7. Bluetongue: an emerging vector-borne disease outbreak in North-western Europe

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Abstract

The animal vector-borne disease bluetongue (BT) was discovered in the Netherlands and neighbouring areas of Belgium, France, Germany and Luxemburg for the first time in August 2006. The BT virus was identified as serotype 8. This serotype had never before been found in Europe. Vector surveillance in the outbreak area revealed nine different potential vector species, with >90% belonging to the *Culicoides obsoletus* and *C. pulicaris* group of midges. BT virus was found in *C. dewulfi*, a member of the *C. obsoletus* group. Following a winter period free of reported cases in the affected areas, renewed outbreaks were reported on 17 July 2007, indicating that the virus had survived undetected throughout the winter of 2006/2007. It is argued that the introduced BT virus may have benefited from the unusually high temperatures in July 2006 in northwestern Europe, and that climate, vectors and virus conspired to cause a major epidemic in farm animals. Aspects of this outbreak are discussed, with relevance to the origin of the serotype, the vector ecology and competence, the climate, and the route of introduction.

Keywords: Bluetongue virus, North-Western Europe, *Culicoides*, outbreak, control

Introduction

Climate change and increasing international trade have been blamed for the dissemination of vector-borne diseases at an unprecedented speed in recent years. Dengue fever, a disease previously limited to S.E. Asia, has become endemic in the Caribbean and Central- and South America; West Nile fever has arrived in the continental USA and Chikungunya fever has hit hard on the island of Réunion (Jetten and Focks 1997, Morse 2003, Paganin *et al.* 2006). In addition, the incidence of several tick-borne diseases is rising in the northern hemisphere, e.g. Lyme disease, granular ehrlichiosis (anaplasma) and tick-borne encephalitis (Parola 2004, Piesman and Gern 2004). Now, another infectious disease can be added to this list: bluetongue (BT) was confirmed in sheep in the Netherlands on 15 August 2006, the first case ever reported north of the Alps.

BT is endemic in South Africa, most of southern Asia, Australia and the Americas, but since 1998 it has also been present at one time or another in many parts of Mediterranean Europe. Cyprus, certain Greek Islands and the Iberian peninsula have previously suffered occasional outbreaks of BT probably caused by the wind-borne spread of vectors infected by bluetongue virus (BTV) from Israel and Turkey, or North Africa (Purse *et al.* 2005). These early incursions were short lived and involved only a single serotype on each occasion. However, this picture has changed since 1998, with new introductions each year except 2003, involving BTV strains of five distinct serotypes (1, 2, 4, 9 and 16) killing many thousands of sheep. In southern Europe, the competent vector was found to be the well-known vector of BT, *Culicoides imicola* Kieffer, a blood feeding midge with a distribution from South Africa to southern Europe. In Europe, however, *C. imicola* is a relatively recent arrival. Since 2000, Italy has witnessed yearly epidemics of BT, which are mostly controlled by vaccination. In northern Italy and the Balkans, the disease is most likely transmitted by C.

obsoletus (Meigen), *C. scoticus* Downes and Kettle, and *C. pulicaris* (Linnaeus), midge species that tolerate a cooler and wetter climate than *C. imicola* (De Liberato *et al.* 2005, Gomulski *et al.* 2006). *Culicoides obsoletus* and *C. scoticus* belong to the subgenus Avaritia Fox and *C. pulicaris* to the subgenus *Culicoides* Latreille, respectively. Recent epidemiological models predicted that the distribution of BTV in Europe would not reach beyond the Balkan countries or southern France (Purse *et al.* 2005).

First outbreaks of BTV

The index case of BT in the Netherlands occurred in Kerkrade, in the far south of the country, on the border with Germany and Belgium. That same day, five other flocks of sheep were recorded as suspect (Figure 1). By 17 August, three farms had been confirmed positive for BTV, with eight others suspected. All cases were confirmed by PCR in combination with antibody detection. By 19 and 21 August, several cases were also recorded from neighbouring areas in Belgium and Germany, respectively. On 26 August, the isolate was typed by the European Community Reference Laboratory at Pirbright in the UK as a BT serotype 8 using RT-PCR and sequence analysis of genome segment 2. The virus is derived from a sub-Saharan African lineage but is distinct from the reference and attenuated vaccine strains of BTV-8. It is the first time that this serotype has been isolated from animals in Europe. Moreover, this strain not only affected sheep but also cattle with clinical symptoms.

By late August 2006, 28 farms in the Netherlands had been confirmed positive with BTV, all within an area of 400 km^2 in Limburg province. Three cows were found positive 150 km north of the outbreak area, at an animal exportation centre near Utrecht. The three animals had been brought there from the infected area shortly before confirmation of the BT introduction. A further 46 and 21 farms were infected in Belgium and Germany, respectively. Shortly thereafter, numerous cases were reported to the authorities in Belgium, Germany, Luxemburg and the Netherlands, and there were a few cases reported in northern France (Mehlhorn *et al.* 2007, Toussaint *et al.* 2007) (http://www.efsa.europa.eu/en/in_focus/bluetongue/bluetongue_report_s8.html). By the end of 2006, more than 450 infected farms had been reported in the Netherlands, with many more in

Figure 1. Sheep on a farm in the affected area in Limburg province, August 2006.

Belgium, Germany and Luxemburg (Figure 2). The weekly number of new infections is shown in Figure 3, with a clear peak of cases by the end of October. Only in France the number of infected farms remained low (n=6) and confined to the Northeast. Adhering to contingency plans adopted by the European Community, a series of regulatory steps were issued to the farming community with regard to animal movement and other aspects of their business. According to these rules, by 17 November 2006 about 50% of the Netherlands was declared to lie within the infected area (Figure 4). Livestock owners in the infected area were also required to treat animals with a pour-on insecticide (deltamethrin or permethrin or pyrethrin/piperonylbutoxide) and treat walls of the

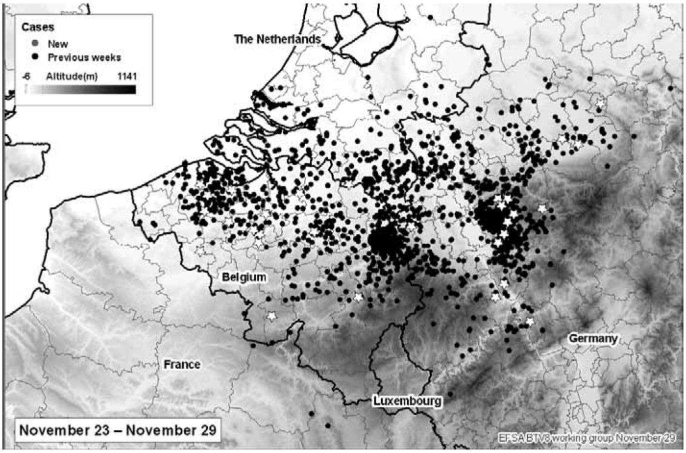

Figure 2. Overview of cases of BTV 8 recorded in North-western Europe between 17 August 2006 and 27 February 2007 (source: DEFRA, UK).

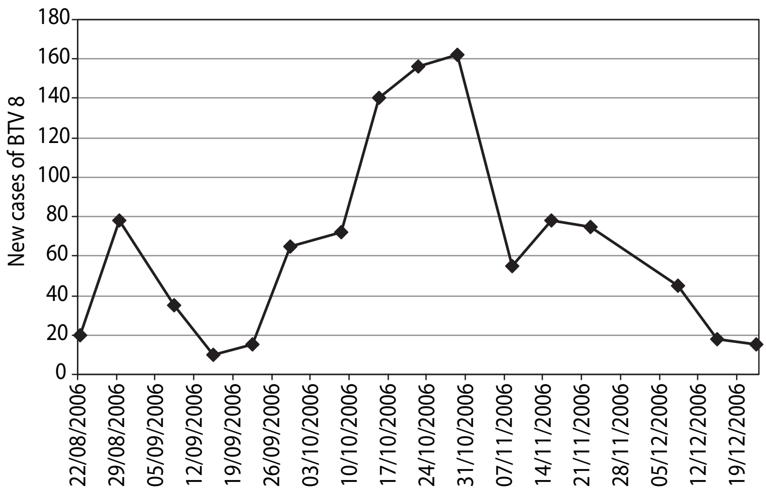

Figure 3. Weekly number of BTV cases during the bluetongue outbreak in North-western Europe in 2006 (source: EFSA, Parma, Italy).

Figure 4. Restricted zone for live ruminant transport in the Netherlands, November 2006 (modified after Dutch Ministry of Agriculture, Nature and Food Quality).

stables with this insecticide. At the early start of the outbreak, domestic animals were required to be kept indoors from one hour before sunset to one hour after sunrise (http://www.minlnv.nl/portal/page?_pageid=116,1640524&_dad=portal&_schema=portal).

Vector surveillance

We conducted a rapid survey of putative BTV vectors in the heart of the outbreak zone between 22 August and 28 September 2006, in order to obtain information on the presence and density of *Culicoides* spp. in the affected area. This surveillance was conducted with Liberty plus counterflow CO_2 traps (Mosquito Magnet® Liberty Plus, American Biophysics Corp., North Kingstown, RI 02852, USA) and with Onderstepoort light traps (Figure 5) (Kline 2002, Meiswinkel 1998, Venter *et al.* 1996). The study focused on four of the affected livestock farms in southern Limburg province, close to the borders with Belgium and Germany. During this survey, we collected 6,441 *Culicoides*. Of these, 3,902 specimens were identified to species or species group, representing at least nine different species. The *C. obsoletus* group was the most abundant species group present (88%), followed by the *C. pulicaris* group (9%) (Table 1). Other *Culicoides* species were relatively rare among the catches. These data are in agreement with recent studies on *Culicoides* in the Netherlands, which show that members of the *C. obsoletus* and *C. pulicaris* complexes are widely present throughout the country, often in association with animal farms (Takken *et al.* in press). The only notable species absent from the catches was *C. impunctatus* Guetghebuer, which is abundantly present elsewhere in the Netherlands (Takken *et al.* in press). Light trap collections showed considerable daily variations in numbers of midges collected, with the *C. obsoletus* group remaining the most abundant throughout the period of surveillance (Figure 6). The light trap collected much larger numbers of *Culicoides*, but the CO_2 trap was in continuous operation and therefore could also

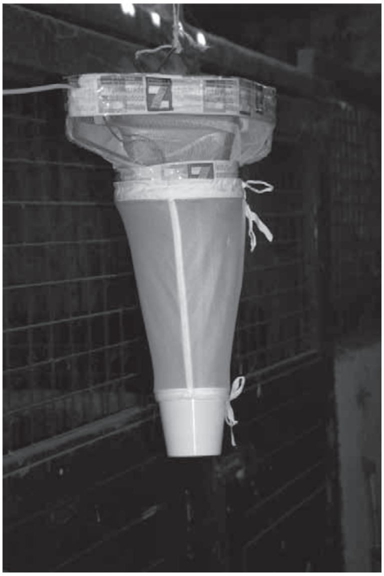

Figure 5. Onderstepoort light trap in one of the sites of the Culicoides survey in September 2006.

Table 1. Total catch of Culicoides *spp. in Onderstepoort light traps during the survey in Limburg province, 22 Aug – 28 Sept 2006.*

Species	Total number collected	Percentage of total
C. obsoletus group[1]	3,449	88%
C. pulicaris group	351	9%
C. punctatus	28	1%
C. newsteadi	6	0%
C. festivipennis	35	1%
C. circumscriptus	5	0%
C. stigma	2	0%
C. nubeculosus	2	0%
Unidentified *Culicoides* spp.	24	1%
Totaal	3,902	100%

[1]The *C. obsoletus* group includes *C. obsoletus*, *C. scoticus*, *C. chiopterus* and *C. dewulfi.*

collect midges during daylight hours, a time when in northwestern Europe midges can be very active (Service, 1971). Interestingly, the daily numbers of midges in the catches were relatively low (1–50 *Culicoides* spp. per light trap per night) unlike *Culicoides* catches in southern Europe, where often hundreds of midges are collected during one night (De Liberato *et al.* 2003).

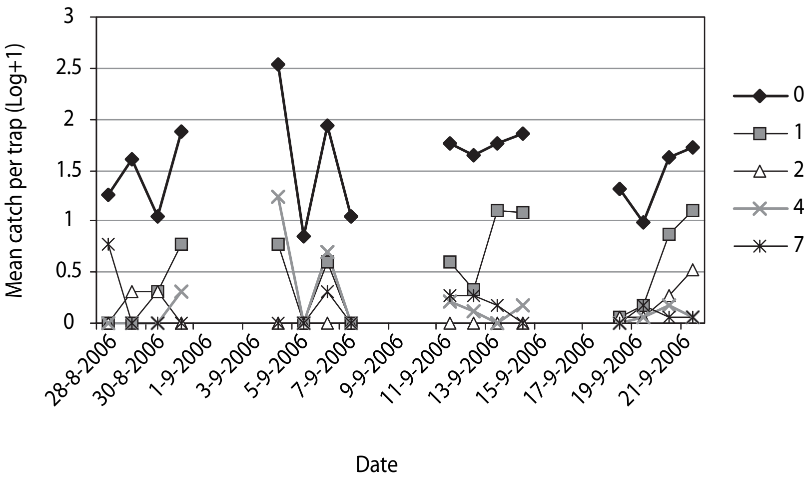

Figure 6. Mean number of Culicoides spp. collected in Onderstepoort light traps between 28 August 28 2006 and 23 September 2006 in the outbreak area in the Netherlands. 0 – C. obsoletus group; 1 – C. pulicaris group; 2 – C. punctatus; 4 – C. festivipennis; 7 – unidentified Culicoides spp.

Overwintering and new outbreaks

During the winter of 2006/2007 no new confirmed infections of BTV were reported, whereas newly found BT positive animals may have resulted from infections in late 2006. This suggests that active viral transmission had halted due to lower temperatures leading to the death of adult (infected) midges. Although no information about overwintering of adult biting midges in Europe is available, we frequently caught adult midges throughout the winter in an outdoor trap on a livestock farm near Afferden, the Netherlands (51º52’52”N, 5º38’21”E, 5 m above sea level), where in May 2006 large numbers of *C. obsoletus* had been caught. Numbers of *Culicoides* spp. in the trap, however, were much lower between December 2006 and March 2007 compared to summer and autumn populations (W. Takken, unpublished results). The activity of adult *Culicoides* throughout the winter was also reported by Losson *et al.* (2007), who frequently caught adult midges in a light trap in a calving unit near Liège in Belgium between November 25, 2006 and March 9, 2007. Although catches were initially high, they dropped to <10 *Culicoides* per night after December 10, 2006.

On 17 July 2007 the first new case of BT was reported from Germany, ostensibly from an animal taken sick on 6 July 2007. This case was followed by several cases in Belgium and the Netherlands and one case in France (Anonymous 2007a,b). By 1 August 2007, BT had been recorded in the Netherlands from more than 22 farms, all located within the 2006 affected areas. The southern part of the Netherlands was, once more, declared a BTV infected area, requiring restrictions for transport of live ruminants (Figure 4)[2]. By 22 August 2007 more than 336 farms were reported affected with BT, with the disease having also spread into the northern provinces of the Netherlands.

[2] On August 3, 2007, the British authorities reported a case of foot and mouth disease on a livestock farm. As a preventive measure, the Dutch government on August 4, 2007, issued a complete ban on all ruminant transport throughout the country. The ban was lifted when it was clear that the FMD outbreak had been contained.

Discussion

This BT outbreak in North-western Europe in 2006 and 2007, caused by a novel BT serotype for Europe, raises several important questions that need further attention in the future. Although southern Europe has experienced recurrent BT outbreaks in recent years, some involving *C. obsoletus* and *C. pulicaris*, until 2006 the virus had limited its distribution to the Iberian peninsula, France (Corsica), Italy, the Balkan countries, European Turkey and Greece (Calistri *et al.* 2003). Recent epidemiological models, incorporating climatic factors, did not predict an outbreak in the Netherlands, not even under future climate scenarios (Purse *et al.* 2005, Tatem *et al.* 2003). Although members of both the *C. obsoletus* and *C. pulicaris* complexes have been incriminated as vectors in the Balkans and northern Italy, and both species complexes are widely distributed in central and northern Europe, it was thought that temperature would be the limiting factor for establishment of the virus and indeed, the 2006 record high temperatures recorded in some parts of central and northern Europe may have been a factor in the observed virus spread. Thus, while competent vectors are present in the Netherlands, we should question how the virus has arrived this far north, leaping across a gap of hundreds of kilometres. A second aspect is that this outbreak was caused by a virus isolate that is new to Europe. Bluetongue virus serotype 8 is found in Africa and the Americas, and suspected on the Indian subcontinent, but had, prior to 2006, not been recorded from Europe[3]. Sheep and cattle, although widely traded across Europe, are rarely imported from outside the continent. Therefore, accidental importation through an exotic animal should be considered. A third, curious, aspect of this epidemic is the initial patchy distribution. Within Limburg province, BTV had been found on 28 farms by 29 August 2006. Many of these farms are not adjacent to each other, but are often separated by several km in a highly diverse terrain. In addition to commercial livestock holders, there are numerous smallholder or hobby farms, with <15 sheep. Midges are found throughout the area, mostly concentrated in river valleys, where they find shade and moisture. A first analysis of the epidemic showed that not all farms were affected. However, as BTV is vector-borne, one might expect a rapid spread affecting all livestock holdings indiscriminately. Clearly this farm to farm variation requires urgent investigation.

Given that the epidemic was present across borders, affecting at least five countries, control of the epidemic proved difficult. A ban on animal movement was implemented within an area of 20 km around the affected farms, with further restrictions within a 150 km radius. This zone reached across Luxemburg into northern France and far into Germany, covering all of Belgium and about 50% of the Netherlands. The fact that infected animals were not slaughtered and hence may have served as infectious reservoirs for midges, may have resulted in many more animals becoming infected and an increased risk of further spreading of the disease. It seems more likely, however, that viral distribution is accomplished by the *Culicoides* vectors, which can disperse over several hundred m per day, or be rapidly distributed over a large distance by wind (Bishop *et al.* 2000). Whereas infected ruminants are thought to lose infectious BTV after 60 days, the infection can persist the entire life of adult *Culicoides*, which may vary from two weeks to several months. Hence containment of infectious midges, if possible, would provide an effective strategy for BTV control. Livestock holders were required to spray barns and stables with insecticides, and treat their animals with insecticide as well. However, there is no proven evidence demonstrating the efficacy of these measures and in the 2006 outbreak they failed to halt BTV dispersal. It is reported

[3] There are reports of sheep positive with BT serotype 8 from Bulgaria, but no virus has been isolated from these animals.

from Italy and the USA that treatment of farm animals with insecticides failed to stop the spread of BTV to adjacent herds (Mullens *et al.* 2001, Satta *et al.* 2004).

The month of July 2006 was the warmest on record in the Netherlands (http://145.23.254.254/VinkCMS/news_detail.jsp?id=33586) with an average monthly temperature >22.3 ºC (the historic mean temperature for July is 17.4 °C). These high temperatures may have favoured the development of BTV in *Culicoides* vectors and its transmission to susceptible animals, given the presence of an infected animal imported into the region. Climate change has already been blamed for changes in the distribution of vector-borne diseases (Epstein 2005), which are widely considered to affect the health of humans and animals. It was assumed that the epidemic would fade out in the winter of 2006/2007, but recent studies in the Netherlands and Belgium demonstrated that at least a very small proportion of *Culicoides* survived as adults, thus presenting a possible reservoir of BTV (Losson *et al.* 2007; Takken *et al.*, unpublished results). The reported outbreaks in Belgium, Germany, France and the Netherlands in late July 2007 support the hypothesis that BTV remained active in the affected areas. Although at the time of writing it is too early to speculate about its 2007 distribution, it is likely that a larger area than in 2006 may become affected. The month of July 2007 was, in stark contrast to that of 2006, relatively cool and very wet. This suggests that high summer temperatures are not required for BTV distribution, and that the indigenous *Culicoides* species are competent vectors. Considering the size of the infected areas and the large number of farms, vector control seems not feasible. One could consider to focus vector control on the overwintering adult vectors, which are likely to be concentrated in animal stables and barns. Here, a focussed campaign with insecticides targeted to kill the overwintering adult midges might be effective and is expected to result in a drastic reduction of the vector reservoir. Alternatively, vector control could be started when the population of the responsible *Culicoides* spp. starts to grow, therewith delaying the spread of BT. Extensive knowledge of the competent vector(s) and communication with, for instance, weather forecasters and farmers is needed to effectively reduce the growth of the vector population. Ultimately, vaccination seems to be the only way to eradicate BT.

Although at present we have little knowledge about the origin of the current BTV outbreak, its vectors or epidemiology, and the possible effect of climate change, the fact that the disease occurred this far north and its ability to spread rapidly are reasons for serious concern about the risk of similar emerging diseases and our preparedness to diagnose and control them.

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