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PROPOSAL AND ECONOMIC EVALUATION OF A NEW APPROACH TO SANITARY DECISION IN ERADICATION OF CONTAGIOUS BOVINE PLEUROPNEUMONIA

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La pleuropneumonie contagieuse bovine (CBPP) est une maladie bovine très sévère appartenant à la liste A de l'OIE. Elle sévit en Entre-Douro e Minho et Beira sur la région du littoral au nord du Portugal depuis 1983. Bien que sa maîtrise dans cette région soit réussie, son éradication n'est toujours pas possible, à cause des infrastructures particulières liées aux systèmes de production. L'utilisation d'un seul test sérologique entraîne un problème pratique pour la détermination du statut sanitaire individuel, et par la même, la certification de l'élevage.

Les récents progrès dans le diagnostic de Mycoplasma mycoides subs. Mycoides S. C. ont permis de valider en pratique courante, un test sérologique 100 p. cent spécifique, basé sur le test d'immunoblotting (IBT). Des évaluations de cette technique ainsi que d'autres, la fixation du complément (CFT), l'examen bactériologique et histologique du poumon, ont été conduites afin d'estimer les valeurs de la sensibilité et de la spécificité des tests. Parmi les résultats de ce travail, une nouvelle approche de diagnostic de CBPP dans le but de l'éradiquer, combinant en série CFT et IBT, est discutée. L'intérêt du test post-mortem est aussi discuté. Un arbre décisionnel a été développé, permettant le changement de l'échelle du niveau animal au niveau élevage ainsi qu'une meilleure garantie et la validité des résultats. L'évaluation financière et l'efficacité sanitaire des protocoles possibles sont également présentées.

INTRODUCTION

Contagious Bovine Pleuropneumonia (CBPP) is a severe cattle disease placed in the A list of O.I.E. It was eradicated from most of the European countries in the beginning of this century, but outbreaks have occurred in France (1980, 1982, 1984 - 15 outbreaks), Spain (1989/91 - 19 outbreaks) and Italy (1989/92 - 34 outbreaks) (Ter Laak, 1992). In Portugal CBPP is endemic since 1983, restricted to three provinces of the north (Entre Douro e Minho (EDM), Trás-os-Montes and Beira Litoral), after 1987.

The evolution of the epidemic in EDM have an irregular pattern, but a consistent and progressive reduction in farm incidence have been achieved from 1990, with the establishment of a regular serological control (every 6 months). This decreasing trend was broken in 1991/92 and in 1997 by two epidemic outbreaks involving about 50 farms each (some 1500 dairy cattle) concerning two small counties.

The introduction of CBPP in a disease free area is only possible by the introduction of infected bovine, usually asymptomatic, either chronic carriers or recently infected animals. CBPP can also spread by short distance aerial inter-herd transmission, in specific situation, which have been reported in EDM (*Almeida *et al., 1992*). If infected farms are not all identified and depopulated, CBPP turns endemic with chronic carriers spreading the disease between the farms.

POSSIBLE DIFERENT TEST STRATEGIES FOR ERADICATION

None of the tests available at the moment for CBPP diagnosis is 100% sensitive. Therefore the test and slaughter procedure at individual level is not effective for eradication purposes because false negative animal (in the prodromic and chronic stages) are left behind in infected herds.

Three different possible strategies for eradication, based in different combinations of CFT with *post mortem* testing or with immunoblotting test (IBT) (Regalla et al., 1996) in a serial testing sequence were compared in terms of the risk profile and of the associated expected economical value of each strategy. A decision tree analysis (Marsh, 1993) was developed for this purpose and as shown in Figure 1. The list of notations used, the events they referred and values conferred in the model are the following:

Notation	*EVENTS*	*VALUES*	*Notation*	*EVENTS*	*VALUES*
HD+	infected herd	herd prevalence (HP)	CFT+	positive result in CFT	herd apparent prevalence (HAP)
HD-	non infected herd	1-HP	CFT-	negative result in CFT	1-HAP
H ++	test+ infected herd	HPPV of last test	H/B+	positive result in H/B	HAP of serial testing
H +-	test+ non infect.herd	1-HPPV of last tes	H/B-	negative result in H/B	1-HÁP of serial testing
H -+	test- infected herd	1-HPNV of last test	IBT+	positive result in IBT	HAP of simple or serial testing
H --	test- non infect.herd	1-HNPV of last test	IBT-	negative result in IBT	1-HÁP of simple or serial testing
IF	infected herd	same as DF	SL	slaughter of + animals	financial cost of slaughter
DF	disease free herd	financial benefit	SO	herd stamping out	financial cost stamping out

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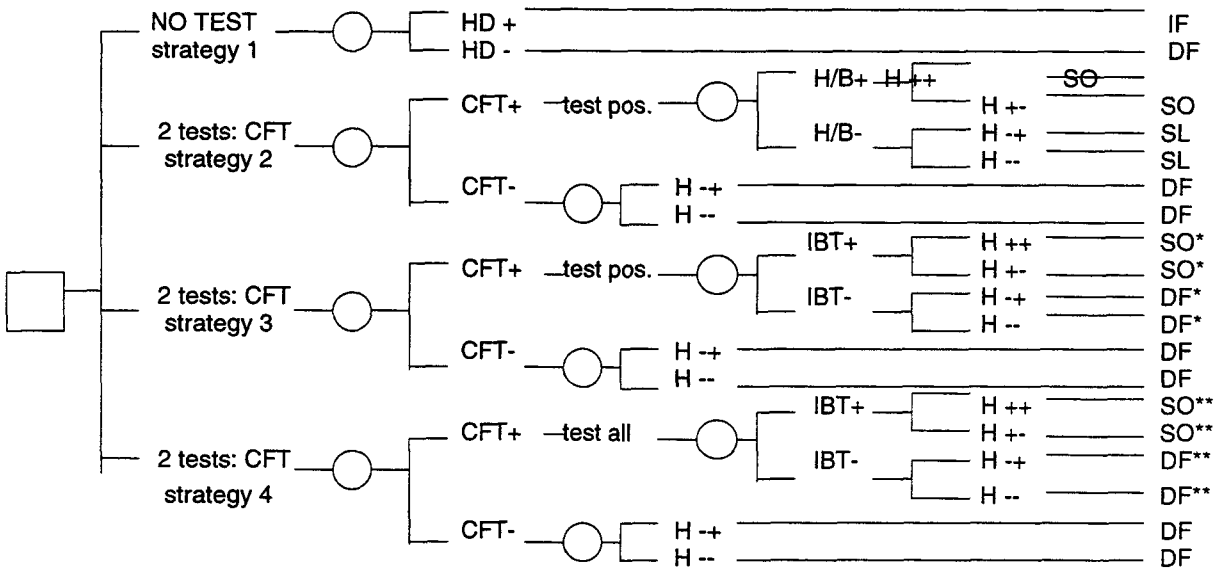
Figure 1
Decision tree for CBPP eradication strategies



Strategy 2 is the one followed presently in Portugal: positive animals to CFT are slaughtered and tested with (H/B). In case of confirmation of infection by isolation, stamping out of herd is carried out. If no evidence of infection is found the sampling of the herd for CFT is repeated until all results are negative or H/B is positive. This can be a very resource consuming practice especially in big herds were some bovine are culled before a herd negative result is achieved, due to decreased HSP of the test.

The assessment of this and alternative strategies was made using available epidemiological data on the population, the disease and the tests. The average number of bovine per herd is 8 in the EDM region and the CBPP prevalence inside infected herds is accepted to be higher than 0.2, and there are about 35,000 herds.

IBT and CFT Sensitivity (SE) and Specificity (SP) values derived from a recent evaluation of CBPP diagnosis tests (Immunoblotting, Complement fixation test, Histological examination and Bacteriological examination) conduced in Portugal by Regalla *et al.* (1996). The results obtained are presented in Table I.

Table I
Quality of the CBPP diagnosis tests

Description	CFT	Histopathology and Bacteriology	IBT
SE	79.9*	49.1*	91.6*
SP	99.5**	100	100*

*Regalla *et al*, 1996; ** OIE, 1995[5]

Based on the presented figures, the epidemiological value of the tests at herd level, Herd Specificity (HSP) and Herd Sensitivity (HSE) were calculated according to *Martin, 1992*. The cutpoint number of reactors was set at one or more positive result. Subsequent apparent prevalence (HAP) and predictive positive and negative values (HPPV and HNPV respectively) were derived from HSE and HSP.

The decision tree was built in Microsoft EXCEL spreadsheet and simulations were made for different herd prevalence, 1%, 0.1% and 0.01%. Results of one branch of the decision tree, named strategy 4, are presented in Table II.

Table II
Probability values in the fourth branch of the decision tree analysis

Notation	Prevalence herd level (%)			Notation	Prevalence herd level (%)		
	1	0.1	0.01		1	0.1	0.01
CFT+	0.0472	0.0401	0.0394	H++	0.0072	0.0007	0.0001
CFT-	0.9528	0.9599	0.9606	H+-	0.0000	0.0000	0.0000
IBT+| CFT+	0.0072	0.0007	0.0001	H-+	0.0026	0.0003	0.0000
IBT-| CFT+	0.0400	0.0394	0.0393	H--	0.9901	0.9990	0.9999

Table III presents the risk values and the financial benefits resulting from each policy. For this simulation, prevalence at herd level is considered at four different levels. The value of the possible outcomes for the financial

[5] R. Groupe Ad Hoc de l'OIE sur les Systèmes de Surveillance de la Péripneumonie Contagieuse Bovine, Off. Int. Epiz. Paris, 1995.

analysis was estimated as follows from (**Almeida, *et al.*1992): Strategy 1,DF and IF herds - financial benefit of 358; Strategy 2, SO cost of 1,090, SL benefit of 384, DF benefit of 711; Strategy 3, SO* cost of 1,060, DF* 707 and DF benefit of 711; Strategy 4, SO** cost of 1,221, DF** 690 and DF benefit of 711(values in 10^6 PTE). The risk assessment evaluation was based on the proportion of false negative herds resulting from each strategy (1-Eficacy).

Table III
Risk and financial values of the different strategies at different prevalence levels

Strategy	*Financial analysis (10^6 PTE)*				*Risk analysis*			
Prevalence herd level (%)	*30*	*10*	*1*	*0. 1*	*30*	*10*	*1*	*0. 1*
Not Test	12,723	12,723	12,723	12,723	0.30	0.1	0.01	0.001
H/B on positive CFT sera	19,060	22,897	24,597	24,769	0,2466	0,0822	0,0082	0,0008
IBT on positive CFT sera	21,570	24,015	25,116	25,226	0,1935	0,0651	0,0065	0,0007
Herd IBT on CFT positive herd	14,118	21,516	24,845	25,117	0,0789	0,0263	0,0026	0,0003

DISCUSSION AND CONCLUSIONS

The main reasons for the occurrence of the outbreaks in EDM are strongly related to the infrastructure conditions of dairy farming in the north region, which is characterised by small herds, very dependant on external replacement. The very low prevalence (<0.1%) already achieved, lowered the predictive positive value of the CFT to about 10%, with further interference of cross reactions (specially the "*Mycoides* cluster" organisms). These problems and the failure of CFT in detecting prodromic and carrier states make extremely difficult the identification of focus and the decision to proceed with the stamping out. Furthermore, the low sensitivity of the isolation of M. mycoides S.C., the criteria presently used to identify a focus of disease, have not help to improve the situation. To achieve eradication is, therefore, necessary the assessment of two important problems: the identification of infected herds and the certification of disease free herds.

Identification of infected herds

Results from the eradication strategies analysed, are presented in Table III. The new strategies 3 and 4 are better then strategy 2 both from the risk and the financial point of view.
The more efficient strategy from risk point of view is strategy 4; in all stages of prevalence analysed the risk of false negative herds remains always the lowest. However the financial value of strategy 3 is the best but differences between strategies 3 and 4 reduces as prevalence goes down.
Using the present model we can simulate the expectations of evolution of the eradication process if serological control of the region is completed every 6 month. With strategy 4 eradication can be achieved in two years. According to the model strategy 3 will not allow eradication: after four years (eight controls) at least 1 infected herd in 35,000 would remain not detectable. With strategy 2 only 6 years would be possible to have 2 infected herd in 35,000. Both strategies will not go down these figures and extend the eradication process in time.
The best situation could be achieved by 4; performing IBT first in CFT positive sera and in case of negative results from these sera to test the rest of the negative CFT sera. This procedure could slightly reduce diagnostic cost.

Certification of disease free herds

A successful CBPP eradication program requires the introduction cattle coming from disease free certified herds after depopulation. The certification of herds it would bring financial profit stimulating o farmers involvement, and guarantee the sanitary status of the replacement stock.
Shifting the diagnostic evaluation of the herd from the individual result (negative predictive value) to herd result (HNPV) it is possible to use the contribution of serological testing to the certification of the disease free herds.
The 1-HNPV (probability of a false negative herd result) is independent between serological control in the same herd - (P(B|A) = P(B)) and thus $P(A \cap B \cap \ldots N) = P(A) * P(B)^* \ldots ^* P(N)$. Using the 1-HNPV calculated to each specific herd it is possible to retest the herd the number of times necessary to achieve a pre-determined probability of 1-HNPV. The sera would be tested with IBT which is 100% specific and more sensitive than CFT; therefore the danger of false positive results in the certification process would be null.

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