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EPIDEMIOLOGY AND ANIMAL DISEASE CONTROL PROGRAMMES BLUETONGUE IN NORTHERN EUROPE: APPEARANCE OF NEW SEROTYPES WITHIN AN ENZOOTIC GROUND

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ABSTRACT

Due to its significant socio-economic impact and its major repercussions on international trade in animals and animal products, bluetongue is a disease that must be notified to the World Organisation for Animal Health (OIE) (7, 8). In August 2006, the unexpected emergence of bluetongue virus serotype 8 (BTV-8) in northern Europe caused an unprecedented epizootic of bluetongue, which affected cattle more than previously (exacerbated virulence with the appearance of severe clinical signs including reproductive disorders) and was carried by culicoid vectors indigenous to northern Europe. New elements dating from 2008 are described in this update, which postdates the publication by the World Organisation for Animal Health of 'Bluetongue in northern Europe' (10).

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Spread of bluetongue virus infection in northern and Mediterranean Europe in 2008

Between the first declaration (17 August 2006) and 1 February 2007, 2,122 outbreaks of bluetongue were recorded in the European Commission's Animal Disease Notification System (ADNS). The first new upsurge of bluetongue (BTV-8) in Belgium, Germany, the Netherlands, northern France, and Luxembourg in 2007, its subsequent spread to other countries (Denmark, Czech Republic, Switzerland, Italy) and its incursion into the United Kingdom were reported. A second upsurge in 2008, notably in France, and its further spread to Austria, Spain and Sweden suggest that bluetongue has become enzootic in northern Europe (9). The inexorable spread of BTV-8 through Europe, coupled with the recent progression of BTV-1 in the southwest of France from outbreaks in Spain, increases the risk of combined infection by both these serotypes, as well as between these and other serotypes, in particular those circulating in the Mediterranean basin. Nor can we rule out the possibility of the latter serotypes spreading from the Mediterranean zone to more northern latitudes. This progression also increases the risk of BTV-8 reaching a geographical zone where the vector *Culicoides imicola* is present and active for a longer period of the year, which could influence the occurrence of BTV-8 outbreaks. Weekly changes in the number of bluetongue outbreaks in European Union Member States can be monitored using the information recorded in the ADNS (ec.europa.eu/food/animal/diseases/adns/index_en.htm). Weekly spatial changes can be displayed using the EU- BTNET system (eubtnet.izs.it/btnet/). This system is closely linked to the ADNS system for information on European Union Member States and to the animal health information in the OIE WAHIS system (www.oie.int/wahis/public.php?page=home) for information on other countries. Additional information is available from the OIE Reference Laboratory (Pirbright Laboratory, Institute for Animal Health, United Kingdom, www.iah.bbsrc.ac.uk/). The accuracy of the information at any given time nevertheless depends on how quickly each Member State notifies validated information on bluetongue. Figure 1 above shows a map of the restricted zones for each of the serotypes registered.

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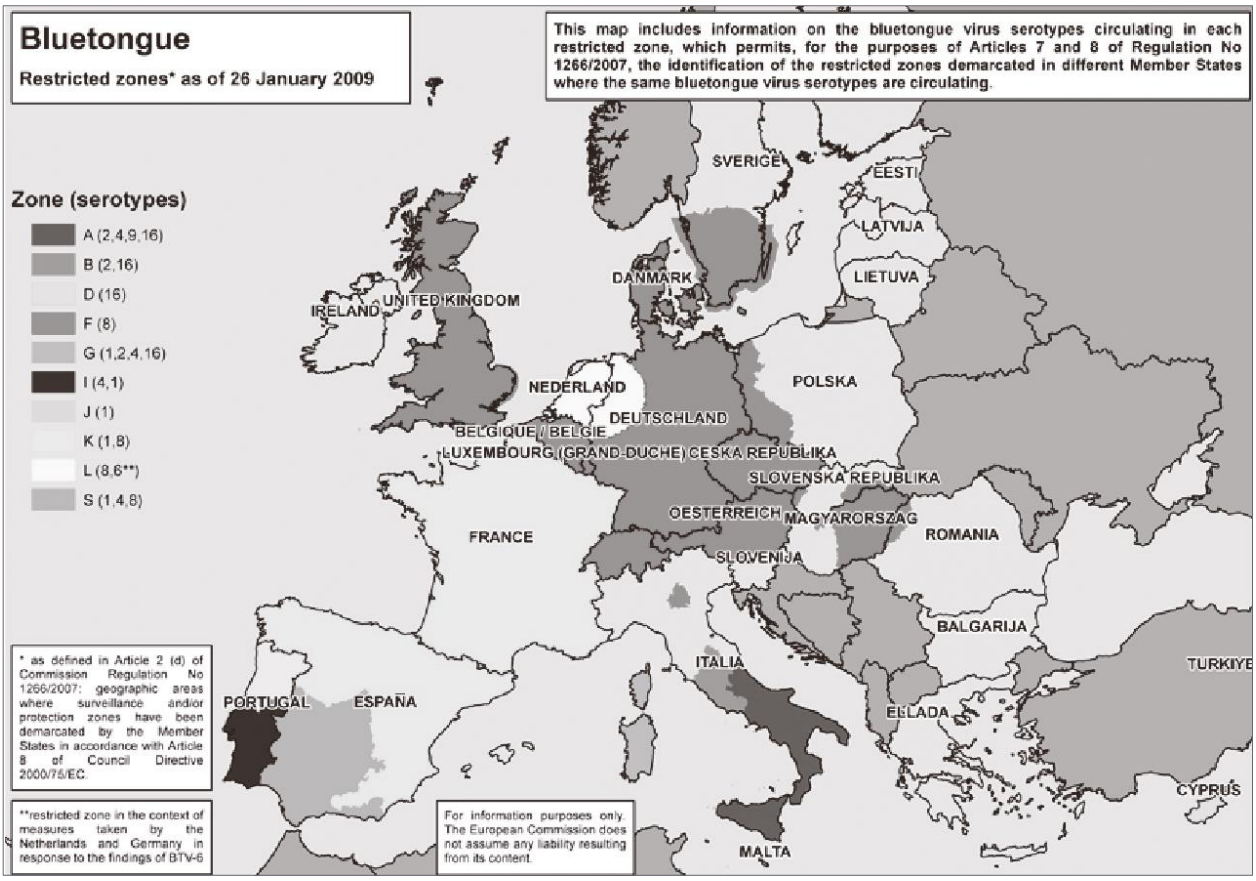
Figure 1. *Restricted zones linked to outbreaks of bluetongue in Europe (see the map in colour page 69)*



Appearance of an attenuated vaccine strain of serotype 6 in the Netherlands

October 2008 was marked by a surprising discovery in the east of the Netherlands of four outbreaks of bluetongue in cattle, caused by BTV-6, a serotype not previously encountered in Europe. Vaccination against serotype 8 had been used in the infected farms. The clinical signs associated with this infection were quite mild (inflammation of coronary bands) and the morbidity rate remained low in the infected farms (in percentage terms). A cautious approach is needed given the special context of this infection. It occurred in a population naturally and heterologously immunised against bluetongue serotype 8. Until this new occurrence, BTV-6 had been identified only in sub- Saharan Africa, the Arabian Peninsula, Central America and the Caribbean. A more detailed characterization of the virus was carried out at the OIE Reference Laboratory (Pirbright Laboratory), which showed it to be related to a strain of BTV-6 present in a polyvalent attenuated vaccine produced in South Africa. Moreover, it also appeared to be a reassorted virus. The illegal use of a live vaccine was put forward as an hypothesis to explain this outbreak, but it is not the only possible explanation. More complete molecular and epidemiological data will be needed before

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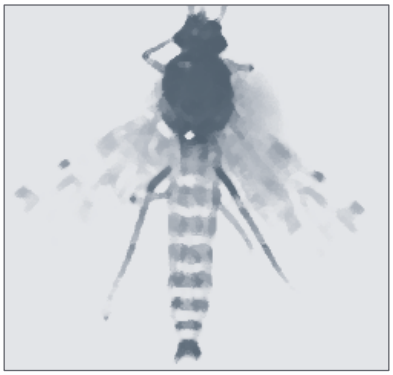
the outbreak can be definitely confirmed as vaccinal in origin. The risks of using multivalent attenuated vaccines include reversion to virulence, reassortment between the genomic segments of a vaccine strain and a wild virus, and the introduction of exotic serotypes into countries previously free from the disease. Cases of infection with serotype 6 have also been reported in Germany, with similar clinical signs. No cases of mortality have been reported in either the Netherlands or Germany.

Possible new serotype in goats in Switzerland (serotype 25?)

A potential new orbivirus, named Toggenburg virus (after the region where it was identified) has been isolated in a goat in Switzerland (4). The molecular profile, based on the sequencing of 7 of the 10 genome segments in this virus, is distinctive, and it could be a 25th serotype of bluetongue virus. Laboratory observations of naturally infected adult goats showed a very low level of specific antibodies and viraemia with no visible clinical signs. Experimental infections were used to demonstrate the transmissibility of the infectious agent and its multiplication in goats (receptive species), with no clinical signs. Subsequent research also detected a few herds in other Swiss cantons with seropositive and polymerase chain reaction-positive goats. To date, none of the cattle on the same holdings as the goats has tested seropositive. Infection with Toggenburg virus thus seems to be restricted to small ruminants. Only time will tell whether this virus can definitely be considered as the 25th serotype of bluetongue virus.



Overlapping of infections with serotypes 1 and 8 in France and of serotypes 6 and 8 in the Netherlands

The current epidemiological situation raises the possibility of viral super-infection and co-infection within a given host or vector with, for example, serotypes 1 and 8 (France) or serotypes 6 and 8 (Netherlands), the clinical and epidemiological consequences of which cannot currently be

evaluated. In the event of a cell becoming co-infected by two viruses of different strains (serotypes), newly generated viruses may have acquired some of their genomic segments from one of the two parental viruses and the remainder from the other. Genetic reassortment in this way is particularly important for the development of RNA viruses such as BTV. The likelihood of reassortment occurring and the potential changes in virulence of reassorted viruses are difficult to predict, but such phenomena have already been observed in the past between wild strains or between a wild strain and an attenuated vaccine strain. Depending on vaccination, the appearance of new serotypes as a result of reassortment or from other orbiviruses, the clinical signs associated with bluetongue may evolve. Any animal presenting clinical signs consistent with bluetongue after vaccination should lead one to suspect the presence of a serotype not covered by the vaccination, the emergence of a new orbivirus or a reassorted virus. In this situation, veterinary practitioners and livestock farmers must alert the authorities so that additional tests can be carried out to check for the presence of a bluetongue virus antigenically different from the serotype(s) against which the animal was vaccinated and to investigate the source of any newly introduced animals

Other modes of transmission

Although vector transmission is the predominant mode, other modes of transmission have recently been documented in cattle for serotype 8; transplacental transmission in the absence of vector activity and, less commonly, horizontal transmission by ingestion of infected placenta (6). A field study carried out in Belgium examined the virological and serological status of cow–calf pairs and estimated that transplacental transmission occurs in 10% of cases (2). These modes must also be taken into account in the control strategy in the longer term, since they enable the disease to become endemic in Europe by helping to maintain the virus in winter (a phenomenon known as overwintering).

Vaccination campaigns in Europe using inactivated vaccines

Faced with a situation where bluetongue becomes enzootic, two measures must be given priority : strategic vaccination (based on existing scientific knowledge) using inactivated vaccines and a reduction in the number of contacts between the vectors and susceptible and/or receptive animals. The countries affected or threatened have implemented large-scale vaccination campaigns using inactivated vaccines (BTV-8, BTV-1) in order to minimise the clinical incidence of the disease and to protect susceptible livestock. Regular monitoring of these campaigns is possible at the following Web site :

ec.europa.eu/food/ committees/regulatory/ scfcah/animal_health/index_en.htm

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An update on the culicoid vectors involved

Following the emergence of bluetongue in 2006, entomological surveillance was carried out in the affected countries using culicoid traps. From the data obtained, it transpires that *C. imicola* is not present, unlike the *C. obsoletus*/*C. scoticus* complex, which was regularly observed, and to a lesser degree, *C. dewulfi* (phylogenetically quite close to *C. imicola*) and *C. chiopterus* (3, 5). The parity rate was quite high, which is conducive to vectorial transmission. It was also found that Culicoides could be captured gorged with blood in sheep and goat sheds, even during the winter (the period when vectors are normally considered to be inactive). *C. pulicaris* was only rarely captured. Since the above-mentioned midges are well established in central and northern Europe, the entire region must now be considered to be at risk of bluetongue. In addition, the susceptibility of *C. obsoletus*, *C. scoticus*, *C. dewulfi* and *C. chiopterus* has recently been evaluated following the experimental infection of Culicoides with BTV-8 and it was demonstrated that *C. obsoletus* and *C. scoticus* were receptive, the viral load being three times greater in *C. scoticus* (1). This experiment opens the way for more extensive research throughout Europe to more accurately plot the vectorial competence and capacity of the Culicoides found in these regions.

The need for modelling

There is now a clear need for modelling since it would help to predict the dynamics of the infection and contribute to decision-making to improve control of bluetongue.

Improvements to existing models will require a multi-disciplinary approach and be informed by our improved understanding of the biology of the infection and the ecology of the vectors involved.

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