Overview of the Mediterranean Basin Bluetongue Disease Outbreak, 1998-2004

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Bluetongue viruses (BTV) are arthropod-borne pathogens in the *Orbivirus* genus that infect most ruminants, causing clinical illness primarily in sheep and some deer species. Bluetongue (BT) disease was first described in South Africa in the early 1900s. In the United States , BTV was first isolated from California sheep in 1953, although a disease resembling BT was reported in Texas in 1948 (McKercher 1953). BT is currently a World Organization for Animal Health (OIE) listed disease (OIE List A disease)[1].

During 1998-2004, the largest known outbreak of BT occurred in the Mediterranean basin involving countries where BTV had not been previously reported. The purpose of this document is to summarize the Mediterranean basin BT outbreak as well as recent advances in BT knowledge.

Background – ecology and epidemiology of bluetongue disease

Worldwide, there are at least 24 BTV serotypes vectored by biting midges of the genus *Culicoides* spp. Bluetongue viruses are amplified by ruminant hosts including cattle and sheep. A total of 1,210 *Culicoides* species have been reported globally, but only 15 appear capable of transmitting BTV (Calistri 2003). Bluetongue virus is not transmitted transovarially in the vector.

Bluetongue viruses exist in discrete, stable ecosystems; virus spread occurs within geographic regions, as described below in the Mediterranean basin outbreak, but there has been minimal translocation of BTV virus strains between regions, despite substantial animal movement globally (Caporale 2003, European Commission 2000, Gould 1994). Phylogenetic analysis of BTV strains from 5 regions has revealed that isolates segregate into groups based on their geographic origin: Asia/Australia, Americas/Caribbean and Africa/Europe (Balasuriya 2003). Bluetongue viruses were originally thought to have disseminated globally from Africa, although as early as 1966, it was hypothesized that BTV serotype distribution was based on host and vector limitations within geographic regions (Gibbs 1994 citing Della-Porta 1966). Subsequent research has revealed that BTV serotypes have a common ancestor, but evolved in close affiliation with competent *Culicoides* species unique to geographic regions of the world.

The northern- and southernmost boundaries of BTV have historically been 40º north and 35º south latitudes, respectively; however, it is now documented that BTV occurs to 50º north (Caporale 2003) (Figure 1). The northernmost incursion of BT during the Mediterranean basin outbreak has, to date, been 44º north. The geographic distribution of BTV is categorized into three ecologic zones: *endemic*, *epidemic* and *incursion*. *Endemic* zones are defined as typically tropical regions where BTV transmission occurs throughout the year and subclinical infection is common. In endemic zones, clinical disease generally occurs only in introduced, immunologically naïve susceptible species (Gibbs 1994, Caporale 2003). *Epidemic* zones include temperate areas where outbreaks occur seasonally,

generally in the late summer when vector populations peak. *Incursion* zones are areas that experience outbreaks infrequently when climatic conditions favor disease transmission by vectors.

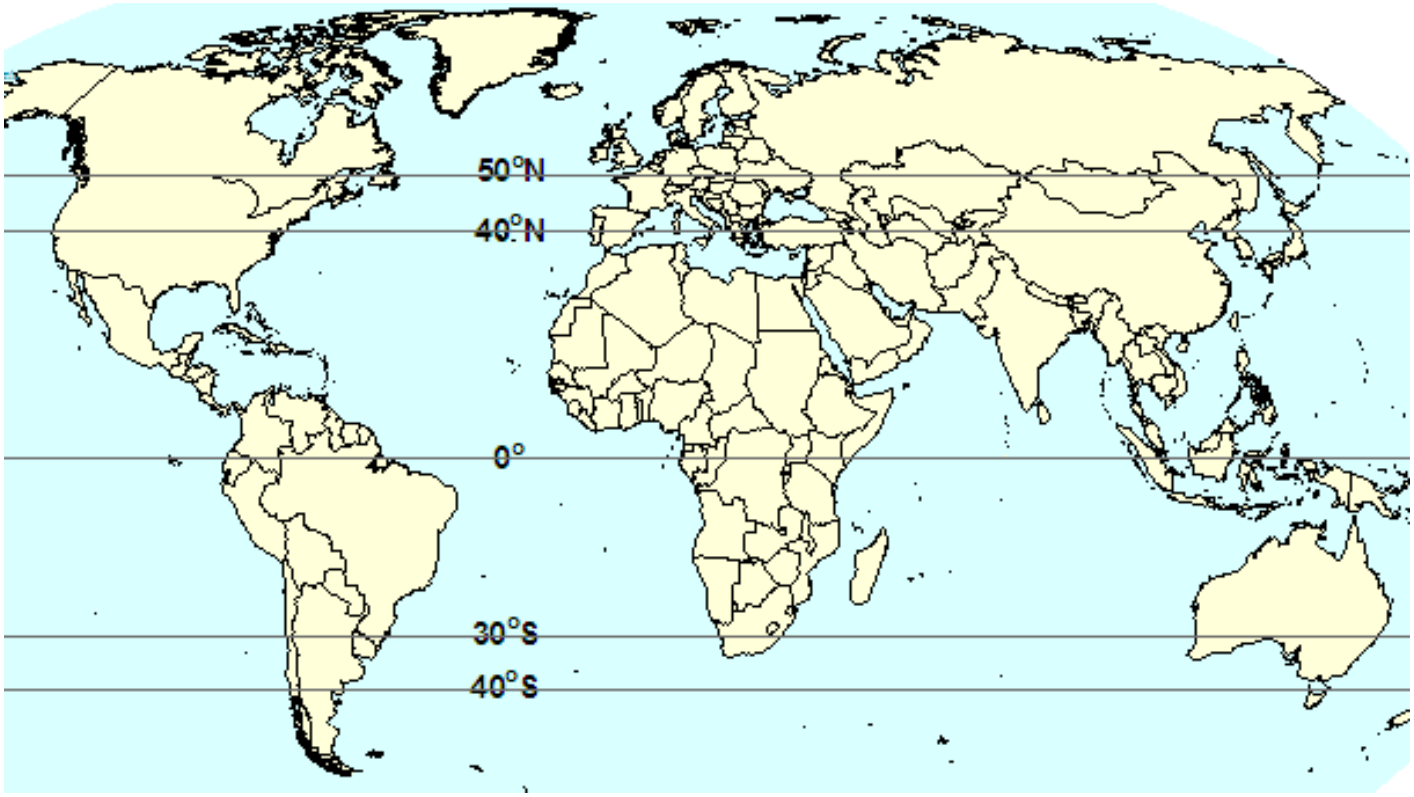

Figure 1. The northern- and southernmost occurrence of bluetongue virus (BTV) has historically been defined as 40º north and 35º south latitudes, respectively. BTV has been reported as far as 50º north.

Table 1. Global distribution of bluetongue virus (BTV) serotypes and primary *Culicoides* spp. vector, by geographic region.

Region	BTV Serotypes	Vector Species*
Africa	1-16, 18, 19, 24	*C. imicola, C. bolitinos*
Asia	1-4, 7, 9, 10, 12,16, 17, 20, 21, 23	*C. imicola, C. schultze grp., C. fulvus, C. actoni, C. actoni, C. brevitarsis, C. orientalis*
Australia	1, 3, 9, 15, 16, 20, 21, 23	*C. fulvus, C. wadai, C. actoni, C. brevitarsis*
Europe	4, 10	*C. imicola* sensu stricto, *C. obsoletus, C. pulicaris*
North America	2 (southern Florida), 10, 11, 13, 17	*C. sonorensis; C. insignis* in southern Florida
South and Central America, Caribbean	1, 3, 4, 6, 8, 12, 17	*C. insignis*

*Some of the species listed consist of a complex of two or more subspecies.

Summary of the Mediterranean Basin Bluetongue Outbreak

From 1998-2004, five serotypes of BTV caused outbreaks in 17 countries in the Mediterranean basin and southern Europe (Table 2, Figure 2). These outbreaks represent the first reported occurrence of BT for 11 (65 percent) of the affected countries and is the largest known outbreak of BT. The seven year period of successive outbreaks were predominantly due to BTV serotypes 2 and 9, although in late 2004, several outbreaks were caused by BTV-4 in the western Mediterranean basin. Mechanisms for spread of BTV during the outbreak are thought to include illegal movement of viremic animals and wind translocation of vector *Culicoides* spp. (Mellor 2002). Most of the reported outbreaks of BT in 2004 occurred during September through December 2004; outbreaks were reported in Croatia , Corsica Island (France), Morocco , Portugal , and mainland Spain (OIE, 2004). Cyprus , where BTV is known to be endemic, reported disease outbreaks in April and May 2004. Bluetongue virus serotype 16 was isolated for the first time in Croatia and Corsica Island (France) in 2004.

The first wave of outbreaks began in 1998, when BTV-9 was reported on several Greek islands and spread along the eastern Mediterranean basin, north through Bulgaria, Turkey, mainland Greece, Serbia and Montenegro, Macedonia, Croatia, and Italy (Table 2, Figure 2) (Breard 2004). Other serotypes reported include BTV-1, BTV-4 and BTV-16. The northernmost incursions of BTV during this series of outbreaks occurred in Serbia at 44’30º (Mellor 2002).

The second wave of outbreaks began in 1999, when BTV-2 was reported from Tunisia, then spread along the western Mediterranean basin to Algeria, Corsica Island (France), Sardinia Island (Italy), and Menorca and Mallorca Islands (Spain, collectively known as the Balearic Islands) (Figure 2). Serotype BTV-4 was reported in Italy and France at this time. Both BTV-2 and BTV-9 outbreaks occurred in Italy . In 2000, serologic evidence of BTV infection was documented in Morocco , adjacent to Algeria , but did not appear in OIE records (Mellor 2002). Overall, the extended BT epidemic resulted in over 500,000 sheep deaths due to illness or culling (OIE 2003). Data from OIE suggest that a higher proportion of these deaths may have occurred due to culling than illness mortality. Approximately 85 percent of Italy ’s sheep and goat populations were located in the outbreak regions of Italy .

Of the outbreak serotypes, BTV-2 isolates are most closely related to BTV-2 isolates from sub-Saharan Africa (Maan 2003). The outbreaks in the eastern Mediterranean due to BTV-9 are related to Asian BTV isolates, while BTV-1 outbreak isolates from Greece are most closely related to BTV isolates from India .

Several European countries implemented mass vaccination for BTV, including Italy , Corsica, and Menorca and Mallorca Islands. Vaccination is an effective control measure for BT; however, vaccination is serotype specific. In addition to vaccination, recommended methods to control BT include animal movement restrictions, vector control, slaughter of viremic animals, and management to reduce animal vector exposure (Mellor 2002).

During the course of the epidemic, BTV transmission occurred in areas of Europe outside of the known range of *C. imicola* (Mellor 2002). BTV incidence is dependent on the distribution, prevalence and competence of *Culicoides* spp. Vector presence and ability to transmit BTV is related to climatic factors including temperature, precipitation, humidity and wind conditions (Mellor 2002). *Culicoides imicola* is not known to occur in outbreak areas of northern Greece and Bulgaria (Mellor 2002) and has only recently been reported on mainland Italy, where the vector may have gone undetected historically (Calistri 2003, Meiswinkel 2003, Breard 2004). In outbreak areas apparently without recognized vector species, it has been hypothesized that the range of *C. imicola* is expanding or there is an unidentified vector (Mellor 2002). Mounting evidence, much of it from Italy, supports the involvement of novel vectors in the outbreak, primarily *C. obsoletus sensu lato* (a complex of at least two members) and *C. pulicaris* (Purse 2004, Breard 2004, Dallas 2003, Caracappa 2003, de Liberato 2003, Calistri 2003, Meiswinkel 2003).

Table 2. Mediterranean basin and southern European countries reporting bluetongue disease to the World Organization for Animal Health (OIE), 1998-2004.

		Reported Outbreaks, Year						
Country* (last reported outbreak < 1998)	**Other sero-types**	**1998**	**1999**	**2000**	**2001**	**2002**	**2003**	**2004**
BTV Serotype 9 Outbreak								
Greece (mainland and islands) (1989)	1,4,16	X	X	X	X			
Bulgaria			X		X	X		
Turkey (1979)	16		X	X				
Serbia and Montenegro (includes Kosovo)					X	X		
Former Yugoslav Republic of Macedonia					X	X**	X**	
Croatia	16				X			X
Italy (southern mainland, Sicily Island)	16			X	X	X	X	
Bosnia and Herzegovina						X	X	
BTV Serotype 2 Outbreak								
Tunisia			X	X		X		
Algeria				X				
Italy (central mainland, Sardinia and Sicily Islands)	4			X	X	X	X	
Spain (Menorca and Mallorca Islands)(1960)				X			X	
France (Corsica Island)	4, 16			X	X		X	X***
Other, or serotype not reported								
Albania						X		
Israel	16	X			X		X	
Cyprus (1977)	16	X**	X**	X**	X**	X**	X	X
Morocco	4							X
Spain (mainland) (1960)	4							X
Portugal (1959)	4							X

***BOLDED** country names indicate the first reported occurrence of bluetongue disease for that country.

**Detection of BTV antibodies or virus isolation, no clinical disease reported.

***Only serotypes 4 and 16 have been reported on Corsica Island in 2004.

Figure 2. Countries reporting bluetongue disease to the OIE, 1998-2004. Countries with outbreaks attributable to predominantly BTV-9 are represented in white; BTV-2 in dark gray; BTV-16 in black; BTV-4 in cross hatch. Italy is shown in light gray, representing outbreaks due to both BTV-2 and BTV-9. *Abbreviations:* B/H, Bosnia and Herzegovina; S/M/K, Serbia and Montenegro including Kosovo; FYRM, Former Yugoslav Republic of Macedonia; Alb, Albania; Switz, Switzerland.

Bluetongue in North America

In the US , BTV infection is rare to absent in northern latitudes, becoming more common in southern and western states (Dargatz 2003). The predominant US BTV vector is *C. sonorensis*, except in the northeastern US where *C. sonorensis* and BT do not occur (Tabachnick 1996). The low prevalence of BT in northwestern states is probably related to environmental limitations affecting the capacity of *C. sonorensis* to transmit virus. *C. sonorensis* had previously been considered part of the *C. variipennis* complex, but is now considered a separate species. BTV serotypes 10, 11, 13, and 17 occur throughout the range of *C. sonorensis* in the US ; BTV-2 is limited to Florida. BTV-2 was first isolated in Florida in 1982 and is thought to be vectored solely by *C. insignis*, although *C. sonorensis* is also present in Florida (Mecham 2003). Canada is free of BT, with the exception of the Okanagon Valley, British Columbia.

Bluetongue disease and trade

The duration of BTV viremia in domestic ruminants has been a critical issue in international trade and placement of trade barriers. The OIE currently recognizes a 100 day infective period (Article 2.1.9.1, Terrestrial Animal Health Code, OIE 2003). Using virus isolation, BTV is detectable in cattle and sheep blood for less than 63 and 54 days post-infection, respectively. Using PCR, BTV genetic material is detectable in the blood of cattle and sheep for up to 180 and 119 days post-infection, respectively (Katz 1993, 1994). However, subsequent studies found that only cattle or sheep with viremia detectable by virus isolation were infectious to *C. sonorensis* (Bonneau 2002). During a 2003 international meeting on BTV, it was recommended that this new information about reservoir host infective period be incorporated into risk assessments for trade purposes (Caporale 2003).

In the US , no additional safeguards were implemented during the Mediterranean basin outbreak beyond existing United States Department of Agriculture protocols regarding BT. Existing protocols include testing and quarantine within vector-free facilities, for animals imported from countries that have BT serotypes other than those endemic to the US .

Conclusion

From 1998-2004, the largest known outbreak of BT occurred in 17 countries in the Mediterranean basin and southern Europe; 11 of these countries reported BT to the OIE for the first time. The outbreaks were primarily caused by serotypes BTV-2 and BTV-9. BTV-2 spread from northern Africa north to France and then into Italy . BTV-9 was first reported from the southeastern Mediterranean basin, and moved north and east to Italy . Mechanisms for spread of BTV are thought to include illegal movement of viremic animals and wind translocation of infected vector *Culicoides* spp. The northernmost incursion of BT during this epidemic occurred in Serbia at 44º north.

During the outbreak, several countries implemented emergency use of mass vaccination using attenuated virus vaccine. Preliminary evidence indicates that mass vaccination may have been a useful tool in controlling the outbreak, though additional research is needed regarding use of vaccine during outbreaks. Traditional control measures for BT include animal movement restrictions, vector control, slaughter of viremic animals, and management to reduce animal vector exposure.

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[1] -OIE is in the process of eliminating List A and B designations in favor of a single notifiable disease list categorized by reporting urgency and other factors (http://www.oie.int/eng/edito/en_lastedito.htm).