

The changing global face of Bluetongue: from the beginning

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Bluetongue virus,
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Global ecology.

Summary

Bluetongue (BT) was first recognized and described in Southern Africa, and only later elsewhere. It is now known that the causative agent of BT [BT virus (BTV)] occurs throughout temperate and tropical regions of the world. Previous OIE symposia in 1984, 1991 and 2003 clarified the global distribution of BTV and its epidemiology, pathogenesis, and diagnosis. Since the 3rd symposium in 2003, however, there have been significant developments. Notably, BT has emerged in Northern Europe and novel BTV serotypes have appeared in other endemic areas raising substantial questions regarding the environmental and anthropogenic drivers of emergence of BTV, including the invasion and spread of laboratory propagated viruses. Additional BTV serotypes with novel properties have recently been identified in Europe and the Middle East. Recent studies also confirm the importance of the *Culicoides* vector as the essential overwintering reservoir of BTV in temperate regions such as California and not ruminant livestock, proving wrong the prevailing thesis circulated prior to the 1st symposium in 1984. The challenge for participants of this 4th symposium is to predict collectively what the future might hold in terms of emergence of BTV globally, and what strategies are likely to be most feasible, justified, and effective for its control.

Evoluzione della Bluetongue: storia dalle origini

Parole chiave

Virus della Bluetongue,
Culicoides,
Ecologia.

Riassunto

La presenza della Bluetongue (BT) è stata registrata per la prima volta in Africa meridionale. È ormai accertato che l'agente eziologico (BTV) si è diffuso nelle regioni dal clima temperato e tropicale. I convegni organizzati dall'OIE (1984, 1991 e 2003) hanno permesso di accertare oltre alla distribuzione globale del virus anche l'epidemiologia, la patogenesi e la diagnosi della malattia. Dall'incontro OIE del 2003 ad oggi sono stati registrati sviluppi importanti: la BT è stata riscontrata in Europa settentrionale e nuovi sierotipi sono emersi in diverse regioni europee e medio orientali. La diffusione del virus ha portato alla luce nuovi interrogativi riguardanti i fattori ambientali e antropici, compresa la circolazione di virus adattati in laboratorio. Studi recenti hanno confermato l'importanza dei *Culicoides*, e non dei ruminanti, come principali artefici della sopravvivenza del virus durante il periodo invernale nelle regioni temperate, permettendo così di rivedere la tesi dominante durante il primo convegno OIE nel 1984. L'articolo si conclude evidenziando che la sfida per gli esperti che hanno partecipato al convegno OIE è quella di collaborare per poter approfondire la conoscenza dell'evoluzione del BTV su scala mondiale e per definire le strategie più realistiche, giustificate ed efficaci per il controllo del virus.

Historical perspective, including prior OIE symposia

Bluetongue (BT) is an historic disease of Africa that was recognized soon after European sheep were introduced to the region (MacLachlan 2011, Verwoerd 2012). Hutcheon, Spreull, Theiler, and later DuToit, Neitz and Neville, did especially pioneering work in defining the epidemiology and cause of the disease. Theiler identified the causative agent as a virus – BT virus (BTV) – soon after the turn of the 20th century and, because of its highly seasonal occurrence, early investigators also concluded that the disease was most likely to be transmitted by an insect vector, *i.e.* an arboviral disease, the specific vector (*Culicoides* biting midges) later being confirmed by DuToit. Although outbreaks were described among sheep on Cyprus during the early 20th century, BT was considered to be an African disease until it was recognized in the US in the late 1940s.

Subsequent to the identification of BT in the US, the disease or its causative agent (BTV) were recognized in other regions of the world, including Asia, Southern Europe, elsewhere in the Americas, and Australia. This led to the dogma of the 1960s and thereafter that the disease was ‘emerging’ globally, a concern further fuelled by reports of persistently infected and immunotolerant cattle, which could ‘silently’ spread the virus and maintain it between seasonal periods of transmission (so-called virus overwintering). Thus, BT was included in the World Organization for Animal Health (OIE) List A of those pathogens “that have the potential for very serious and rapid spread, irrespective of national borders, that are of serious socio-economic or public health consequence and that are of major importance in the international trade of animals and animal products”, which in turn lead to BTV-free countries imposing non-tariff barriers to import of livestock and germplasm from BTV-endemic countries (MacLachlan and Osburn 2006).

The First International Symposium on Bluetongue and Related Orbiviruses was held in Asilomar, California, January 16-20, 1984. The symposium was organized by Bennie I. Osburn in an effort to gather concerned scientists and regulators from the global community to rationally address relevant issues pertaining to pathology, immunology, virology, epidemiology, and entomology (Barber *et al.* 1985). Osburn also was the catalyst behind the Second International Symposium on Bluetongue, African Horse Sickness and Related Orbiviruses that was held at the OIE in Paris from June 17-21, 1991. This symposium built on the theme of the first and working teams of international experts again analysed and addressed critical aspects of BT and BTV infection including their international impacts

(Walton and Osburn 1992). The Third Symposium was promoted by Vincenzo Caporale and held from October 26-29, 2003 in Taormina, Sicily, following the introduction and unprecedented spread of BTV in Southern Europe (MacLachlan and Pearson 2004). The legacy of these symposia is an increased understanding of BT, the global epidemiology of BTV infection and its insect vector, viral diagnostics and prevention, all of which provide the transparent and science-based criteria for rules-based international trade as mandated by the World Trade Organization through the OIE Terrestrial Animal Code.

Developments since the 3rd symposium

The recent appearance of BTV serotype 8 in Northern Europe was highly disconcerting for multiple reasons, including:

1. the unusual virulence of this strain of BTV for all ruminant livestock and a wide variety of non-African ungulate species, along with other distinctive properties that distinguish it from the field strains of BTV that typically circulate elsewhere in the world *e.g.* its propensity to cross the ruminant placenta to cause fetal infections;
2. the virus was efficiently spread by species of *Culicoides* midges that previously had not been viewed as likely vectors of BTV. Some of these new vector species have been clearly shown to exhibit unexpected behaviours, including their capacity to live and reproduce indoors (endophily);
3. the virus appeared first in Northern Europe, without spreading from Southern Europe, where multiple other BTV serotypes were actively circulating at the time. Importantly, strains of BTV serotype 6, 11, and 14 also have appeared recently in Northern and Eastern Europe and these viruses are all apparently live-attenuated vaccine viruses, raising significant concerns regarding the role of as yet unexplained human activities in their introduction.

In addition to the ‘vaccine-like’ BTVs that have emerged and spread in Northern Europe, 3 new serotypes (25-27) have been identified among small ruminants in Europe and the Middle East (Batten *et al.* 2014, Vogtlin *et al.* 2013). These viruses have distinct properties that distinguish them from other BTVs, including their capacity to cause persistent infections (BTV-25) and for contact transmission (BTV-26).

Climate change has apparently exerted an important role in mediating regional expansion of the global range of BTV (Purse *et al.* 2008). Coincident with the spreading of BTV into Southern Europe at the

end of the last century, multiple novel serotypes of BTV also were detected in the Southeastern US and it is assumed that these viruses originated from a different BTV epizootic in the adjacent region of the Caribbean Basin. Studies in both Europe and Australia have confirmed the long-distance spread of novel strains of BTV by virus-infected midges, a finding that is consistent with the genetic grouping of field strains of BTV into regional topotypes that sometimes share members. Identification of the specific environmental and meteorological drivers of emergence of BTV is central to predicting the associated risk thereof, and ultimately to disease prevention and control (MacLachlan and Mayo 2013).

Although, the mainstream thesis among some who attended the First Symposium was that persistently infected cattle were responsible for both the overwintering and global spread of BTV, this thesis has since been soundly refuted. The advent of the modern diagnostic assays (particularly BTV-specific real time polymerase chain reaction), which are now used in many countries, has confirmed that infection of livestock with BTV serotypes (other than the new small ruminant ones, *i.e.* BTV 25-27) is prolonged but not persistent, reflecting an erythrocyte-associated viraemia (MacLachlan 2011). Similarly, recent studies confirm BTV infection of vector midges rather than sentinel cattle during the overwintering period in California (Mayo *et al.* 2014).

The future

The challenge to those gathered for this 4th International Symposium on Bluetongue and Related Orbiviruses is to further clarify the climatic and anthropogenic drivers that are responsible for the emergence and spread of these infections. Those discussions must of necessity focus on the potential impacts of climate change and, in particular, what its effects may be on 'non traditional' vector species and long-distance translocation of virus-infected vectors. However, it is critical, and even more urgent, that anthropogenic drivers are identified, such as those responsible for the introduction and spread of several novel and apparently laboratory-modified viruses in Europe and perhaps elsewhere. The importance of newly identified small ruminant serotypes of BTV also requires clarification, including their potential relevance to livestock movement and trade.

In summary, it is critical that strategies for control of BT and related diseases continue to be refined so that the economic impact of these diseases is minimized in the future – experiences from the recent past would indicate that this is not always a simple challenge, and that efforts should include both vector and animal-based strategies (MacLachlan and Mayo 2013). Similarly, the understanding of each disease and of its ecology is central to the logical design of science-based and transparent regulation of animal movement and trade.

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