Bluetongue control using vaccines : experience of the Mediterranean islands

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Summary

Following the emergence of bluetongue (BT) virus serotype 2 on the island of Corsica in 2000, annual monovalent vaccination campaigns of the ovine population were conducted between 2001 and 2003. Despite vaccination, outbreaks were reported from several areas in 2001, but since November 2001, the absence of clinical cases in Corsica proves that vaccination is effective. This experience in Corsica is examined and, using available data, compared to the situation and the vaccination strategies on other Mediterranean islands. In light of the expansion of a new serotype of BTV onto these islands, a Mediterranean information network for BT and other emerging diseases is proposed.

Keywords

Bluetongue – Mediterranean – Vaccination – Vaccine – Virus.

As the ability to control vector populations of insects is limited, vaccination against bluetongue (BT) remains a very useful disease control tool. Four objectives can be sought when using this tool, as follows:

1) prevention of the establishment of BT virus (BTV) in an area
2) reduction of the number of clinical BT cases
3) eradication of BTV infection
4) immunisation of animals that will be introduced into the affected region.

After defining the objectives of BT vaccination, the following questions remain:

1) What level of vaccination should be reached?
2) Which species should be immunised?
3) Is the objective of eradication feasible?
4) When should vaccination cease?
5) How can the arrival of new serotypes be prevented?

In this review we will first present the example of BT in Corsica between 2000 and 2002. After a summary of the epidemic, the use of vaccination is evaluated and then compared with experience in the other islands of the western Mediterranean (the Balearic islands, Sardinia and Sicily) (Fig. 1).

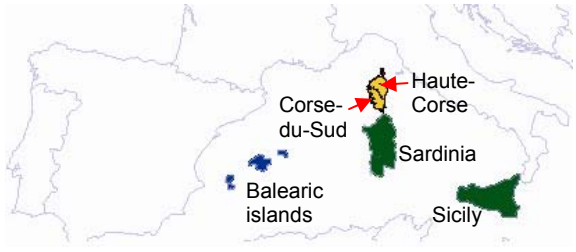

Figure 1
The larger islands of the western Mediterranean

History of bluetongue in Corsica

2000 and 2001 bluetongue epidemic

Following the first description of the principal vector (*Culicoides imicola*) in Corsica at the beginning of October 2000 (6), 49 outbreaks of BT (involving approximately 12 000 sheep) were later recorded on the island, whereas BT did not occur in continental France (Fig. 2). Serological surveys showed that BTV spread throughout the island. Corse-du-Sud was more infected with a 41% morbidity rate and twice the seropositivity rate of Haute-Corse (24% vs 40% in cattle, 16% vs 38% in sheep). Sheep were vaccinated with homologous vaccine against BTV-2 during the winter of 2000-2001. On average, 78% of the sheep flocks were vaccinated. Nevertheless, 335 outbreaks of BT were recorded between July and November 2001 and Haute-Corse was more affected than Corse-du-Sud (7). The last outbreak of BT in Corsica with serotype 2 was recorded on 8 November 2001. The 2000 and 2001 data confirm that BT commenced late in 2000 and ceased after the onset of cooler weather in November. A relatively mild winter allowed the persistence of infection and outbreaks began again the following July.

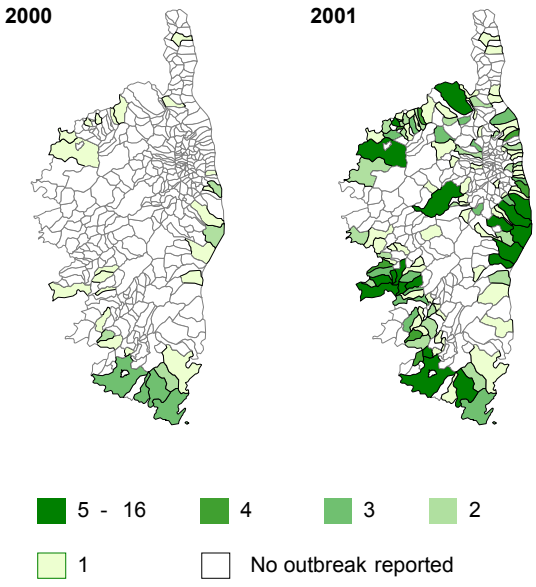

Figure 2
Spatial distribution of bluetongue cases in Corsica, 2000 and 2001
Source: National Food Directorate (Direction générale de l'Alimentation: DGAL)

Serological prevalence in non-vaccinated cattle and sheep

A total of 113 cattle herds were sampled in spring 2002, and 48% of the animals were seropositive. Corse-du-Sud has a significantly higher prevalence (68%) than Haute-Corse (39%). The serological rate of infection increased in cattle between the winters of 2000-2001 and 2001-2002 (increase of 63% in Haute-Corse and 70% in Corse-du-Sud) with a stable difference between the two regions. The geographic distribution of samples influenced these results, as the seropositivity rates (>75%) were higher in coastal areas and lower (<25%) in the mountains (Fig. 3). At this stage of the epidemic, a substantial portion of the cattle population (32% in Corse-du-Sud and 61% in Haute-Corse) was still susceptible (seronegative) and so could play a role in virus multiplication and dissemination. Nevertheless, the highest proportion of seronegative cattle occurred in the central areas of Corsica where the altitude is high and vector abundance is limited. The more affected areas in 2000 and 2001 were those with more seropositive cattle. The amplifying role of cattle in high altitude areas would, therefore, seem to be limited.

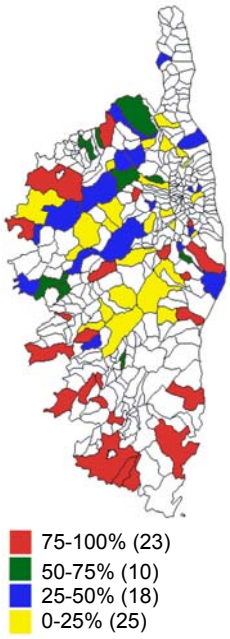

Figure 3
Seropositivity against bluetongue virus in cattle in Corsica in 2002
Source: National Food Directorate (Direction générale de l'Alimentation: DGAL)

Assessment of bluetongue virus circulation through serological analyses in sentinel cattle

Despite the vaccination campaign, circulation of BTV was observed in sentinel herds of cattle in 2002. Although the percentage of seroconversion at herd level is similar, the raw numbers show that the circulation of BTV was higher in Haute-Corse (Table I). This has to be compared with the presence of *C. imicola* during eight months from May to December 2002. The principal vector of BT is now permanently established in Corsica. To summarise

the situation in France in September 2003, neither *C. imicola* nor cases of BT have been found in mainland France and clinical BT due to BTV-2 has not been observed in Corsica since 8 November 2001. Vaccination was very effective in reducing clinical symptoms but BTV still circulates at a low level.

Table I
Seroconversions in cattle in Corsica in 2002

Herds	Corse-du-Sud	Haute-Corse
Herd level		
Number of herds	35	48
Percentage of herds with at least one seroconversion	37.1% (13/35)	64.6% (31/48)
Animal level		
Number of animals	229	1 495
Seroconversion	16.6%	12.9%

Evaluation of vaccination in Corsica

The possible use of vaccination against BT was discussed by the European Union scientific committee on animal health and welfare on 27 June 2000, prior to the initial report of BT in Corsica. At the national level, the case was submitted to the official risk assessment institution, the French Agency for Food Safety (AFSSA: Agence française de Sécurité sanitaire des Aliments). The choice to vaccinate was largely based on the assumption that *C. imicola*, which had been captured for the first time in Corsica, would survive the winter of 2000-2001. It was decided to vaccinate sheep, but not other species, with the South African attenuated monovalent BTV-2 vaccine as only BTV-2 had been isolated in the outbreaks of 2000 and 2001.

Impact of vaccination on serological status of ruminants

Serological status after the first vaccination campaign (2000-2001)

Assuming that there was no contact with vectors because of altitude, a sample of 13 herds (1 461 animals) vaccinated in February 2001 and 9 non-vaccinated herds (306 animals) was selected (4). These flocks went to summer pastures in 2001. Seven months after vaccination they were tested using the competitive immunosorbent assay (c-ELISA). The seropositivity rate was significantly different ($\chi^2 = 36.88$, $p<0.05$) (Table II) between the two populations. Some positive results in the vaccinated population were due to previous infection. The non-vaccinated population was taken as a control population to calculate the effect of vaccination. From the 1 461 animals vaccinated, 43% were positive before vaccination and 275 became positive after vaccination (out of 831 negative animals before vaccination). Vaccination caused seroconversion of only 33% of the seronegative animals (Fig. 4). This very poor result has been explained by the delay between vaccination and serology (7 months), the vaccination protocol (single vaccination of all sheep, regardless of age) and vaccination failure (i.e. excessive delay between vaccine reconstitution and injection). These results fully explained the poor protection of sheep herds during the 2001 epidemic.

Table II
Serological results in transhumant sheep

Sheep population	**c-ELISA**		**Seropositivity rate**	**Standard deviation**
	+	**–**		
Vaccinated transhumant population	905	556	62%	0.0127
Non vaccinated transhumant population	132	174	43%	0.0283

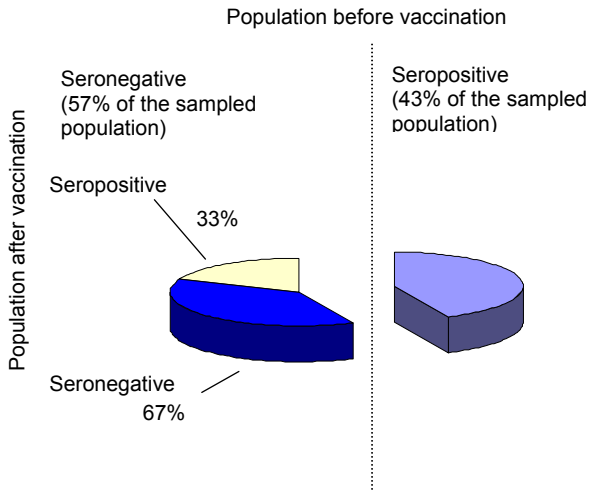

Figure 4
Effect of vaccination in transhumant sheep

Serological status after the second vaccination campaign (2001-2002)

The proportion of BT-seropositive animals is 91% on average. The northern and southern areas of Corsica show the same results (Table III). The serological prevalence in 2002 is obviously very high and is the result of a more efficient vaccination campaign during the 2001-2002 winter, and also because of the very high levels of virus circulating during the 2001 epizootic. These data are consistent with the absence of clinical BT amongst ruminants in Corsica in 2002.

Effect of vaccination

A comparison of mortality and morbidity rates between vaccinated and non-vaccinated animals shows that non-vaccinated animals are more affected, which validates the decision to undertake massive vaccination in 2000 (Table IV).

Table III
Serological status of vaccinated sheep flocks in Corsica

Flocks	Corse-du-Sud	Haute-Corse	Total
Number of flocks	57	50	107
Number of samples	1 118	1 058	2 176
Positive	91%	91%	91%
Negative	7%	7%	7%
Doubtful	2%	2%	2%

Table IV
Bluetongue outbreaks in Corsica in 2001

Flocks	Haute-Corse	Corse-du-Sud	Total
Infected flocks			
Total number	211	124	335
Sheep belonging to infected flocks	63 274	21 664	84 938
Vaccinated sheep in infected flocks	48 833	17 678	66 511
Morbidity rate			
Infected flocks	16.67%	14.18%	16.03%
Vaccinated animals belonging to infected flocks	6.06%	6.99%	6.31%
Non vaccinated animals belonging to infected flocks	52.52%	46.04%	51.12%
Mortality rate			
Infected flocks	12.77%	12.43%	12.68%
Vaccinated animals belonging to infected flocks	4.65%	6.41%	5.12%
Non vaccinated animals belonging to infected flocks	40.22%	39.11%	39.98%

Source: National Food Directorate (Direction générale de l'Alimentation: DGAL)

Comparison with the other Mediterranean islands

The situation in Corsica is best compared to that of the other islands in the western Mediterranean where BT outbreaks due to BTV-2 were recorded, namely: Sardinia, Sicily and the Balearic islands (Fig. 5). The presence of *C. imicola* was confirmed in all of these islands except Ibiza (5). After one annual vaccination campaign from October 2000 to spring 2001, no clinical cases of BT were recorded in the Balearic islands (1). Only two annual vaccinations of sheep were necessary to obtain the same results in Corsica. In Sardinia, the vaccination coverage was between 94.58-99.97% and in Sicily between 22.93-93.90% in 2002 (2). In Sicily and Sardinia, clinical cases of BT were still recorded during 2002-2003 despite annual vaccination (10 and 53 outbreaks compared to 6 090 and 6 in 2001-2002, respectively) using the same attenuated vaccine against BTV-2. Three important factors may explain this contrast: First, the sheep population is much greater on Sardinia and Sicily than on the other islands (Table V). It is also possible that an 'island effect' played a role in the extinction of BTV infection in the Balearic islands as the susceptible population may not have been sufficient to maintain the infection; similar findings have been observed with other contagious diseases like measles (3). Second, the geographic position of the different islands has to be taken into account. The Balearic islands are located 200 km from continental Spain but 350 km from Sardinia, whereas Corsica and Sardinia are separated by only 12 km, and Sicily and continental Italy are almost connected. It is then probable that only the Balearic islands can be considered an independent entity from an epidemiological perspective. The close interaction between Sicily and continental Italy is illustrated by the presence of the same serotypes of BTV in Sicily and Calabria (BTV serotypes 2 and 9). Third, vaccination in the Balearic islands was implemented very rapidly whereas it took three months in France.

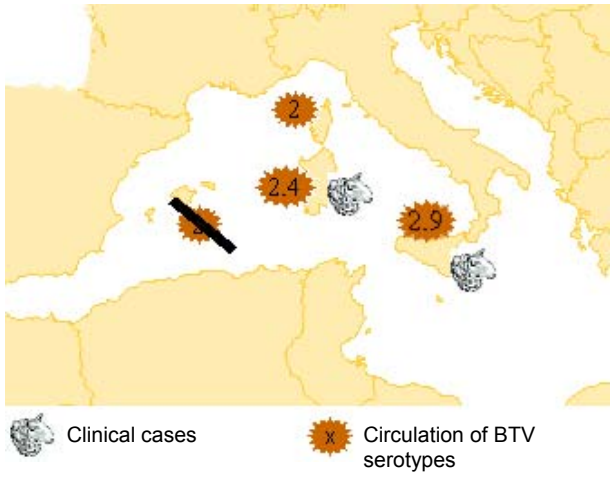

Figure 5
Bluetongue in the larger islands of the Mediterranean, September 2003

It is very important to evaluate the level of vaccination coverage that should be attained to eradicate disease, specifically the herd immunity threshold (HIT). An empirical evaluation gives 80% (Charles Nicolle's law) but it has been shown that HIT calculation should be based on the evaluation

of the strength of spread of the disease measured by the basic reproduction ratio R0. Basically, if R0<1, the disease cannot persist in a population. Let R0 be the reproduction ratio in a population; to decrease R0 to a value below 1, a simple calculation indicates that the proportion of vaccinated animals should be more than 1-1/R0. In vector-borne diseases, several factors attributable to the vector will change the approach (biting rate, trophic preferences, survival rate, incubation period and vectorial competency). Consequently, even with high vaccination coverage, it is still possible that the virus will persist in small areas or in reservoir animals. There is then a risk of re-emergence when coverage declines. For instance, the very high coverage in Sardinia in 2002 (from 95% to 99%) did not prevent all outbreaks.

Table V
Bluetongue in the larger islands of the Mediterranean

Island	Area (km²)	Sheep	Goats	Cattle	BT clinical cases	
					First	Last
Sardinia	24 090	3 283 000	283 000	230 000	18 August2000	Ongoing
Sicily	25 700	1 032 000	197 000	465 000	10 October 2000	Ongoing
Corsica	8 682	137 000	24 800	55 860	18 September 2000	08 November 2001
Ibiza	572				No outbreak	
Majorca	3 639	334 775	19 228	46 934		
Minorca	702				9 September 2000	27 November 2000

Conclusion

The experience in the Balearic islands, Corsica, Sicily and Sardinia showed that attenuated vaccine can safely be used to reduce the direct costs of BTV infection, i.e. morbidity and mortality in sheep. Even when side effects were reported by farmers, investigations did not confirm them. In September 2003, the question for the French authorities was whether to stop vaccination after two years without any outbreaks of BT. However, this question has been negated by the occurrence of new outbreaks of BT due to serotype 4 in Sardinia. On 25 August 2003, outbreaks were reported in Sardinia and serotype 4 was confirmed on 15 September 2003. It was then decided to vaccinate animals in Corsica against serotypes 2 and 4. In this case, the vaccination strategy was to prevent the establishment of the new serotype in Corsica. This experience illustrates the need for regional collaboration to define optimal vaccination strategies. The importance of information about circulating serotypes has also to be stressed. For this purpose, it is proposed that a Mediterranean information network be established for BT and other emerging diseases.

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