Systems for prevention and control of epidemic emergencies

Paolo Calistri[1*], Annamaria Conte[1], Fabrizio Natale[2], Luigi Possenti[1], Lara Savini[1], Maria Luisa Danzetta[1], Simona Iannetti[1] & Armando Giovannini[1]

[1] *Istituto Zooprofilattico Sperimentale dell'Abruzzo e del Molise 'G. Caporale', Campo Boario, 64100 Teramo, Italy*
[2] *European Commission, Joint Research Centre, Institute for the Protection and Security of the Citizen, Ispra (VA), Italy*

** Corresponding author at: Epidemiology Unit, National Reference Centre for Veterinary Epidemiology, Programming, Information and Risk Analysis, Istituto Zooprofilattico Sperimentale dell'Abruzzo e del Molise 'G. Caporale', Campo Boario, 64100 Teramo, Italy. Tel.: +39 0861 332241, e-mail: p.calistri@izs.it.*

Veterinaria Italiana 2013, **49** (3), 255-261. doi: 10.12834/VetIt.1206.06
Accepted: 25.07.2013 | Available on line: 28.08.2013

Keywords
Animal movements,
Diseases modelling,
Early detection,
Epidemic emergency,
Network analysis,
Risk assessment,
Risk maps.

Summary

The development of early warning systems is fundamental for preventing the spread of infectious diseases. Data collection, however, is a costly activity and it is not possible to implement early warning systems everywhere and for all possible events. Hence, tools helping to improve the focus of surveillance efforts are of paramount importance. Risk assessment methods and other provisional modelling techniques may permit to estimate the probability of introduction and spread of infectious diseases in different geographical areas. Similarly, efficient information systems must be in place to assist the veterinary services in case of epidemic emergencies in order to support the prompt application of control measures for the containment of the infection and the reduction of the magnitude of negative consequences. This review describes two recent approaches to the estimation of the probability of introduction and spread of infectious diseases based on the use of risk maps/spatial modelling and Social Network Analysis (SNA) techniques. The review also describes a web application developed in Italy to help official veterinary services to trace animals in case of outbreaks of infectious diseases.

Strumenti per la gestione delle emergenze epidemiche

Parole chiave
Analisi di network,
Emergenza epidemica,
Mappe di rischio,
Modelli predittivi,
Movimentazioni animali,
Rilevazione precoce,
Valutazione del rischio.

Riassunto

I sistemi di allerta rapida sono fondamentali nella prevenzione della diffusione delle malattie infettive. La raccolta dei dati è, tuttavia, un'attività economicamente dispendiosa e pertanto non è concretamente possibile mettere in atto tali sistemi per ogni evenienza. Tutti gli strumenti che consentono di indirizzare meglio le attività di sorveglianza risultano, quindi, significativamente importanti. In particolare, le metodologie per la valutazione del rischio e altre tecniche di previsione permettono di stimare la probabilità d'introduzione e di diffusione delle malattie infettive in diverse aree geografiche. Analogamente, devono essere disponibili sistemi informativi efficienti per supportare i servizi veterinari nell'applicazione delle misure di controllo dell'infezione e nel contenimento degli effetti avversi in caso di epidemie. Questa rassegna descrive due recenti approcci utilizzati per la stima della probabilità d'introduzione e di diffusione delle malattie infettive basati sull'uso di mappe di rischio/modelli spaziali e tecniche di Social Network Analysis (SNA). Infine, viene descritta un'applicazione web sviluppata in Italia a sostegno dell'attività dei servizi veterinari finalizzata a tracciare gli spostamenti degli animali da e per i focolai di malattia.

Introduction

The existence of surveillance systems able to function as effective early warning systems is pivotal in preventing the spread of infectious diseases (6). So much so that early surveillance warning systems are widespread across Europe. The current Italian sentinel system for Bluetongue (12) and the ornithological surveillance system for West Nile virus (5) may be considered two typical examples of such surveillance programmes.

However, data collection is costly and it is not possible to implement ubiquitous early warning systems. The resources are limited and the deployment of such systems is regulated so to achieve the maximum level of efficiency. Therefore, any tool improving the deployment of surveillance measures is fundamental, and the identification of risk factors for the introduction and spread of infectious diseases is becoming a priority. Risk assessment methods and other provisional modelling techniques allow for calculating the probability of introduction and spread of infectious diseases in different geographical areas, as well as the epidemiological analysis of the available data on animal trade. Similarly, efficient information systems must be in place to support veterinary services in case of epidemic emergencies. In fact, the quick reaction of veterinary services and the rapid application of control measures are related to the prompt availability of reliable information. This review describes two recent approaches for the estimation of the probability of the introduction and spread of infectious diseases based on the use of risk maps/spatial modelling and Social Network Analysis (SNA) techniques. It also describes a web application developed in Italy for helping veterinary services in tracing back and forward animals in case of outbreaks of infectious diseases.

Estimation of probability of introduction and spread of infectious diseases

Risk maps and modelling

The probability of the introduction and spread of an infection into a new territory is often modelled through risk maps. Probability values are estimated through the application of mathematical and statistical models using explanatory variables.

A model can be seen as a tool simulating or estimating how an object or a system of objects will behave. When applied to biological sciences, models aim to reduce the complexity of biological systems into basic rules and equations. Models are increasingly being applied to extrapolate knowledge and results in time and space (23). These techniques may be used to identify disease risk factors, to better understand epidemic dynamics and for more efficient targeting, control and preventive measures. However, they are still not fully exhaustive. It is impossible to build a fully accurate model due to the complexity of biological systems and due to the limitations of explanatory variables to be used. Models are based on the knowledge of the studied object and it often happens that a fair share of such a knowledge is not (yet) available. This leads to the need to carefully assess the results of any model in relation to the uncertainties existing behind the model itself (15).

One of the most frequent approaches in modelling the probability of the spread of an infectious disease is the use of spatial models, which represent a valid method for the identification and quantification of the effect of a set of explanatory variables on the spatial distribution of a specific event/disease (17).

The development of risk maps for *Culicoides* vectors in Europe and in the Mediterranean Basin is an example of application aiming at predicting the possible areas for Bluetongue endemisation. Several maps for the Mediterranean Basin (21, 18) and Italy (8, 9) were developed for the major vector, *Culicoides imicola*, and for other potential vector species. It is noteworthy that *Culicoides imicola* could also be the vector for Africa Horse Sickness (AHS) and Epizootic and Haemorrhagic disease (EHD) currently not present in Europe. However, risk maps developed for *Culicoides* distribution and abundance are a typical example of the possible drawbacks following such an approach. Prior 2006, the absence of the major vector, *Culicoides imicola*, above 42°N led to the false belief that Northernmost European territories were not susceptible to Bluetongue infection and endemisation. The large Bluetongue outbreak that started in August 2006 and progressively interested almost all European countries during the following two years proved wrong all previous beliefs about the inability of non-Imicola species to sustain an epidemic course. In this case, the limited forecasting of *Culicoides* risk maps was mainly due to the limited knowledge of vector competencies, although the potential role of non-Imicola vectors was previously observed in the Balkans and in other Mediterranean areas (19, 20).

Other risk maps are based on ecological niche models (ENM), which assume that each species is distributed according to its ecological potential. This approach takes into account the details of the ecological patterns responding to the characteristics of individual species' ecology. More in details, it allows for spatially representing the species ecological niches disguised as 'suitability' maps (22). This approach has been endorsed in order to predict the areas of potential colonization by several species of ticks, potential vectors of many important diseases, including the emergent Crimean-Congo Haemorrhagic Fever (CCHF) (10).

Identification of crucial herds/flocks for the spread of infectious diseases

In spatial models the contacts between sub-populations or individuals that may determine the spread of diseases are implicitly incorporated in the idea of geographic proximity. An alternative approach is to consider more explicitly in the model the relations that are at the basis of these contacts. In the case of diseases transmissible by transported animals, the information concerning animals' transportation logged in national livestock databases according to EU rules on traceability may be used to understand the possible pathways of introduction and spread of pathogens transmitted by animal-to-animal contacts. In recent years, Social Network Analysis (SNA) techniques have been applied for the analysis of the network represented by the movements of animals. These movements, in fact, can be represented as a network where the premises of origin and destination are defined as 'nodes' and the transports of animals between premises as 'relations' or 'edges'. In this type of network edges have a direction from the holding of provenience to that of destination and the strength of the relation can be quantified on the basis of the number of animals that have been transported.

The movement of animals along the edges of the network represents a major source of contact between the populations of the two premises of origin and destination and can be considered as a path for the diffusion of a disease, especially in the case of diseases transmissible mainly by direct contact. Social Network Analysis techniques use centrality measures to quantify the role and the importance of each node within the network. The simplest centrality measure is the 'degree', which is calculated counting the number of relations that the node has with its direct neighbours. In a directed network, like the one based on animal movements, in addition to counting the total number of edges linked to a node it is possible to consider the 'in-degree', which is the number of edges arriving to the node and the 'out-degree', which is the number of edges leaving from the node.

Other centrality measures take into account the structure of the network more globally (24):

- the 'closeness' is a measure of the number of steps required to reach all the other nodes along the shortest paths;
- the 'betweenness' is the measure of the number of times the node falls on the geodesic paths between other pairs of nodes in the network;
- the 'eigenvector' is a measure of centrality proportional to the sum of the centralities of the nodes to which a node is connected (4).

The results of a recently published analysis of the Italian network of cattle movements show that 48.5% of movements take place within a short distance, about 20 km from the origin (Figure 1), while only a few transports involve longer paths (16). In addition, the distribution of the number of movements indicates that there is a relative abundance of premises with a very high number

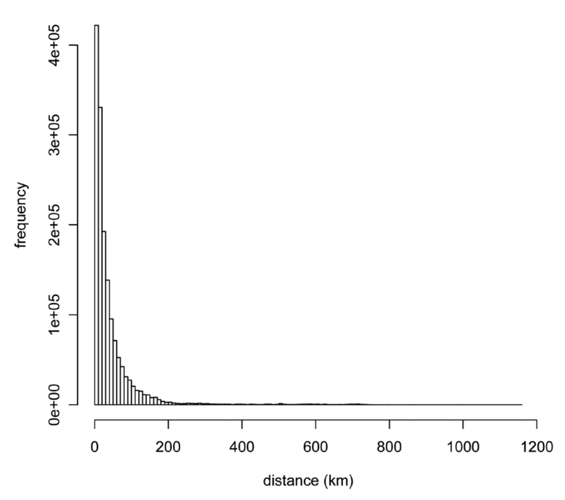


Figure 1. *Distribution of the number of movements of cattle in Italy in 2007 by geodesic distance.* Distances are measured between centroids of the municipalities of the premises of origin and the premises of destination (16).

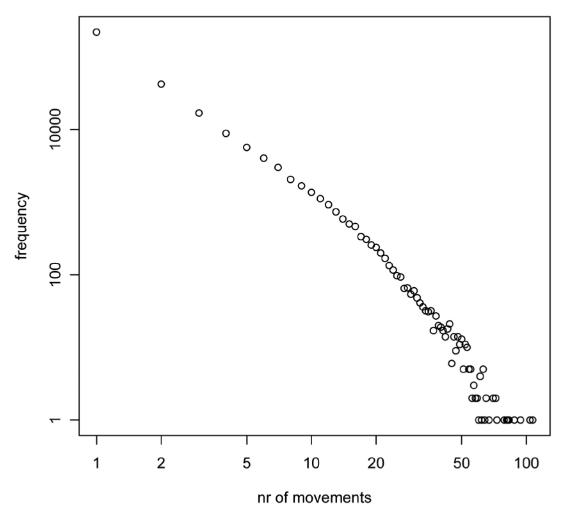


Figure 2. *Frequency distribution of the number of movements of the premises in the network of cattle movements in Italy in 2007.*

of connections having a prominent position in controlling trade flows (Figure 2). This, coupled with the information on the type of premise (dairy or fattening farm, market, assembling or genetic centre), strongly points out the importance of specific nodes as possible 'super spreaders' in case of infection (Figure 3).

The results of the analysis on the Italian cattle network are similar to those obtained by other Authors in Denmark (3) and in Great Britain (14).

A further confirmation of the importance of 'super spreaders' is given by the comparison of the results, in terms of reduction of infection spread, obtained after simulating epidemics under different scenarios of movement blockage (16). When control measures are applied taking into account the centrality values of premises to be blocked, the efficacy of the measures is much higher (Figure 4).

Systems for the management of epidemic emergencies

The rapidity of the application of appropriate control measures is crucial for the success of any intervention, once the presence of an infectious

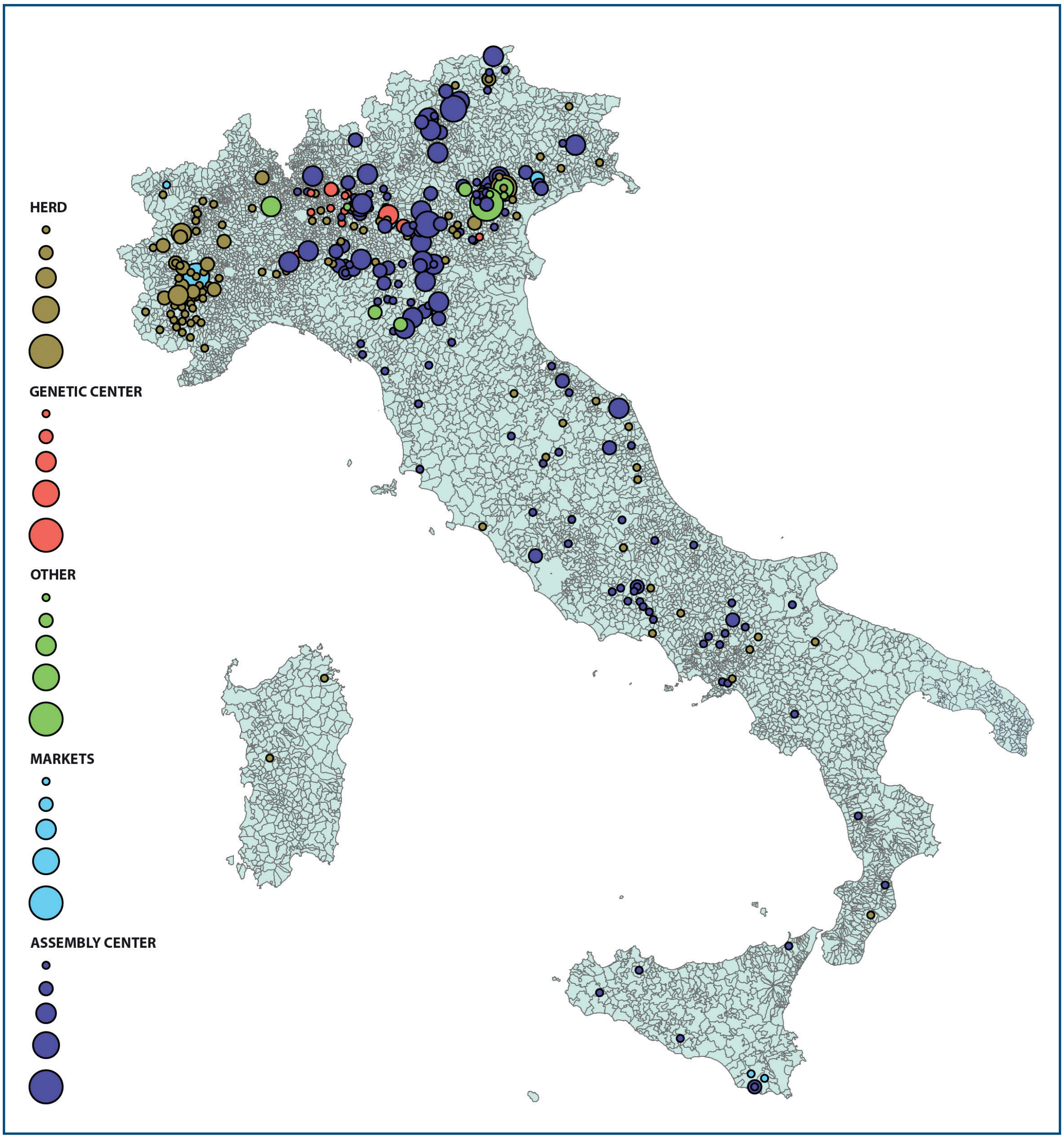


Figure 3. *Spatial distribution of premises in Italy with the higher CDC (Complex Degree Centrality) values in 2007.* CDC is based on geometric average between the number of connections (degree) and the number of animals moved.

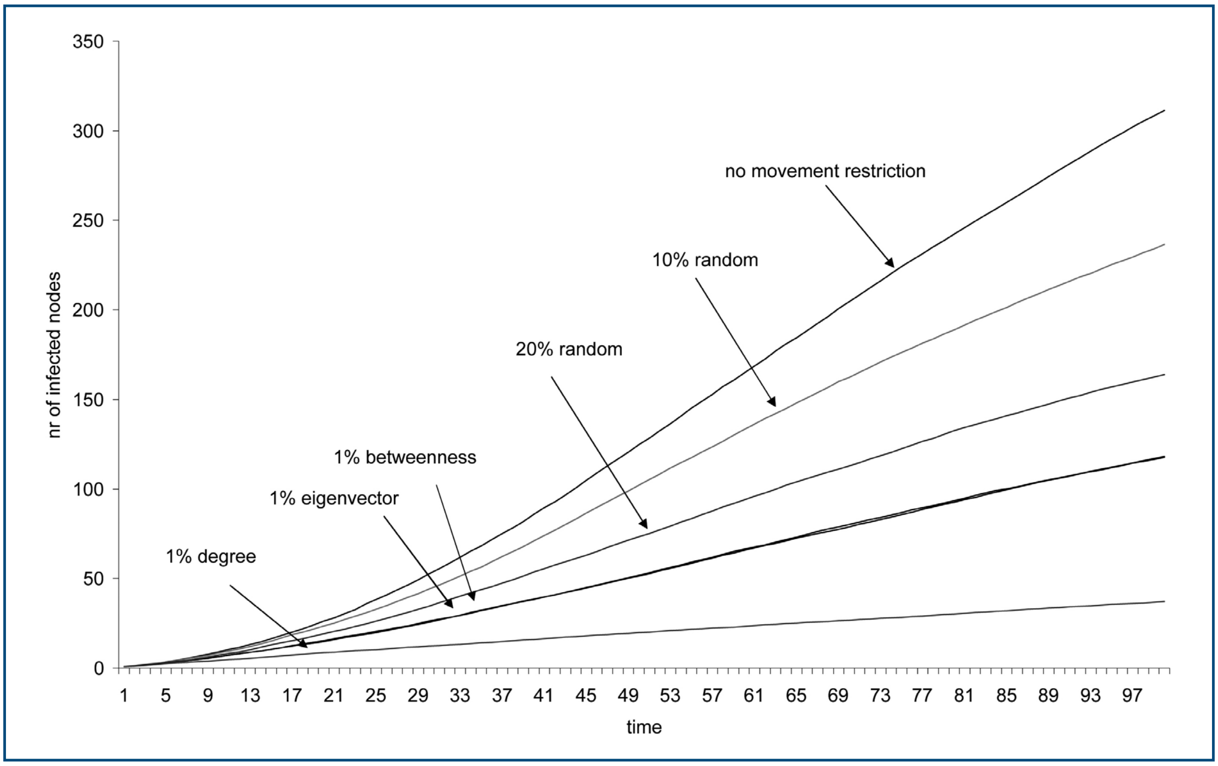


Figure 4. *Number of infected nodes by time for different scenarios of control measures applied on the network of cattle movements in Italy in October 2007.* Control measures are simulated by cancelling outgoing movements from selected premises on the basis of their values of centrality (16).

disease potentially causing an emergency situation has been confirmed. In other words, the 'action' must follow the 'decision' in the shortest possible time. However, the efficacy of the reaction rests on the following factors:

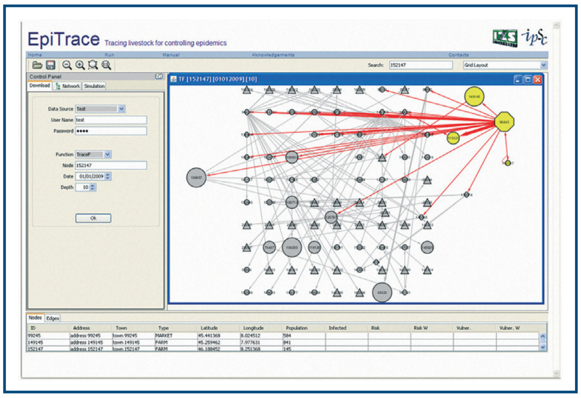
- the existence of a short command chain with a clear distribution of competencies and responsibilities;
- the presence of standard and clear procedures, already validated during simulations or previous emergencies;
- the availability of well trained personnel, appropriate equipment and diagnostic materials;
- the availability of adequate financial funds for the compensation of farmers and for other expenses.

However, all the above listed requisites would not be sufficient as long as the decision-makers and in-field personnel will lack a good quality of data collection and an efficient information system able to provide updated and reliable information.

Several information systems have been developed at national and international level with the aim of helping veterinary services in the management of epidemic emergencies. The World Animal Health Information System (WAHIS), developed by the World Organisation for Animal Health (OIE), is considered the international reference for all national or regional systems. In fact, through its web interface and e-alert system, WAHIS collects and disseminates a large quantity of information on animal disease outbreaks occurring worldwide (2).

In Italy a similar application, called Information System for the notification of Animal Diseases (SIMAN) has recently been developed (7). SIMAN website encompasses several tools for data dissemination, including a web-GIS (Geographic Information System) application. It also allows for the collection and communication of data on animal disease outbreaks occurring in Italy according to OIE and European Union standards.

More recently, in collaboration with the Institute for the Protection and Security of the Citizen of the European Commission, a new web application, called 'Epitrace', has been developed for tracing animal movements between cattle herds. Actually, when an outbreak of a contagious disease is confirmed, two of the most pressing issues are the pin-pointing of most likely infection sources and the identification of the animals that might be infected by a further spread of the disease. The availability of a system able to provide veterinary services with the data of movements in and out the infected establishment in few minutes is, therefore, of paramount importance. Epitrace allows for quickly extracting from the Italian Cattle National Database



Search: 152147

Data Source: Test
User Name: test
Password: ••••
Function: TraceF
Node: 152147
Date: 01/01/2009
Depth: 10

ID	Address	Town	Type	Latitude	Longitude	Population	Infected	Risk	Risk W	Vulner.	Vulner. W
99245	address 99245	town 99245	MARKET	45.441368	8.024512	584					
149145	address 149145	town 149145	FARM	45.259462	7.977631	841					
152147	address 152147	town 152147	FARM	46.188452	8.251368	145					

Figure 5. *Epitrace web application for the prompt visualization of all direct and indirect links of a specific herd in a given period of time.* The application utilises the in real time data stored in the Italian Cattle National Database.

all contacts from or towards a specified outbreak herd during a given time span. These contacts are represented as a network (Figure 5), the application can also access details about the identity of premises and the dates and number of animals transported. The analysis can be further extended by expanding specific areas of the network and interrogating the database interactively and in real time.

Time is clearly a crucial factor in case of highly transmissible infectious diseases. Delays in recognition of the disease and application of proper control measures may lead to economically devastating consequences and to the choice of inappropriate control measures (1).

Conclusions

Epidemiological modelling, risk maps and SNA techniques may help to better prioritize the interventions and the use of resources in the planning of early warning systems and in the management of control actions in case of epidemic emergencies.

However, to avoid drawing wrong conclusions, the uncertainties behind any model should not be underestimated. The use of epidemiological models, for example, was strongly debated in the United Kingdom during the 2001 Foot-and-Mouth epidemic (13), especially in their ability of predicting the true magnitude of the epidemic and to supply valuable information for the evaluation of alternative control strategies.

Especially in the case of vector-borne diseases, the poor knowledge of vector biology and behaviour frequently introduces uncertainties into models, greatly reducing the accuracy of the predictions.

Therefore, although sophisticated airborne and ecological models may be beneficial, sometimes relatively simple analyses of basic epidemiological data can be more appropriate. In Italy, for example, a quite uncomplicated risk assessment based on animal movement data allowed for identifying the areas at risk for Bluetongue serotype 8 virus introduction (11). This shows that the general approach of parsimony in the model complexity should always be followed.

A different problem is related to the need for prompt and easily accessible information in case of emergency. Nowadays the broad range of technical solutions helps the development of new tools for information dissemination, but the quality of data gathered, stored and processed by the information systems is still the crucial aspect for any surveillance system. Therefore the respect of unambiguous rules and the existence of clear procedures for data collection and updating are essential to provide the decision-makers with reliable and useful information. In this regard, the availability of clear case definition and the presence of well trained personnel, both official veterinarians and practitioners, are all prerequisites for the efficiency of any passive surveillance system, thus facilitating a prompt recognition and response in case of disease occurrence.

References

1. Bates T.W., Thurmond M.C. & Carpenter T.E. 2003. Description of an epidemic simulation model for use in evaluating strategies to control an outbreak of foot-and-mouth disease. *Am J Vet Res*, **64**, 195-204.
2. Ben Jebara K. 2007. WAHIS and the role of the OIE's reference laboratories and collaborating centres. *Dev Biol* (Basel), **128**, 69-72.
3. Bigras-Poulin M., Thompson R.A., Chriel M., Mortensen S. & Greiner M. 2006. Network analysis of Danish cattle industry trade patterns as an evaluation of risk potential for disease spread. *Prev Vet Med*, **76** (1-2),11-39.
4. Bonacich P. & Lloyd P. 2001. Eigenvector-like measures of centrality for asymmetric relations. *Social Networks*, **23**, 191-201.
5. Calistri P., Giovannini A., Savini G., Monaco F., Bonfanti L., Ceolin C., Terregino C., Tamba M., Cordioli P. & Lelli R. 2010. West Nile virus transmission in 2008 in North-Eastern Italy. *Zoonoses and Public Health*, **57**, 211-219.
6. Childs J. E. & Gordon E. R. 2009. Surveillance and Control of Zoonotic Agents Prior to Disease Detection in Humans. *Mt Sinai J Med*, **76** (5), 421-428.
7. Colangeli P., Iannetti S., Cerella A., Ippoliti C., Di Lorenzo A., Santucci U., Simonetti P., Calistri P. & Lelli R. 2011. The national information system for the notification of animal diseases in Italy. *Vet Ital*, **47** (3), 303-312.
8. Conte A., Giovannini A., Savini L., Goffredo M., Calistri P. & Meiswinkel R. 2003. The effect of climate on the presence of *Culicoides imicola* in Italy. *J Vet Med B Infect Dis Vet Public Health*, **50**, 139-147.
9. Conte A., Goffredo M., Ippoliti C. & Meiswinkel R. 2007. Influence of biotic and abiotic factors on the distribution and abundance of *Culicoides imicola* and the Obsoletus Complex in Italy. *Vet Parasitol*, **150**, 333-344.
10. Estrada-Peña A. & Venzal J.M. 2007. Climate Niches of Tick Species in the Mediterranean Region: Modeling of Occurrence Data, Distributional Constraints, and Impact of Climate Change. *J Med Entomol*, **44** (6), 1130-1138.
11. Giovannini A., Calistri P., Conte A., Goffredo M., Paladini C., Lelli R. & Caporale V. 2008. Bluetongue virus serotype 8 in Europe in 2007–2008 and the risk of virus introduction and spread in Italy. *In* Symposium on 'Bluetongue in Europe back to the future'. Brescia (Italy), 7 June 2008.
12. Giovannini A., Paladini C., Calistri P., Conte A., Colangeli P., Santucci U., Nannini D. & Caporale V. 2004. Surveillance system of bluetongue in Italy. *Vet Ital*, **40** (3), 369-384.
13. Kao R.R. 2002. The role of mathematical modelling in the control of the 2001 FMD epidemic in the UK. *Trends Microbiol*, **10** (6), 279-286.
14. Kao R.R., Danon L., Green D.M. & Kiss I.Z. 2006. Demographic structure and pathogen dynamics on the network of livestock movements in Great Britain. *Proc Biol Sci*, **273** (1597), 1999-2007.
15. Keeling M.J. & Rohani P. 2008. Modeling infectious diseases in humans and animals. Princeton University Press. Princeton (US) and Oxford (UK), 366 p.
16. Natale F., Giovannini A., Savini L., Palma D., Possenti L., Fiore G. & Calistri P. 2009. Network analysis of Italian cattle trade patterns and evaluation of risks for potential disease spread. *Prev Vet Med*, **92**, 341-350.
17. Feiffer D.U., Robinson T.P., Stevenson M., Stevens K.B., Rogers D.J. & Clements A.C.A. 2008. Spatial Analysis in Epidemiology. Oxford University Press. 142 p.
18. Sarto I Monteys V., Ventura D., Pages N., Aranda C. & Escosa R. 2005. Expansion of *Culicoides imicola,* the main bluetongue virus vector in Europe, into Catalonia, Spain. *Vet Rec*, **156**, 415-417.
19. Savini G., Goffredo M., Monaco F., De Santis P. & Meiswinkel R. 2003. Transmission of bluetongue virus in Italy. *Vet Rec*, **152**, 119.
20. Savini G., Goffredo M., Monaco F., Di Gennaro A., Cafiero M.A., Baldi L., De Santis P., Meiswinkel R. & Caporale V. 2005. Bluetongue virus isolations from midges belonging to the Obsoletus complex (Culicoides, Diptera: Ceratopogonidae) in Italy. *Vet Rec*, **157**, 133-139.
21. Tatem A.J., Baylis M., Mellor P.S., Purse B.V., Capela R., Pena I. & Rogers D.J. 2003. Prediction of bluetongue vector distribution in Europe and north Africa using satellite imagery. *Vet Microbiol*, **97**, 13-29.
22. Townsend Peterson A. 2007. Ecological niche modelling and understanding the geography of disease transmission. *Vet Ital*, **43** (3), 393-400.
23. Van Ittersum M.K., Laffelaar P.A.,VanKeulen H., Kropff M.J., Bastiaans L. & Goudriaan J. 2002. Developments in modelling crop growth, cropping systems and productions systems in the Wageningen School. *NJAS - Wageningen Journal of Life Sciences*, **50** (2), 239-247.
24. Wasserman S. & Faust K. 1994. Social Network Analysis: Methods and Applications. New York and Cambridge, Cambridge University Press, 825 p.