotypes and strains of BTV. Antibodies detected by cELISA persist for long periods following BTV infection of animals, although cELISA does not distinguish animals that were naturally infected with BTV from those that were immunised with current commercial BTV vaccines (DIVA: Differentiating Infected from Vaccinated Animals). It is to be stressed that the detection of BTV-specific antibody by cELISA indicates only prior exposure to BTV and implies nothing about disease causality or when that infection occurred. Serotype-specific antibody is assessed using virus-serum neutralisation assay in cell cultures, a procedure that takes several days and requires specialised laboratory facilities to complete.

Identification of BTV infection in animals is most readily accomplished using a group-specific quantitative reverse-transcription polymerase chain reaction (RT-qPCR) assay. Such assays are now routinely available in many diagnostic laboratories, and at least one of these assays (based on detection of the S10 gene that encodes NS3 [36, 38]) has, to date, consistently identified all field strains of BTV, regardless of serotype and region of origin (genetic topotype). A distinct advantage of RT-qPCR over conventional PCR assays is that the amount of viral nucleic acid in a sample can be quantitated, which can be useful in ascribing disease causality; specifically, acutely affected animals generally have large amounts of BTV nucleic acid in their blood and tissues, which is reflected by low cycle threshold (Ct) values on the RT-qPCR assay. Critically, ruminants remain positive for BTV nucleic acid by PCR assay for up to six months or longer following infection, meaning that the mere detection of viral nucleic acid by RT-qPCR is not proof of disease causality nor the presence of infectious virus (1, 17, 90, 91). Serotype-specific PCR assays can be used to serotype the virus present in samples that are positive by group-specific assay (30, 95). The availability of these assays has largely obviated the need for virus isolation, which is complex, laborious, expensive, and typically takes several weeks to perform. Hence, virus isolation requires specialised laboratory facilities. Furthermore, some virus strains require initial propagation in embryonated chicken eggs before they will grow in cell culture systems.

Control measures

Control of BT is attempted using either preventive (prophylactic) or therapeutic strategies (2, 23, 96, 97). Treatment of BT-affected ruminants is often unrewarding and logistically challenging during outbreaks as it involves only nonspecific supportive and nursing care. Prevention of BT and/or BTV infection of ungulates can be achieved either

by protecting animals from insect attack or prophylactic immunisation (vaccination). Elimination of *Culicoides* midges from the environment is not practical generally, particularly in extensive pastoral settings. However, housing sheep in protected buildings during the peak of activity (dusk, early evening) to minimise exposure to biting midges can be beneficial for vector species that exhibit strictly outdoor (exophagy) feeding behaviour, but less so with those species that exhibit indoor (endophagy) feeding behaviour. Especially valuable animals can be housed in fully insect-protected enclosures to prevent any contact with vector midges during outbreaks, or treated with repellents to minimise the likelihood of vector attack.

Vaccination is central to prevention of BT in many endemic areas, and also to the response to incursions of the disease into previously unaffected regions (2, 86, 98, 99). Both inactivated and live attenuated (modified live) BTV vaccines are available in some parts of the world, and logically these should be based on the local virus strains and serotypes. Although more costly and less immunogenic, inactivated vaccines are inherently safer than live attenuated ones, because the latter have the potential for transmission in nature, reversion to virulence, and the capacity to cross the placenta. There is little cross-protection between BTV serotypes, so to achieve comprehensive protection, animals should be vaccinated against all BTV serotypes that circulate in a given region. Extensive use of inactivated vaccine in livestock preceded the disappearance of BTV-8 from much of Europe (97). Live attenuated vaccines should be administered prior to breeding to avoid fetal infections (and subsequent fetal losses and teratogenic defects). Vaccination should also be carried out prior to the seasonal period of virus transmission (late summer and autumn in temperate zones) to prevent infection of vectors with the virus strains contained in the vaccine, thus minimising the likelihood of recombination of vaccine and field viruses. New-generation BTV vaccines have been developed, including vectored recombinant vaccines. In addition to being very safe, these next-generation vaccines also have the potential for DIVA (98, 100).

Conclusions

Viruses included in the BTV serogroup are genetically diverse, even within individual serotypes. These viruses are usually transmitted by *Culicoides* midges; however, there is considerable diversity in the epidemiological features of virus transmission within each (geographically restricted) global episystem. New epidemiological patterns of transmission continue to be recognised, most recently for BTV-25 and BTV-26 in goats, although critical aspects of these are yet to be characterised. The determinants of the highly variable patterns of BTV virulence to livestock are also yet to be ascertained. Specifically, although virulent viruses can elicit disease syndromes with characteristics of haemorrhagic fevers, apparently identical viruses of the same serotype can vary greatly in their virulence to livestock and there are currently no well-characterised molecular markers that allow their differentiation. Some host factors, such as animal species, and virus factors, such as whether the virus has been passaged *in vitro*, are recognised as important to virulence and other biological properties of individual strains of BTV. Protective immunity to BTV infection is serotype-specific and so vaccination can be problematic in geographical areas where multiple serotypes of BTV occur. A major complication is that some live attenuated BTV vaccines may cause more disease than many wild-type viruses. Although BT is not a zoonosis, infections of carnivores are well recognised, which raises concern of potential 'species-jumping' of BTV (23). Better characterisation of the environmental and anthropogenic drivers of emergence of BTV infections is clearly a prerequisite for predicting future occurrence and distribution of the disease, and to its control.

Fièvre catarrhale ovine

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Résumé

La fièvre catarrhale ovine (FCO), maladie virale transmise par des arthropodes, affecte les ovins et d'autres espèces d'ongulés non africains. Les lésions vasculaires associées à la maladie sont analogues à celles observées chez l'homme lors de fièvres hémorragiques virales, avec un infarctus caractéristique, une hémorragie, une fuite vasculaire, un œdème et un choc hypovolémique. Fait important, la FCO n'est pas une zoonose. L'infection des ruminants et du vecteur (le moucheron piqueur du genre *Culicoides*) par le virus de la fièvre catarrhale ovine est endémique dans nombre de régions tropicales et tempérées du monde entier ; néanmoins, à l'intérieur de cette distribution mondiale, le virus est présent dans des écosystèmes relativement discrets (synonyme : épisystèmes) au sein desquels certaines espèces de moucherons piqueurs assurent la propagation de constellations spécifiques de sérotypes viraux. Certains virus de la FCO rapportés récemment chez les caprins, en particulier le sérotype 25 du virus (BTV-25) en Europe centrale, sont apparemment dotés de propriétés biologiques spécifiques. Leur épidémiologie ne semble pas dépendre des *Culicoides* en tant que vecteurs assurant la transmission virale. L'infection des ruminants par le virus de la FCO se manifeste souvent sous forme infra-clinique, mais des foyers de maladie clinique grave surviennent à intervalles réguliers aux franges septentrionale et méridionale de la distribution mondiale du virus, où l'infection est clairement saisonnière. Récemment, une évolution de la distribution mondiale de l'infection par le virus de la FCO a été constatée au niveau régional, en particulier en Europe. Ce phénomène s'explique probablement par le changement climatique et par son impact sur les espèces vectrices de moucherons piqueurs. Néanmoins, le rôle des facteurs anthropiques dans l'émergence du virus de la FCO dans de nouvelles zones est encore mal compris ; par exemple, on ne sait pas encore très bien jusqu'à quel point ces facteurs ont été responsables du déplacement vers le nord et l'est de l'Europe de souches vaccinales à virus vivant atténué et d'une souche du BTV-8 particulièrement virulente et dotée de caractéristiques singulières. À défaut d'une définition complète de l'ensemble des facteurs environnementaux et anthropiques à l'origine de la récente émergence de la FCO dans le nord de l'Europe et ailleurs, il sera difficile de prédire ce que le futur nous réserve en termes d'émergence de l'infection par le virus de la FCO au niveau mondial. Des tests fiables et pratiques sont disponibles pour le diagnostic sérologique et virologique au laboratoire, permettant d'établir un diagnostic sensible et spécifique de l'infection par le virus de la FCO et de confirmer la présence de la maladie chez les animaux. Les stratégies de contrôle et de prévention de la FCO sont par essence largement fondées sur la réactivité aux foyers et reposent généralement sur la vaccination des espèces sensibles d'animaux d'élevage ainsi que sur les restrictions imposées aux échanges et aux déplacements d'animaux.

Mots-clés

Changement climatique – Fièvre catarrhale ovine – Fièvre hémorragique – Moucheron piqueur *Culicoides* – Virus de la fièvre catarrhale ovine.

Lengua azul

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Resumen

La lengua azul es una enfermedad vírica transmitida por artrópodos que afecta a ungulados no africanos, principalmente a la oveja, y da lugar a lesiones vasculares análogas a las causadas por las fiebres hemorrágicas humanas de origen vírico, con manifestaciones características como tejidos infartados, hemorragias, extravasación capilar, edema y choque hipovolémico. Es importante destacar que no se trata de una enfermedad zoonótica. La infección por el virus de la lengua azul de rumiantes y de los jejenes *Culicoides* que constituyen su vector es endémica en numerosas regiones tropicales y templadas del mundo, aunque dentro de este área de distribución mundial el virus está presente en ecosistemas relativamente discretos (sin. episistemas), en los que diferentes especies del género *Culicoides* propagan constelaciones específicas de serotipos víricos. Últimamente se han descubierto ciertos virus de la lengua azul asociados a la cabra, especialmente el serotipo 25 en Europa Central, que parecen revestir propiedades biológicas características y presentar una epidemiología en la cual la transmisión del virus no depende de la presencia de vectores *Culicoides*. La infección de rumiantes por el virus de la lengua azul no suele acompañarse de manifestaciones clínicas, aunque regularmente se producen brotes de casos graves en los límites superior e inferior de la distribución mundial del virus, en los cuales la infección es claramente estacional. Últimamente, la distribución mundial de la infección ha experimentado cambios en ciertas regiones, sobre todo en Europa. Los autores postulan que esos cambios responden a la influencia del cambio climático sobre los jejenes que actúan como vector. Pero se sabe poco sobre la intervención de factores de carácter antrópico como mediadores de la aparición del virus en nuevas zonas. No está claro, por ejemplo, en qué medida se debe a factores antropogénicos el reciente desplazamiento al norte y el este de Europa de virus vacunales atenuados y de una cepa del serotipo 8 especialmente virulenta y dotada de propiedades características. A falta de una caracterización completa de todos los factores ambientales y antrópicos que subyacen a la reciente aparición del virus de la lengua azul en el norte de Europa y otras zonas resulta difícil predecir cómo y dónde se manifestará en el futuro a escala mundial la infección por este virus. Existen pruebas de laboratorio exactas y adecuadas para diagnosticar serológica y virológicamente, con sensibilidad y especificidad, la infección por el virus de la lengua azul confirmar su presencia en animales. Las estrategias de prevención y control son básicamente de tipo reactivo, y en general se basan en la vacunación del ganado sensible y la imposición de restricciones al comercio y el traslado de animales.

Palabras clave

Cambio climático – Fiebre hemorrágica – Jejenes *Culicoides* – Lengua azul – Virus de la lengua azul.

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