OPINION

Climate change and the recent emergence of bluetongue in Europe

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Abstract | Bluetongue, a devastating disease of ruminants, has historically made only brief, sporadic incursions into the fringes of Europe. However, since 1998, six strains of bluetongue virus have spread across 12 countries and 800 km further north in Europe than has previously been reported. We suggest that this spread has been driven by recent changes in European climate that have allowed increased virus persistence during winter, the northward expansion of *Culicoides imicola*, the main bluetongue virus vector, and, beyond this vector's range, transmission by indigenous European *Culicoides* species — thereby expanding the risk of transmission over larger geographical regions. Understanding this sequence of events may help us predict the emergence of other vector-borne pathogens.

Bluetongue virus (BTV) is the type species of the genus *Orbivirus* in the family *Reoviridae* — a large group of double-stranded RNA viruses with 10–12 genome segments[1]. It causes an infectious, non-contagious disease of ruminants[2], and there are 24 SEROTYPES. The virus replicates in all ruminant species, but severe disease is mostly restricted to certain breeds of sheep (particularly fine wool and mutton breeds that are common in Europe) and some species of deer[3]. Most transmission of BTV, particularly in endemic areas, therefore occurs 'silently' in disease-resistant host animals. Cattle are the main such reservoir in most areas, being subclinically infected and sometimes developing prolonged viraemias of up to 100 days[4]. Nevertheless, since its arrival in Europe in 1998, bluetongue (BT), the disease caused by BTV, has caused the deaths of more than one million sheep[5,6]. In addition to morbidity and mortality, BT disrupts the trade in animals and animal products and has been estimated to cause annual losses of US$125 million in the United States alone[7].

BTV is transmitted between its ruminant hosts almost entirely by the bites of certain species of *Culicoides* biting midges (Diptera: Ceratopogonidae). Susceptibility to infection and the subsequent replication and dissemination of viruses in *Culicoides*, is determined by a range of hereditary and environmental factors[8,9]. So far, less than 1% of more than 1,400 *Culicoides* species described have been incriminated in the transmission of BTV — although relatively few species have been studied. The disease is restricted to areas where these competent vector species occur — broadly the tropical and subtropical parts of the world, between latitudes 35°S and 40°N (FIG. 1a). Transmission within this zone is seasonal, and most occurs between late summer and late autumn when adult vectors are abundant. Adult *Culicoides* are not strong fliers but they can be passively dispersed by the wind, possibly up to several hundred kilometres in a single night[10], especially over the sea. For example, wind-borne infected midges (in the absence of animal movements) carried strains of BTV about 20 km from the Turkish coast to the Greek island of Lesvos, and more than 300 km to the Balearic Islands from Tunisia or Sardinia. In view of this potential for extremely rapid spread[8] and its serious consequences for the international trade of animals and animal products, BT is classified as a List A disease by the Office International des Epizooties (OIE), the world organization for animal health (see the Online links box for further information).

Vector-borne pathogens are particularly sensitive to climate[11], a fact that has led to widespread and continued speculation that anthropogenic climate change will increase the incidence and intensity of their transmission[12–14]. There is, however, little evidence supporting such speculations[11,15,16], while at the same time there is an increasing realization that other non-climatic abiotic and biotic factors can also affect disease distribution[17–20]. In this article, we discuss those features of the BTV–*Culicoides* system that make it exquisitely sensitive to changes in climate. We highlight a recent step-change in BTV transmission in Europe and provide evidence to support our conclusion that this has been driven mainly by climate change.

The changing pattern of BT in Europe

Sero-surveys indicate that many BTV serotypes have been circulating on the fringes of Europe for several decades — in sub-Saharan Africa[21], Turkey and the Middle East[22–35]. These fringe areas are linked to Europe and north Africa by traditional livestock trade routes such as the RUMINANT STREET between western Asia and southern Europe[36,37], with more infrequent movements of livestock also occurring across the Sahara and westward across north Africa[38]. SYNOPTIC WEATHER SYSTEMS also drive winds across this region — for example, the Persian trough events that link the Middle East to western Turkey and which are coincident with the summer–autumn period of peak BTV transmission[39,40]. The potential has, therefore, long existed for BTV to enter Europe, either by the movement of infected ruminants or by the wind-dispersal of infected midges.

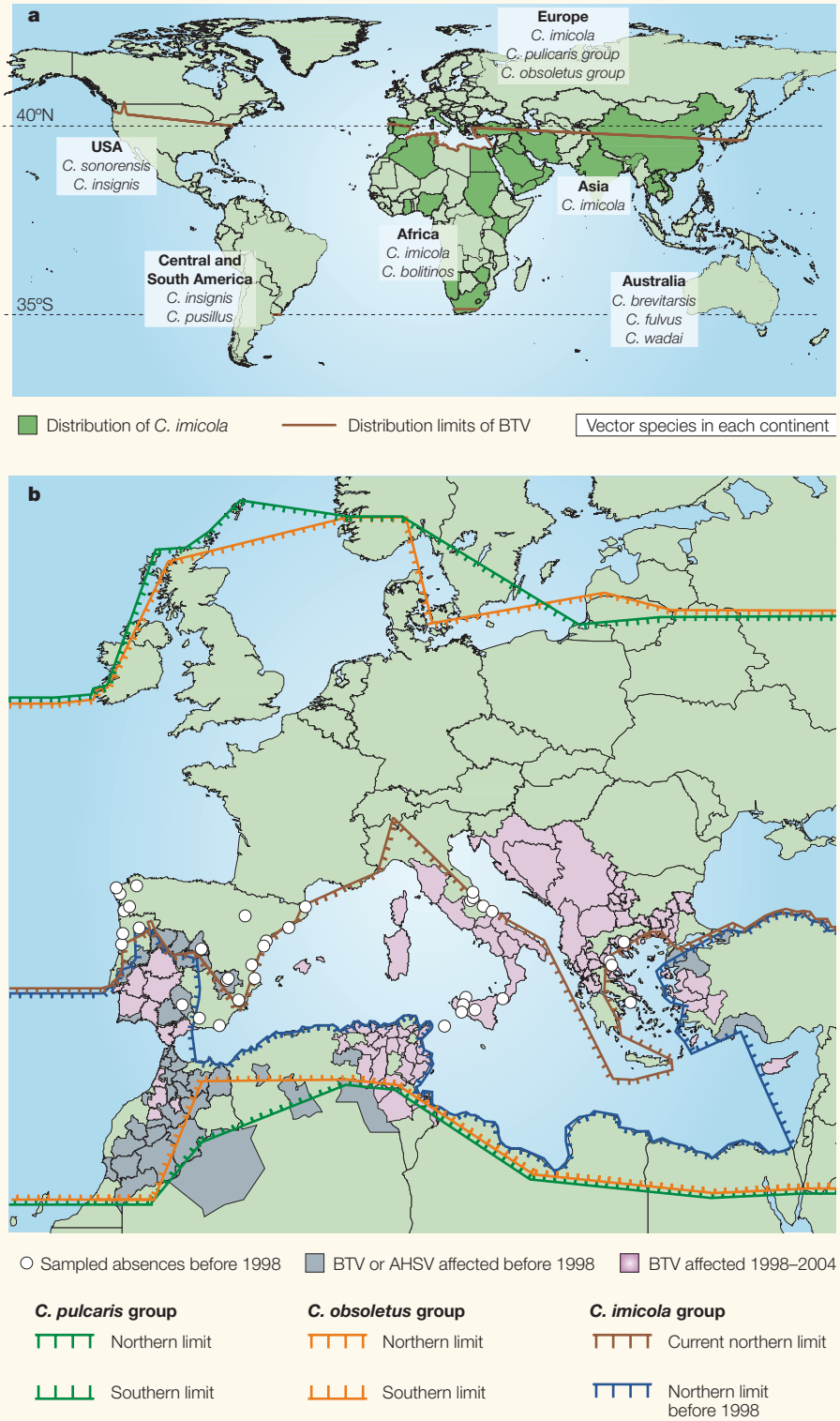


Figure 1 | **Distribution of BTV and *Culicoides* vectors. a** | Map showing the countries where *Culicoides imicola* — the major Old Word bluetongue virus (BTV) vector — has been recorded (indicated in dark green). The current distribution limits of BTV are demarcated by red lines and are located broadly between the latitudes 35°S and 40°N (indicated by dashed lines). Other important *Culicoides* vectors are listed next to the continent in which they are involved in transmission. **b** | Map showing the distribution of BTV and the closely related orbivirus African horse sickness virus (AHSV) prior to 1998 (grey shading) and that of BTV since 1998 (up to November 2004, pink shading). Hatched lines indicate the approximate known northern and southern range limits of the three most important vector groups in Europe (derived from references cited in the text as well as REFS 136–143). Open circles indicate sites where *Culicoides imicola* was found to be absent before 1998.

Despite these potential entry routes, both BTV and African horse sickness virus (AHSV) (which is a closely related orbivirus that is transmitted by the same *Culicoides* species) made only brief periodic incursions into southern Europe before 1998 (REFS 27,41–46; FIG. 1b, grey shading). AHSV affected Europe (southern Iberia) most recently in 1990 and BTV last affected Turkey and Cyprus in 1981. With regard to BTV during incursions only one or two countries were affected at a time and only a single BTV serotype was involved. Only the major Old World vector species *Culicoides imicola* Kieffer was implicated in transmission, and all BT outbreaks occurred within its known northern range limit in Europe[31,47–49]. Up to 1997, this range included Portugal, south-western Spain[50,51] and some Greek islands[52,53] (FIG.1b, blue line). Surveys in several areas beyond this limit failed to detect *C. imicola*[51,54–63] (FIG. 1b, white circles, Bulgarian survey not indicated).

The current BT epidemic. The current BT epidemic began during October 1998, when BTV-9 was detected on four Greek islands close to the Turkish coast (Rhodes, Leros, Kos and Samos). In subsequent years up to 2004, BTV-9 spread northward (into western regions of Turkey, Bulgaria, Kosovo, Albania, Bosnia and Herzegovina, the former Yugoslav Republic of Macedonia, Serbia and Montenegro, and Croatia) and westward (into mainland Greece, Italy, Sicily, Sardinia and Corsica). A further three serotypes, BTV-1, BTV-4 and BTV-16, also entered Europe from the east (through Greece) and then spread westwards. A separate incursion of BTV-2 also occurred in 2000, spreading from Tunisia and/or Algeria into Sardinia, Sicily, mainland Italy, Corsica and the Balearic islands (FIG. 1b, pink shading). In late 2004, further incursions, this time of BTV-4 occurred from Morocco into southwestern Spain and southern Portugal. Some serotypes have now persisted for up to six years in parts of Europe, a pattern that is consistent with frequent OVER-WINTERING as opposed to reincursion of particular strains. For example, BTV-9 entered Bulgaria in 1999 (REF. 64) and was subsequently recorded in the Balkan countries listed above on an annual basis up to and including 2004. Since 2001, BTV-9 has not been recorded in areas to the south of the Balkans (that is, Greece and western Turkey), despite sentinel surveillance that places the nearest potential sources of BTV-9 for reincursion more than 1,000 km away in east Anatolian Turkey. Although such long-distance 'jumps' might be plausible over the sea under favourable wind conditions, the spread of the

virus over land is usually characterized by short-distance jumps that would have been detected by surveillance in the intervening countries, which indicates that BTV has over-wintered in the Balkans for 3–5 years.

Several features of the current epidemic indicate a substantial change in the epidemiology of BT in Europe[5]: first, the expanded distribution of transmission, with at least 12 countries affected over 7 years and outbreaks recorded more than 800 km further north than before (up to latitude 44°30′N); second, the almost simultaneous invasion of six BTV strains (of five serotypes) from at least two directions (BOX 1); third, the increased persistence of transmission, with over-wintering of particular strains; fourth, the marked extension of the northern range limit of the traditional vector *C. imicola* into the Balearic Islands[65], mainland France[66], Switzerland, eastern Spain (REFS 67,68; J. Delgado and P. Collantes, personal communication), mainland Greece[69], Sicily[70] and mainland Italy[71]; and fifth, the extension of transmission beyond the range of *C. imicola*, indicating a vector role for other *Culicoides* species in these areas.

The marked changes in the epidemiology of BT do not seem to be caused by biotic factors (for example, pathogen characteristics and host distribution or movements). Furthermore, the increased transmission of BTV in Europe is unlikely to be due to the circulation of new, more virulent strains of BTV — the strains that are involved are closely related to those that have been circulating in the region for several decades (BOX 1). Although small genetic changes in RNA arboviruses can have marked changes on viral phenotype[72], it is difficult to envisage a factor that would select for such small changes simultaneously and independently in six lineages of BTV, and that would select for them now rather than at any other time in the past few decades.

Although the increase in trade between Europe and the Middle East[73] might have slightly increased the number of host-animal movements, the total number of ruminants has declined since the 1980s, particularly in central areas of Europe[74].

Non-climatic, abiotic factors (such as socio-economy, land use and animal health systems) also seem unlikely to be responsible. Vector species of *Culicoides* breed in a range of moist microhabitats (such as irrigation channels, drainage pipes and dung heaps) that are ubiquitous across many farmyard types. Their distributions should therefore have remained relatively unaffected by changes in agricultural practice or land use.

Most wild-type strains of BTV are highly virulent when they are first introduced into populations of naive, European sheep breeds, so any previous incursions are unlikely to have gone unreported despite recent improvements in animal health and surveillance systems. Control strategies against BTV in fringe regions have also remained relatively unchanged for several decades, with only a few countries using the polyvalent, live-attenuated vaccines on either an *ad hoc* (such as Turkey and Cyprus) or annual (such as Israel) basis.

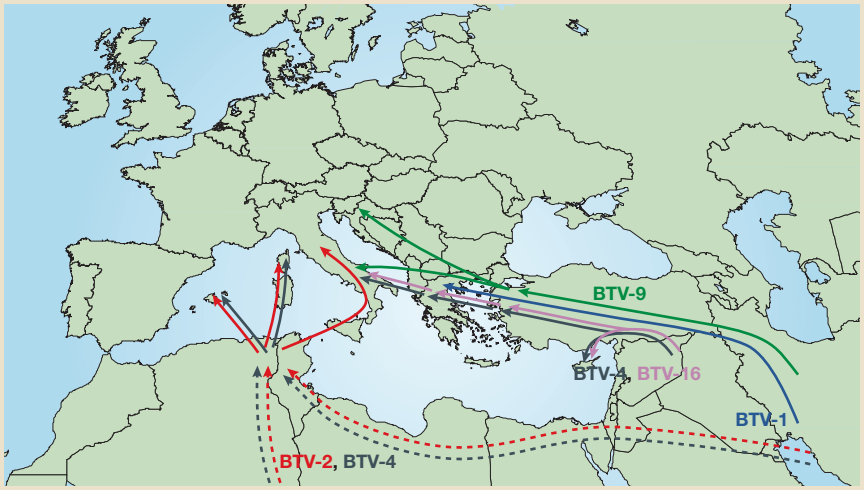
Examining responses to recent, unprecedented climate change across a range of biological systems, Walther *et al.*[75] stated that the "clearest evidence for climate trigger occurs where a suite of species, with different histories of introduction, spread *en masse* during periods of climate amelioration", which is analogous to the more-or-less simultaneous entry of six BTV strains into Europe. As we show in this article, a direct, causal link between BTV emergence in Europe and climate change can be inferred because the nature of the responses of these pathogens adheres

Box 1 | The molecular epidemiology of BTV in Europe

The advent of new, high-throughput sequencing technologies has led to the development of nucleotide and amino-acid sequence databases (containing geographically and temporally referenced isolates) for many pathogens. Analysis of such sequence variation enables the rapid typing of viral populations and identification of the origins of new viral strains[130–132]. A sequence database has recently been established for bluetongue virus (BTV), which contains full-length sequences of the two most variable BTV genome segments, Seg-2 and Seg-6, which encode the outer capsid proteins VP2 and VP5, respectively (see the BTV sequence database in the Online links box). This includes data for reference strains of all 24 serotypes[133,134], additional wild-type virus strains and some live attenuated vaccine strains.

Sequence analysis of the five European BTV serotypes has identified six lineages, which have arrived from at least two sources (see the map, which shows the spread of BTV-1, -2, -4, -9 and -16). The European strain of BTV-1 (Greece 2000/01) belongs to an 'eastern' group of viruses and is similar to viruses that have been isolated in India. By contrast, the European strain of BTV-2, which first appeared in Tunisia in 1998, belongs to a 'western' group of viruses and is similar to strains from South Africa, Nigeria, Sudan and the United States. BTV-2 entered Europe from the south (possibly from sub-Saharan Africa where it is endemic[21]), or could have moved westward through north Africa, via routes previously implicated in the movement of foot-and-mouth disease virus (as a result of animal trade)[131].

The sequence analysis of the other European BTV types indicates that BTV-9 and BTV-16 belong to 'eastern' groups, whereas the European type 4 strain that was initially isolated in Greece in 2000, is similar to viruses that have periodically been isolated from the region since 1969. This indicates that it might have been circulating in the fringes of Europe for many years. However, in late 2003, a new strain of BTV-4, which is distinct from that seen in Greece and Turkey, arrived in Corsica and the Balearics, and therefore might have arrived from north Africa. None of the BTV strains involved in the recent outbreaks is closely related to the vaccine strains currently in use, indicating that vaccine breakdown has not had a role in BTV emergence in Europe. Importantly, distinct strains are still entering Europe on an annual/bi-annual basis.



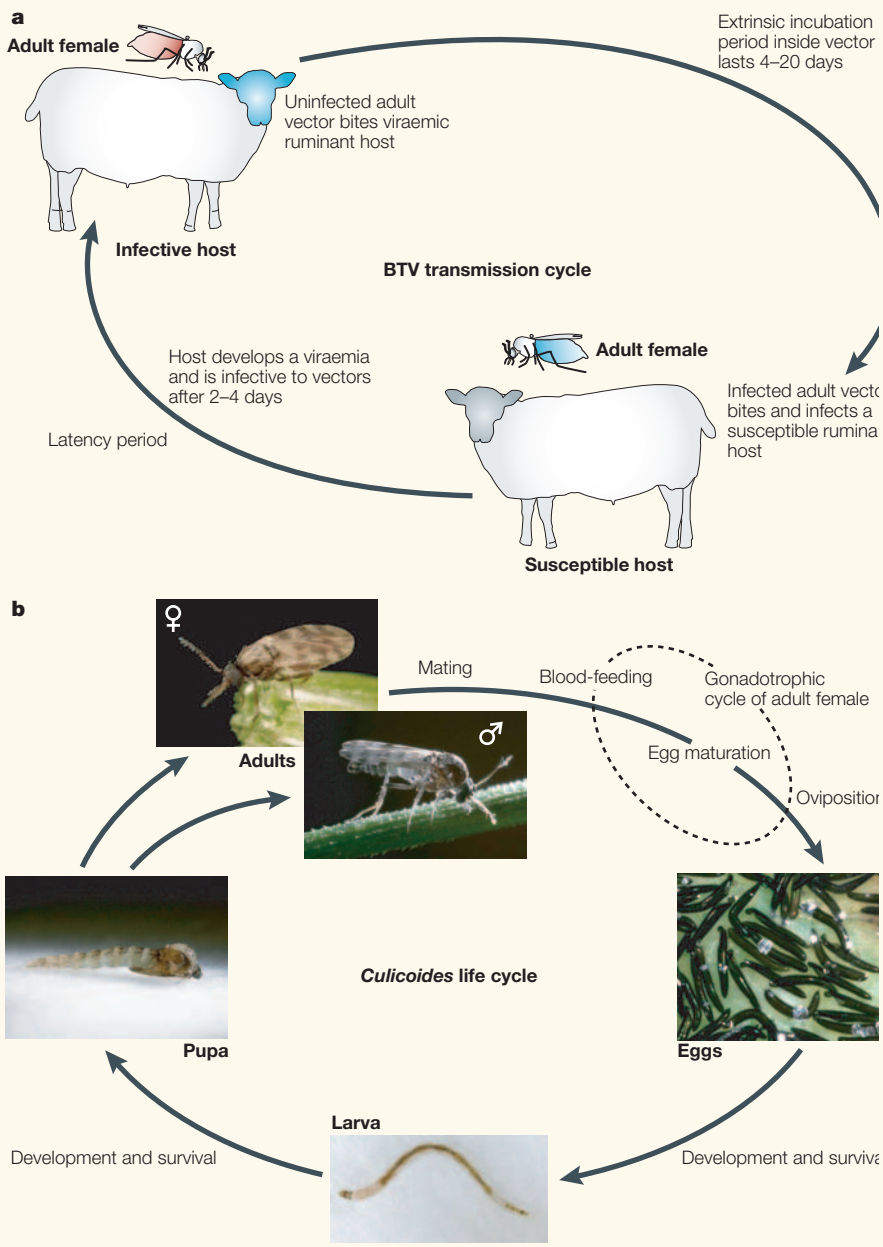


Figure 2 | **The transmission of BTV is affected by changes in temperature.** The transmission cycle of bluetongue virus (BTV) is summarized in (**a**) and the life cycle of the *Culicoides* vector is summarized in (**b**). The extrinsic incubation period of BTV involves the entry of virus into the midgut of the *Culicoides* vector, dissemination through the haemocoel and subsequent infection of the salivary glands. The efficiency of heritable barriers to virus dissemination by the vector might be affected by temperature. Temperature influences vector competence and the rate of virogenesis in *Culicoides*. Temperature also affects most stages of the *Culicoides* life cycle, including the survival of adults and larvae through the winter months (enhanced by high winter temperatures), recruitment to the adult population and activity rates of adult *Culicoides*. Most stages of the *Culicoides* life cycle are also affected by the availability of moisture. Breeding habitats are semi-aquatic — larvae and pupae require moist habitats and adults are prone to dessication.

closely to the criteria that has been set out by earlier researchers[11,15,16]. Several areas of research (for example, theoretical model systems, laboratory experiments and field manipulations and observations) have demonstrated the biological sensitivity of both *Culicoides* vectors and BTV to changes in climatic conditions[16,76]. There is also sufficient meteorological evidence of climate change with sufficient measurements in the study region[16], and significant changes in the climatic drivers of infection have occurred at the same times and in the same places in Europe as changes in the incidence of BT[11].

Sensitivity of BTV to climate

For BTV transmission to occur, a competent adult *Culicoides* vector must feed on a viraemic host and must ingest sufficient virus to exceed its infection threshold. The vector must then survive both the extrinsic incubation period of the virus and the interval to a subsequent blood meal and must then feed on a susceptible host (FIG. 2a). These important events in the BTV transmission cycle are modulated by temperature and moisture availability, and the probability of their completion to effect transmission is relatively low. The large abundances of *Culicoides* vectors under favourable summer/autumn conditions often compensate for this by imposing very high vector–host contact and biting rates.

Considering these climatic effects in more detail, temperature modulates most stages of the *Culicoides* life cycle[8,77] (FIG. 2b). In the seasonal climates of temperate regions, a cold winter or a hot dry summer could substantially reduce vector populations, even if conditions are favourable for most of the year. The starting point for recruitment to the adult population in the spring depends, however, on the survival rates of adults and larvae through the winter, which are enhanced by high winter temperatures — at least 8 months with a mean temperature >12.5°C favoured the presence of *C. imicola* at sites in Iberia[78]. Recruitment to the adult population tends to be optimal in summer/autumn in intermediate temperature ranges (25–30°C), but is inhibited below a threshold temperature of about 8–10°C. The activity rates of adult *Culicoides* in summer/autumn are increased by warm conditions (that is, 18–29°C; REF. 79), particularly at night time as adult *Culicoides* are most active at sunset and sunrise.

Temperature also directly influences the competence of the *Culicoides* vector[80,81] and the rate of virogenesis within individuals[82]. This is partly because *in vitro* viral synthesis (which is dependent on the activity of the RNA-dependent RNA polymerase) is optimal at 28–29°C, but is inhibited below 10°C (REF. 83). Temperature might also affect the efficiency of heritable barrier mechanisms that constrain virus dissemination by an individual vector at various stages after oral infection[84]. These barriers might prevent infection of the midgut or ovaries, or might restrict the virus to the midgut cells or to fat cells even if the virus enters the HAEMOCOEL. Even at low temperatures (for example, <10°C), however, the virus can persist at low titres for up to 35 days inside adult vectors, and is later able to replicate and be transmitted when the temperature increases (as would occur when spring follows a short winter).

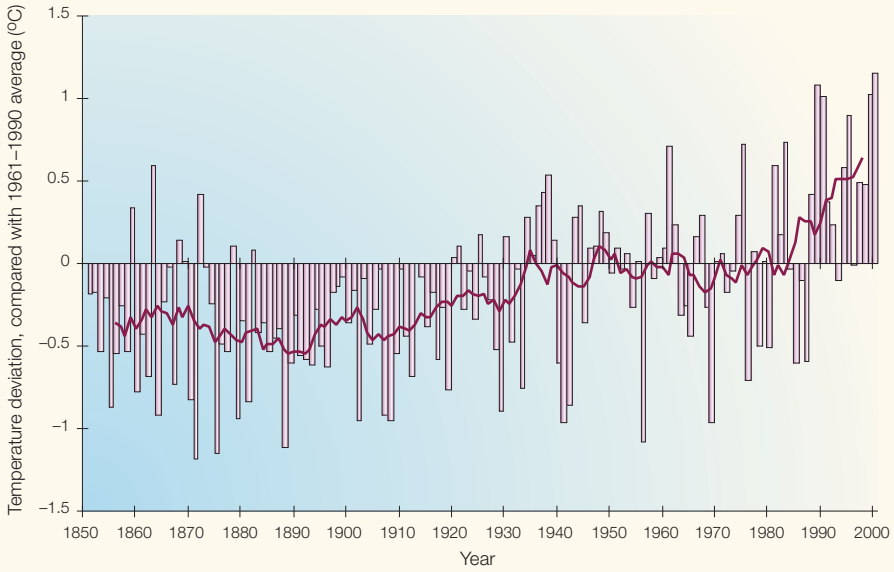


Figure 3 | **Recent warming trends in Europe.** This graph shows the observed annual temperature deviations in Europe over the past 150 years (1850–2000) compared with the 1961–1990 average (°C). Superimposed as a continuous line is the 10-year smoothed trend of these annual temperature deviations. Modified with permission from REF. 144 © (2004) EEA.

The resulting transmission potential of BTV is very sensitive to the balance between the extrinsic incubation period (which is determined by viral replication rates and thus decreases at higher temperatures[80,81,85] such that it lasts 6–8 days at 25°C but only 4 days at 30°C) and the daily survival probability of adult *Culicoides* (which is optimal at 10–20°C and markedly reduced at 30°C). The transmission potential in vector species is therefore probably maximal in summer/autumn at intermediate (approximately 28°C) rather than higher temperature ranges.

However, in 'non-vector' species, only these higher temperatures induce competence. In *Culicoides nubeculosus*, for example, more than 10% of emerging adults can become orally infected after a single infected blood meal when the immature stages have been reared at 33–35°C compared with 0% when the immatures have been reared at 30°C (REF. 85). This phenomenon has been attributed to the leakage of virus directly into the haemocoel, which bypasses the midgut barriers and allows virus replication and dissemination. Considering vector and non-vector species together, an increase in the cumulative frequency of either warm or hot periods in summer/autumn might increase the transmission potential of BTV.

Moisture availability is the second most important extrinsic variable that affects BTV transmission. Precipitation affects not only the size and persistence of semi-aquatic breeding sites[8], but also the availability and duration of humid microhabitats in summer/autumn where adults can carry out important activities and shelter from dessication[86]. Suitable habitat patches are initially colonized by movement of adult *Culicoides* that are dispersed passively on the wind. The direction and extent of this dispersal depends on wind movements (for example, speed, direction and frequency). Medium wind speeds (<8 km per hour) are particularly favourable for this dispersal, especially when combined with thermal conditions that maximize the survival of adults during movement[87].

These interacting effects of climate are manifested in the spatial and temporal distributions of *Culicoides* vectors. In both South Africa and Kenya, the seasonal abundance of adult *C. imicola* depends on the amount of rainfall during the preceding months[88,89]. In Iberia, Morocco and South Africa[90–94], distribution models for *C. imicola* have highlighted the importance of annual average temperatures of the coldest and warmest months, the number of months with mean temperatures above 12.5°C (REF. 78) and a satellite-derived measure of vegetation activity, the NORMALIZED DIFFERENCE VEGETATION INDEX (NDVI), which is correlated with both vegetation biomass productivity and the amount of soil moisture[95]. The latter association arises because rates of both plant photosynthesis and recruitment of *C. imicola* are highest in microhabitats with high levels of soil moisture because this species breeds in wet, but not flooded, organically enriched soil and mud[96,97].

If the various (independent and sometimes opposing) responses of these biological processes to climate are considered together, it is likely that increases in temperature (particularly at night-time and in winter), as well as increases in precipitation (particularly in summer/autumn) will lead to an increased geographical and seasonal incidence of BTV transmission by increasing the range, abundance and seasonal activity of vectors, increasing the proportion of a vector species that is competent and by increasing the development rates of the virus within vectors, thereby extending transmission ability to further *Culicoides* species. More frequent extreme weather events (particularly winds) could increase vector dispersal, thereby aiding colonization events and leading to disease outbreaks in new areas. But have European climates changed in recent years in ways that might increase the incidence of BTV, and in the regions to which BTV has now spread?

Climate change in Europe and BT

Recent climate changes in Europe. The emergence of BT in Europe has occurred during the second of two main periods of warming in the twentieth century (1976–2000), which included the warmest decade (the 1990s) on record. European temperatures have increased by approximately 1.2°C over the past 100 years — twice the average global rate[98] (FIG. 3). The effect of warming is most pronounced on night-time temperatures[99] and winter temperatures[100], which has resulted in fewer frost days[101–103]. The average annual precipitation and the number of wet days have increased in the north but decreased in the south of Europe[99,101,104]. Therefore, there have been marked changes in the climatic drivers of BTV infection (mean winter and night-time temperatures and mean moisture levels) in Europe at the same times as the emergence of BT.

We have quantified changes in temperature and precipitation between the 1980s and the 1990s (which correspond to before and during the current BT epidemics) using monthly climate surfaces from the Climate Research Unit at the University of East Anglia, UK[105]. The change in average temperature and precipitation minima from the 1980s to the 1990s are shown in FIG. 4a and FIG. 4b, respectively.

BT incidence and climate change. BT incidence has increased most markedly in areas where temperature increases are greatest (yellow, orange and red areas in FIG. 4a) in both central (Italy, Corsica and the Balearic Islands) and eastern Europe (western Bulgaria, northern Greece, Albania, the former Yugoslav Republic of Macedonia, Bosnia and Herzegovina,

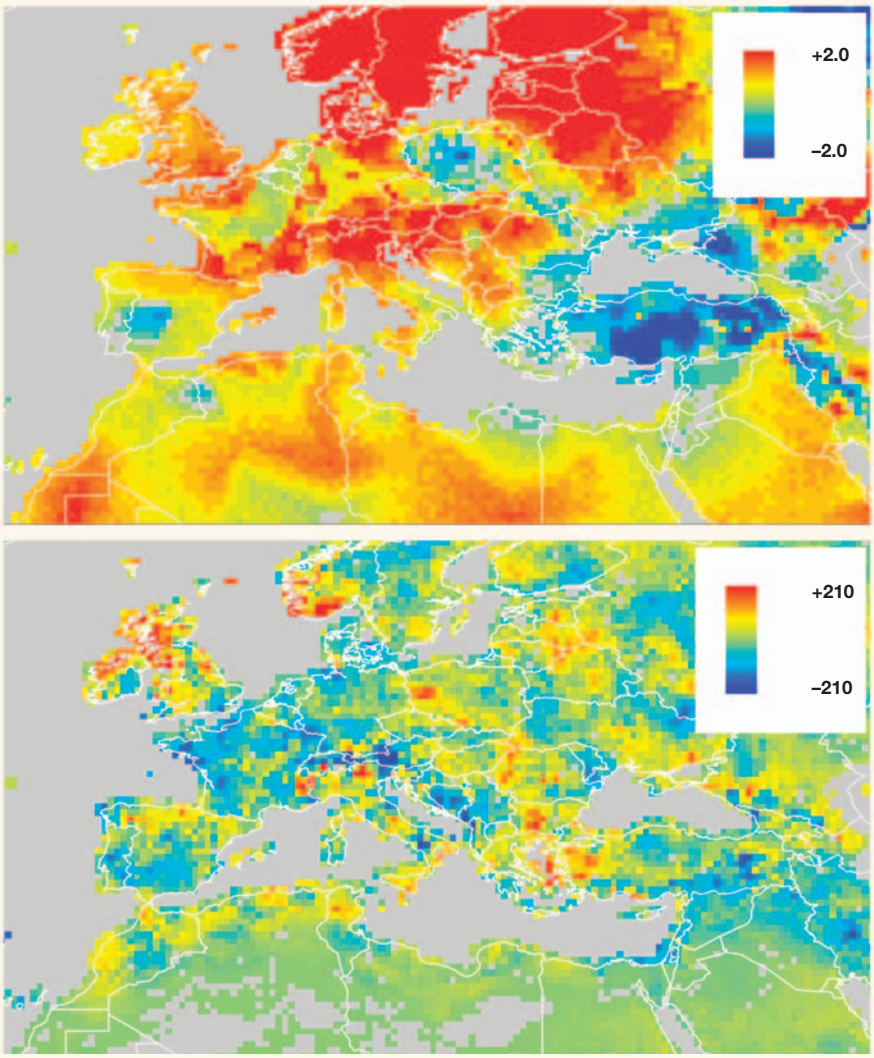


Figure 4 | **Fourier images of spatial variation in recent climate change in Europe.** **a** | The changes in annual minimum temperatures in 0.1°C between the 1990s and 1980s for each 0.5° square of longitude and latitude, on a sliding colour scale ranging from a reduction of 2.0°C (dark blue and –2.0 on inset legend) to an increase of 2.0°C (dark red and +2.0 on inset legend). **b** | The changes in annual mean precipitation in mm between the 1990s and 1980s for each 0.5° square, on a sliding colour scale ranging from a reduction of 210 mm (dark blue) to an increase of 210 mm (dark red). Temperature increases are most marked in both central (Italy, Corsica and the Balearic islands) and eastern Europe (western Bulgaria, northern Greece, Albania, the former Yugoslav Republic of Macedonia, Bosnia and Herzegovina, Serbia and Montenegro, and Croatia), whereas central Iberia and the region around the border between northern Morocco and Algeria have cooled. The pattern of changes in annual precipitation levels are less spatially coherent, with the United Kingdom, northern Iberia, Scandinavia, eastern Europe and western Turkey amongst the areas becoming wetter, and southern Iberia, France, Germany and eastern Turkey amongst the areas becoming drier. To produce these images, continuous monthly climate surfaces (dataset CRU TS 2.0; see the Online links box), constructed by interpolating between ground stations, were obtained from the Climate Research Unit (CRU) at the University of East Anglia, UK[105], at a spatial resolution of 0.5° longitude and latitude (pixel sizes of approximately 50 km^2). The time-series for the 1980s (1980–1989) and 1990s (1990–1999) were FOURIER PROCESSED to extract information about the seasonal (annual, bi-annual and tri-annual) cycles of precipitation and rainfall in each pixel in each decade. Climate-change images were then created by subtraction of the 1980s values from the 1990s values for each seasonal Fourier-processed variable. As the distribution of ground stations across Europe and the Mediterranean is dense and has not varied appreciably between 1980s and 1990s, the changes quantified in the images should not be reflective of changes in station representation.

Serbia and Montenegro, and Croatia). There was little change in minimum temperatures in the BT-affected areas of southern Greece, the Greek islands, southern Bulgaria and Cyprus, but these areas were already sufficiently warm to support BTV transmission; for example, BT occurred sporadically in the Greek islands before the 1980s (REF. 54). The extensive 'cooled' areas (FIG. 4a, blue areas) in central Iberia and along the border between northern Morocco and Algeria might have slowed or prevented the re-entry of BTV into areas of western Europe that were affected in previous epidemics. However, BTV was detected very recently in Morocco[106] (September 2004), mainland Spain (October 2004) and Portugal[106], indicating that the virus has eventually circumvented this barrier (several years into the epidemic). The subsequent progress of the virus from this historical source area could yet indicate whether areas of central Iberia have cooled sufficiently to become unsuitable for BTV transmission.

In general, BTV may not yet have occupied all climatically suitable sites in Europe. Many areas north of the current northern limit of BTV have warmed as much or more than currently affected areas but are still too cool to be suitable for BTV transmission (for example, Scandinavia and mountainous regions of Italy and Switzerland). Other 'warmed' areas in southern and western France, and in the south-western United Kingdom have among the highest population densities of small ruminants in Europe[74], making them likely candidate regions for future spread (dependent on the direction and rates of movement of infected midges or ruminants). In eastern Europe, further spread to the north might be limited by the 'cooled' band along the north Balkans. Several mechanisms might underlie these responses of BTV to climate change in Europe.

Extending distribution of the major Old World vector. Areas that have cooled or shown no temperature changes over the past decade (FIG. 4a) have also shown no changes in the distribution of *C. imicola* (for example, northern Portugal[107] and central Spain[108]; A. Martinez-Salvador, personal communication). By contrast, this vector has spread into areas that have shown obvious warming (for example, north-eastern Spain, southern France, northern Italy and north-eastern regions of Greece). The most northerly detection of a *C. imicola*-infected individual is in Ticino province in Switzerland (A. Cageniard, personal communication), an area that has experienced one of the greatest temperature increases in Europe[109].

Although temperature is an important determinant of the distributional limits of BTV and its vectors in cooler regions (for example, northern Iberia[82]), which are generally wet enough to support larval development, moisture levels limit vector abundance in warmer areas. NDVI time-series data indicate that plant growing seasons, which

can be inferred from high NDVI periods, are lengthening across Europe as the onset of recent springs (1997–2001) have been estimated to occur 25 days earlier on average in eastern Europe[110], where the distribution of *C. imicola* has recently expanded into mainland Greece and European Turkey. Therefore, given the adequate moisture levels of historically cool Europe, it is recent changes in temperature rather than precipitation that are likely to be responsible for the northward spread of *C. imicola* in Europe. This accounts for the poor spatial correlation between changes in precipitation levels since the 1980s and the current incidence of BT and distribution of *C. imicola* (FIG. 4b).

The extent to which *C. imicola* has or will expand into habitats that become newly permissive in Europe depends on natural and wind-dispersed movements from existing occupied patches. Colonization distances of *C. imicola* of about 200–300 km were recorded in the 1990s (200 km between the Balearic Islands and north Africa, 160 km between Corsica and southern France, and 300 km between Lesvos and mainland Greece), which are comparable to range shifts that have been documented for other vectors, such as the mosquito *Aedes albopictus* that moved southwards at a rate of 65 km per year in Florida after its introduction into the United States[111]. Highly dispersive vectors such as *C. imicola*, for which habitats are fairly ubiquitous (see above), are likely to track shifts in their CLIMATIC ENVELOPES relatively rapidly, whereas high reproductive rates might allow more rapid adaptation to new environments[112].

Involvement of novel vectors. The expansion of BTV into areas where *C. imicola* is rare or absent (such as Bulgaria, the Balkans, northwestern Greece, European Turkey and some areas of Sicily, Lazio and Tuscany in Italy) has been facilitated by the involvement of novel vector species[5]. Two widespread and abundant PALAEARCTIC species groups (the *Culicoides obsoletus* group and *Culicoides pulicaris* group) comprise large proportions of trapped *Culicoides* populations in these areas and show fine-scale spatial correlation with BT outbreaks[70,113]. BTV has been isolated from wild-caught individuals of both groups during the current outbreaks (from the *C. obsoletus* group in Italy (REF. 114; C. De Liberato and P. Scaramozzino, personal communication) and from *C. pulicaris* in Sicily[115]). VECTOR-COMPETENCE studies so far indicate low oral-susceptibility rates of these groups to BTV[116], but the recent climate warming in Europe might have increased their importance — by increasing their population sizes and survival rates to compensate for their low competence levels, and by increasing their individual susceptibility through the developmental temperature effects described above. The role of these groups in the transmission of BTV is of real concern as they are common and widespread across the whole of central and northern Europe (FIG. 1b, green and yellow lines).

The increased duration of permissive temperatures for adult *Culicoides* activity in summer and autumn, together with the geographical expansion of *C. imicola*, has increased its spatio-temporal overlap with potential novel vectors. Such overlap enables a 'hand-over' of infection from the subtropical *C. imicola* to the novel, temperate-region vectors[2]. During the current epidemic, in Sicily, Lazio and Tuscany, BTV was initially transmitted in lowland areas by *C. imicola* but was then transferred to *C. pulicaris* and *C. obsoletus* groups, which spread BTV inland[70,113].

Increased duration of adult vector activity might have increased the likelihood of continuous BTV transmission cycles (between adult vectors and hosts) during the winter in many areas of Europe. However, BTV-9 has over-wintered in the Balkans, where long cold winters reduce adult *Culicoides* populations to extremely low levels for several months[8]. BTV transmission (as demonstrated by seroconversion or disease) was not detected during the winter and spring period, indicating that other covert mechanisms of persistence are involved.

Over-wintering of BTV in cool regions. Cold winters often end vector-borne disease episodes by killing virtually all of the adult vectors and thereby preventing transmission for several months of the year. Indeed, it has been noted for more than a century that episodes of AHSV in South Africa are terminated by frost[117]. Over-wintering under such conditions can be difficult to explain. Yet this has been the case for BTV-9, which has recrudesced annually over a 6-year period in the Balkans, a region where reincursion by infected *Culicoides* or animals from other infected regions has, for the reasons stated above, been unlikely. The survival of BTV in the over-wintering larval stages of the vector through TRANSOVARIAL TRANSMISSION is also unlikely. Although the S7 genome segment of BTV has been detected in over-wintering vector

Glossary

CLIMATIC ENVELOPE
The range of climatic variation in which a species can currently persist in the face of competitors, predators and disease.

EL NIÑO SOUTHERN OSCILLATION
A periodic ocean–atmosphere fluctuation in the Pacific Ocean that is an important cause of inter-annual climate variability around the world and which is particularly associated with drought and flood events.

FOURIER PROCESSING
A mathematical technique that expresses a time-series as the sum of a series of sine waves and which is used by climatologists to summarize the seasonal cycles (annual, bi-annual, tri-annual) of multi-temporal climate data.

HAEMOCOEL
The main body cavity of many invertebrates, including insects, that is formed from an expanded 'blood' system.

NORMALIZED DIFFERENCE VEGETATION INDEX (NDVI). A remotely sensed satellite-derived measure of the radiation absorbed by chlorophyll during plant photosynthesis that is a correlate of soil moisture, vegetation biomass and productivity.

OVER-WINTERING
The persistence of a virus in a location between one vector transmission season and the next: by persistence within surviving adult vectors themselves, within the juvenile stages of the vectors following trans-ovarial transmission or by prolonged/persistent infection in viraemic or aviraemic vertebrate hosts.

PALAEARCTIC
One of the eight ecozones into which the world is divided, which extends across Europe, north Africa and north Asia, north of the tropics.

RUMINANT STREET
The 'corridor' between south Asia and Europe that is formed from the connected ruminant populations of Pakistan, Afganistan, Iran and Turkey.

SEROTYPE
An antigen or group of antigens that provokes a specific antibody response in the host that is distinct from those produced against other viruses of the same species.

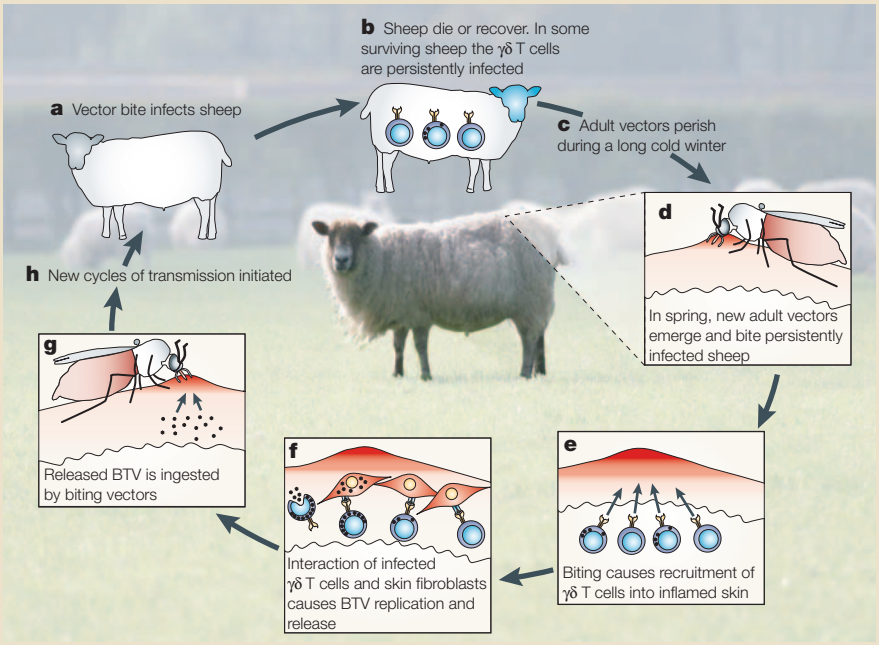
SYNOPTIC WEATHER SYSTEMS
High- and low-pressure systems of the lower atmosphere operating at space and timescales approximately corresponding to those of mid-latitude depressions — spatial scales of several thousand kilometres and timescales of several days.

γδ T CELLS
A subset of T cells that are predominant in skin and mucosal tissues. They probably act as a first line of defence against infection and cancer and have immunoregulatory functions.

TRANSOVARIAL TRANSMISSION
The transmission of microorganisms between generations of hosts via the eggs (vertical transmission).

VECTOR COMPETENCE
The (innate) ability of a vector to acquire a pathogen and to successfully transmit it to another susceptible host.

Box 2 | **A possible over-wintering mechanism for BTV in the absence of the insect vector**



Bluetongue virus (BTV) is transmitted between its ruminant hosts by the bites of the vector species of *Culicoides* biting midges, but adverse climatic conditions that occur during winter can kill the adult vectors. Conventional models of the life cycle of BTV therefore indicate that under such conditions the virus should be unable to persist. However, epidemiological evidence indicates that, in the recent BTV epidemics in Europe, the virus has persisted over several years even in locations where adult vector populations are small or absent for several months each year. In the light of these observations, Takamatsu *et al.*[135] carried out preliminary experimental work in sheep and have postulated a novel over-wintering mechanism for this pathogen as outlined in the figure.

The figure shows how, on being bitten by an infected adult *Culicoides* vector, ruminant hosts become infected with BTV (a). In some infected hosts, the virus establishes a persistent infection of γδ T CELLS. Surviving animals will be seropositive and aviraemic, but will still carry BTV in their γδ T cells (b). In such apparently recovered animals the virus persists, covertly, over the cold vector-free winter months (c). In the following spring, new vectors emerge and commence biting ruminants, some of which are persistently infected (d). Vector biting causes localized skin inflammation, which initiates the recruitment of inflammatory cells, including infected γδ T cells, into the inflamed areas (e). In the skin, interactions between the skin fibroblasts and the γδ T-cell-specific surface molecule WC-1, causes growth arrest in the infected γδ T cells and, through a mechanism that is not fully understood, converts the BTV persistent infection to a productive, lytic infection. This results in BTV replication, cell death and release of the virus into the skin at locations where the vectors are biting (f). The released virus is ingested by the vector *Culicoides*, infecting the vector (g) and initiating a new transmission cycle (h).

In support of this mechanism, Takamatsu *et al.*[135] showed that BTV could persistently infect the γδ T cells of sheep *in vivo* and *in vitro*. When these infected T cells were mixed with sheep fibroblasts in the laboratory, the resultant conversion to a lytic infection increased BTV production 1,000-fold. In sheep, biting by vectors 35 days after the end of viraemia caused an inflammatory response and accumulation of γδ T cells in the skin, and BTV was recovered from skin biopsies at 63 days post-infection. BTV has not yet been recovered from fed vector insects.

larvae in the United States[118], infectious BTV has never been recovered[119,120] — either from over-wintering larvae or from adults derived from these larvae. Indeed, none of the >50 viruses associated with *Culicoides* has been shown to be transovarially transmitted[8]. Interestingly, an elegant mechanism has recently been described that postulates how BTV might be able to over-winter covertly in the ruminant host itself. The basis of this mechanism is described in BOX 2.

Conclusions and future prospects

At least six strains of five serotypes have been involved in the recent unprecedented emergence of BTV across much of southern and central Europe. These changes in BT incidence in Europe have been matched by spatio-temporal changes in regional climates, including the specific climatic drivers of BTV infection. The remarkable spatial congruence that has been observed compensates for the relatively short time period of observation and supports the idea of a causal link between the alterations in BTV distribution and climate change. Interestingly, the timing of epidemics of AHSV over the past 100 years in South Africa has been linked to combinations of drought and rain caused by specific warm phase EL NIÑO SOUTHERN OSCILLATIONS[121]. As the climatic drivers of AHSV and BTV are broadly similar (being transmitted by the same *Culicoides* species and having similar thermal requirements for virogenesis[122]), we predict that the potential distribution of AHSV in Europe has also been extended into the same or similar locations by recent climate change. Although the nearest sources of infection in sub-Saharan Africa are too remote for incursion by wind-borne infected midges, the future introduction of AHSV-infected equines might be expected to produce much more extensive and persistent epidemics further north in Europe than those seen following previous similar introductions.

For several reasons, statistical validation of the spatio-temporal correlation between changes in BTV incidence and climate change was not sought. Many diseases and disease vectors are not routinely surveyed across regions in advance of their emergence. Therefore, the vector and virus surveillance data are sufficient to approximate the extent of the current and past distributions of BTV and *C. imicola* in Europe, but are available at a low resolution compared with climatic datasets and coverage is not complete throughout the region of study. Considering livestock data, current population densities are available on a country level, but data on changes in population density for particular livestock types or on the direction and extent of animal movements do not exist in a form that is compatible with the climate-change data. Such statistical analyses will be the subject of future analyses for particular countries in the study region when data become available. The spatio-temporal association

between changes in BTV incidence and changes in temperature are, nevertheless, compelling, having involved several strains entering Europe from several different directions. Changes in other factors (such as agricultural land-use changes, changes in animal health systems, increases in livestock trade and increases in host density) cannot be shown to follow a similar geographical pattern.

Although climate change has redefined the distributional limits of BTV and its vectors in Europe, local transmission risk will depend on complex local interactions between a range of abiotic and biotic factors — the challenge for risk prediction is to understand these interactions at a finer spatial resolution[123].

Other vector–pathogen systems might undergo a similar climate-driven emergence and it is instructive to identify the features of the BTV–*Culicoides* system that cause it to respond most strongly to climate changes. Unlike most viruses[124], BTV is promiscuous between many host and vector species. Most infected ruminants are subclinically infected and most infections are neither identified nor removed rapidly from the population and so persist as sources of infection for vectors. Furthermore, ruminants tend to be widely distributed and abundant across most agricultural systems.

Each of the three vector *Culicoides* groups in Europe are widespread and abundant, and each has a different distribution (FIG. 1) and climatic envelope[94] for BTV to exploit. The presence of two 'new' groups of *Culicoides* vectors indicate the considerable ability of BTV to adapt quickly to vectors in new regions. Vector competence should therefore be considered a dynamic, sometimes climate-mediated, component of a pathogen's biotic environment. In general, compared with other vectors, *Culicoides* are highly dispersive, capable of reproducing rapidly and are habitat generalists. They occupy, and are able to track shifts in, a range of moist soil/dung microhabitats in farmyards that not only are ubiquitous across different agricultural systems but usually contain susceptible hosts. *Culicoides* vectors have non-specialized biting habits, feeding on any available large mammals, and therefore their distribution and abundance is rarely host limited[90], precluding the significant reduction of transmission by diversion of biting pressure away from susceptible hosts[17]. It is hard to envisage land use or agricultural changes that would have a similar effect to the draining of marshes that reduced *Anopheles atroparvus* mosquito populations and malaria incidence in the nineteenth and twentieth centuries in Britain[17,125] and that could appreciably reduce the distribution of suitable microhabitats for *Culicoides* vectors or allow for their separation from susceptible hosts. By contrast, other vectors, such as ticks and sandflies, are associated with particular, patchily distributed land cover or vegetation types (such as bracken and forest[126,127]) and ticks also rely on the movement of the hosts through these suitable microhabitats[19].

Vector-borne pathogens that share some combination of these characteristics (that is, rapidly evolving, promiscuous agents, transmitted by rapidly reproducing, highly mobile, habitat-generalist vectors) will also probably respond rapidly to increased climatic suitability in Europe. The recent emergence of West Nile virus (a flavivirus) in the United States was attributed to its promiscuity between more than 30 vector species of mosquito and at least 150 bird species — each with different residence ranges or migration routes across north and central America[124]. West Nile virus has also recently re-emerged in Russia, Italy[95] and France. Another pathogen, Rift Valley fever virus (RVFV) (a member of the genus *Phlebovirus* in the Bunyaviridae), is highly promiscuous between vertebrate hosts, ranging from rodents to hippopotamuses, but causes clinical signs only in ruminants and humans. This virus has been isolated from many potential vector species (including 23 mosquito species, a *Simulium* sp. and a *Rhipicephalus* tick[128]) inhabiting a range of habitat types. Epidemics in south and east Africa follow periods of high rainfall that create breeding sites for flood-water vectors (*Aedes* mosquitoes), whereas those in north and west Africa, have followed construction work that created breeding sites for large river and dam-breeding vectors[111]. In 2000, strains of RVFV (that probably originated in east Africa) escaped from Africa for the first time and infected the Arabian Peninsula, an area well connected to Europe by a 'ruminant street'[129]. The timing and mode of pathogen responses will obviously depend on the species-specific climatic drivers.

The continuing entry of new BTV strains into Europe (BOX 1) is likely to be exacerbated in the future by further climatically induced increases in vector competence and extensions in vector distribution and seasonal activity. New strains of BTV might also arise, through re-assortment (exchange of genome segments) of an increasing number of wild-type strains, and between wild-type strains and the live vaccine viruses that have been used in several countries. These vaccines have been shown to cause levels of viraemia in some vaccinated animals that are sufficient to infect *Culicoides* vectors and facilitate their transmission in the field. In the absence of effective inactivated vaccines or targeted vector control programmes, the long-term outlook for BT (and AHS) in Europe is for more disease over a wider area for a longer period of time.

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Competing interests statement

The authors declare no competing financial interests.

Online links

DATABASES

The following terms in this article are linked online to:
Entrez: http://www.ncbi.nlm.nih.gov/Entrez/
Bluetongue virus

FURTHER INFORMATION
BTV sequence database: http://www.iah.bbsrc.ac.uk/dsRNA_virus_proteins/ReoID/BTV-isolates.htm
Ceratoponidae Information Exchange: http://www.belmont.edu/Science/Biology/cienews/
Climate Research Unit: http://www.cru.uea.ac.uk/
CRU TS 2.0 dataset: http://www.cru.uea.ac.uk/~timm/grid/CRU_TS_2_0.html
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CORRIGENDUM

Climate change and the recent emergence of bluetongue in Europe

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On page 172 of the above article, we wrote that: "In subsequent years up to 2004, BTV-9 spread northward (into western regions of Turkey, Bulgaria, Kosovo, Albania, Bosnia and Herzegovina, the former Yugoslav republic of Macedonia, Serbia and Montenegro, and Croatia) and westward (into mainland Greece, Italy, Sicily, Sardinia and Corsica)." In fact, BTV-9 has not been recorded in Sardinia and Corsica. Only three serotypes BTV-2, BTV-4 and BTV-16 have been detected on each of these islands. The authors apologize for this error.