

National monitoring and surveillance

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Summary

The author describes the characteristics of surveillance systems and the use of surveillance in the three following scenarios: absence of infection, appearance of an exotic/emerging infection and endemic infections. In a population free from an infection, surveillance is used mainly to protect, by means of early detection systems, the population itself from the introduction of the infectious agent from other populations, and to document the health status of the population for international trade purposes. When an exotic infection enters a country, the information required to foresee its possible spread and to plan control and eradication activities is very often missing. As an example of the use of surveillance to collect the information needed to plan control and eradication activities, the author describes the response to the incursion into Europe of bluetongue in the early 2000s. The European brucellosis programme (from 1964 to the present) is taken as an example of the use of surveillance to monitor the control/eradication activities and to steer the control/eradication programme. Finally, the principal challenges currently faced by animal health surveillance professionals are discussed, namely: the methods for gathering information from the wild animal populations, and the methods used to evaluate the equivalence between different surveillance systems based on structured non-random activities and random surveys.

Keywords

Control, Early detection systems, Eradication, Freedom from infection, Notification systems, Surveillance.

Sistemi nazionali di sorveglianza e di monitoraggio

Riassunto

L'autore descrive le caratteristiche dei sistemi di sorveglianza ed il loro utilizzo nei seguenti tre scenari: assenza di infezione, insorgenza di una infezione esotica/emergente e infezioni endemiche. In una popolazione indenne, la sorveglianza viene utilizzata principalmente per proteggere la popolazione stessa -attraverso l'utilizzo di sistemi di rilevazione precoce- dall'introduzione dell'agente patogeno, nonché per documentarne lo stato sanitario ai fini del commercio internazionale. Quando una infezione esotica entra in un paese, generalmente mancano le informazioni richieste per prevederne la possibile diffusione e per pianificare le attività di controllo e di eradicazione. L'autore descrive la risposta all'insorgenza della bluetongue in Europa agli inizi degli anni 2000 come esempio dell'utilizzo della sorveglianza per raccogliere le informazioni richieste ai fini della pianificazione della attività di controllo ed eradicazione. Il programma europeo di lotta alla brucellosi (dal 1964 ad oggi) viene preso come esempio per descrivere l'uso della sorveglianza per monitorare le attività e per governare il piano di

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controllo/eradicazione della malattia. Infine, vengono discusse le principali sfide in materia di sorveglianza che si trovano a fronteggiare gli operatori di sanità animale, e precisamente la definizione di metodi per la raccolta di informazioni nell'ambito delle popolazioni di animali selvatici e la definizione di metodi per valutare l'equivalenza tra diversi sistemi di sorveglianza, basati su una raccolta strutturata di dati non randomizzati e su indagini campionarie.

Parole chiave

Controllo, Eradicazione, Qualifica di indenne, Sorveglianza, Sistemi di notifica, Sistemi di rilevazione precoce.

Introduction

The definition of 'monitoring' and 'surveillance' has probably been debated more than any other medical term. There are no definitions of medical terms that give rise to more heated debate than 'monitoring' and 'surveillance'. A clear example of the differing views on the meaning of surveillance is demonstrated in the OIE (Office International des Épizooties or World organisation for animal health) *Terrestrial animal health code* (32), where different expert groups on different occasions gave different definitions. In the *General definitions* chapter, the following definition of surveillance is provided 'Surveillance: means the investigation of a given population or subpopulation to detect the presence of a pathogenic agent or disease; the frequency and type of surveillance will be determined by the epidemiology of the pathogenic agent or disease, and the desired outputs' and in the specific chapter on General guidelines for animal health surveillance, the definition is 'Surveillance: The systematic ongoing collection, collation, and analysis of data, and the timely

dissemination of information to those who need to know so that action can be taken'.

Therefore, in the present paper, the teaching of Karl Popper (33) will be followed and definitions will be avoided. According to Popper, definitions are never really needed and rarely of any use, except in a few specific cases. He says that 'the problem of giving a definition in 'exact' or 'precise' terms is a pseudo problem. It depends essentially upon the inexact and imprecise terms 'exact' and 'precise'. These are most misleading, not only because they strongly suggest that there exists what does not exist – absolute exactness or precision – but also because they are emotionally highly charged: under the guise of scientific character and of scientific objectivity, they suggest that precision or exactness is something superior, a kind of ultimate value, and that it is wrong, or unscientific, or muddle-headed, to use inexact terms [...] Also, a definition must always use undefined terms in its *definiens* (since otherwise we should get involved in an infinite regress or in a circle); and if we have to operate with a number of undefined terms, it hardly matters whether we use a few more'.

When the discussion moves to less philosophical and more practical aspects, such as the outcomes expected by a 'surveillance and monitoring system', a widely shared agreement is usually achieved. Three main scenarios will be considered in this paper, as follows:

- absence of infection – documenting the freedom from infection for the purpose of international trade
- appearance of an exotic/emerging infection – collection of the data required for the planning of control activities
- endemic infections – monitoring the control/eradication activities.

In all three scenarios, if the objectives are to be effectively and successfully achieved, a system

capable of providing the information needed to steer the health system is required. Therefore, the characteristics of the system needed to monitor the activities performed and to evaluate the achievements of the health activities will be analysed.

Historical notes

Descriptive accounts

The first data collections and reports on disease frequency and mortality take the form of descriptive accounts left by the chroniclers that describe the general character of the disease and the number of victims. For example, one of the most ancient detailed chronicles of an epidemic is the account by Thucydides of the Athenian plague in 430-26 BC during the Peloponnesian War (Thucydides, 431 BC) (38). During this epidemic, the plague spread quickly because of overcrowded wartime conditions in the city, killing tens of thousands. In his history of Rome, Titus Livy (60 BC-17 AD) cited a number of epidemics; in particular, he narrated that in the year of Rome 328 (425 BC) a skin disease had affected all livestock and their caretakers (25). However, many of these accounts were embellishments and thus act as supporting evidence and are not completely factual, but they do reflect the situation at the time (2).

Data collections

The first regular data collections of health interest started in the 8th century and are death records from religious institutions and baptism registrations (2).

Case reporting

Case reporting for infectious diseases dates back to the 14th century in Italy and to the 16th century in Great Britain. These reporting systems were also used for specific public health purposes: commencing in 1348, Italian health officials quarantined, for forty days, people infected with plague who were identified on ships arriving at ports (1). The main concern of the Italian health officials was a very modern one indeed: the early

detection of plague epidemics in order to implement preventive action. During the Black Death, the great plague epidemic that swept over Europe between 1347 and 1350, 'guardians of public health' were appointed by the Venetian Republic to turn away ships with infected passengers and to detain travellers from plague-infected areas (28). In the same period, in Florence, following the failure of Galenic medicine, government officers were appointed as 'health officials' (*Ufficiali di sanità*). These health officials were an embryonic form of a public health and surveillance service; their tasks involved the management of the epidemic by overseeing markets, assessing the origin of merchants, ensuring that personal belongings of patients who died of plague were not sold, etc. During the following century, the Italian states implemented a tight information network linking the embryonic health services of the different states notwithstanding the continuous inter-state diplomatic contentions (14). The importance attached to surveillance, however, varied dramatically in the different European countries: in the first half of the 17th century, the health offices of the northern Italian states consistently complained about the underestimation by northern European countries of plague and of checks aimed at preventing plague (12). In England, for example, data collection on the spread of plague, similar to that adopted during the 15th and 16th centuries in northern Italy, did not start until 1592 with the institution of the *Bills of mortality* (24). Surveillance activities in the 16th and 17th centuries led to recording of vital events for health and scientific purposes. The statistics thus compiled were interpreted and distributed in weekly mortality reports to those who could take appropriate action to limit harmful effects (24). This early system illustrates the principles of surveillance in epidemiology, in that it required systematic data collection, analysis, interpretation, and dissemination for the purpose of action (15,

17, 28). By the 18th century, surveillance in European countries was part of a rudimentary public health service that addressed health in schools, injury prevention, maternal and child health, and public water treatment. European officials claimed that the health of the people was the responsibility of the state (28), and parallel efforts were soon under way in colonial America (17).

Bacteriology

It was not until the late 19th century – the period in which the new science of bacteriology identified germs that could be transmitted from person to person as the cause of disease – that most nations began systematic reporting of infectious diseases among individuals by name, often, but not exclusively, for the purpose of initiating quarantine, isolation or vaccination. While bacteriology served as a justification to pursue new public health strategies, such as isolation and name reporting, it was not a precondition for the adoption of those strategies (1). The first laws requiring the reporting of smallpox, yellow fever and cholera in America were passed in the colony of Rhode Island in 1743 (15). In most instances, however, it was bacteriology that gave new impetus to notification by name. The origins of the 1934 national notification system in Italy (the ‘Health Act’ or *Testo Unico delle Leggi Sanitarie*) lay in an 1888 Act compelling physicians to report some eleven infectious diseases. The system in Italy was ‘geared to the isolation and treatment of individual cases of disease rather than to prevent their occurrence in the community’ (28).

Determinants of diseases

In the 20th century, the focus shifted to view disease as a public phenomenon and epidemiologists studied the distribution and effects of diseases and injuries on human populations. In summary, while disease reporting by the late 19th century was undertaken with an eye to tracking individuals to facilitate public health interventions such as quarantine; by the mid-20th century, the uses of

surveillance broadened to include non-infectious diseases and conditions and became more varied and more tailored to the specific goal at hand, and personal and population surveillance began to coexist (1). This change in the focus of surveillance was mainly due to the work of Alexander D. Langmuir, chief epidemiologist at the Communicable Disease Center (later renamed the Centers for Disease Control and Prevention [CDC]). At the CDC, Langmuir expanded the scope of epidemiological surveillance to include the surveillance of populations rather than individuals and used the term ‘surveillance’ to refer to the collection, analysis and dissemination of data. Subsequently, surveillance also incorporated disease control responsibilities. The further progress in the definition of the characters of surveillance occurred in 2005, with the adoption of new international health regulations (IHR) by the Fifty-Eighth World Health Assembly of the World Health Organization (WHO) (3). The IHR constitute an international treaty that deals with the international notification of health-related events of possible international concern. However, the IHR, while dealing with the international component of surveillance, have consequences and effects on national components. This consequence was largely an indirect one in that the 1969 edition of the IHR did not address surveillance infrastructure and capabilities. The 2006 edition of the IHR also defines surveillance and response capacity requirements (3). However, the new IHR were not a change of paradigms in respect to the development achieved in the CDC during the 1950s, but rather an improvement and a revision of the original concept. The main modifications are as follows:

- the definition of health-related events under surveillance, that now include any unexpected or unusual public health event, and are identified by a decision instrument (provided in the IHR), which focuses on risk assessment criteria of public health importance (Fig. 1)

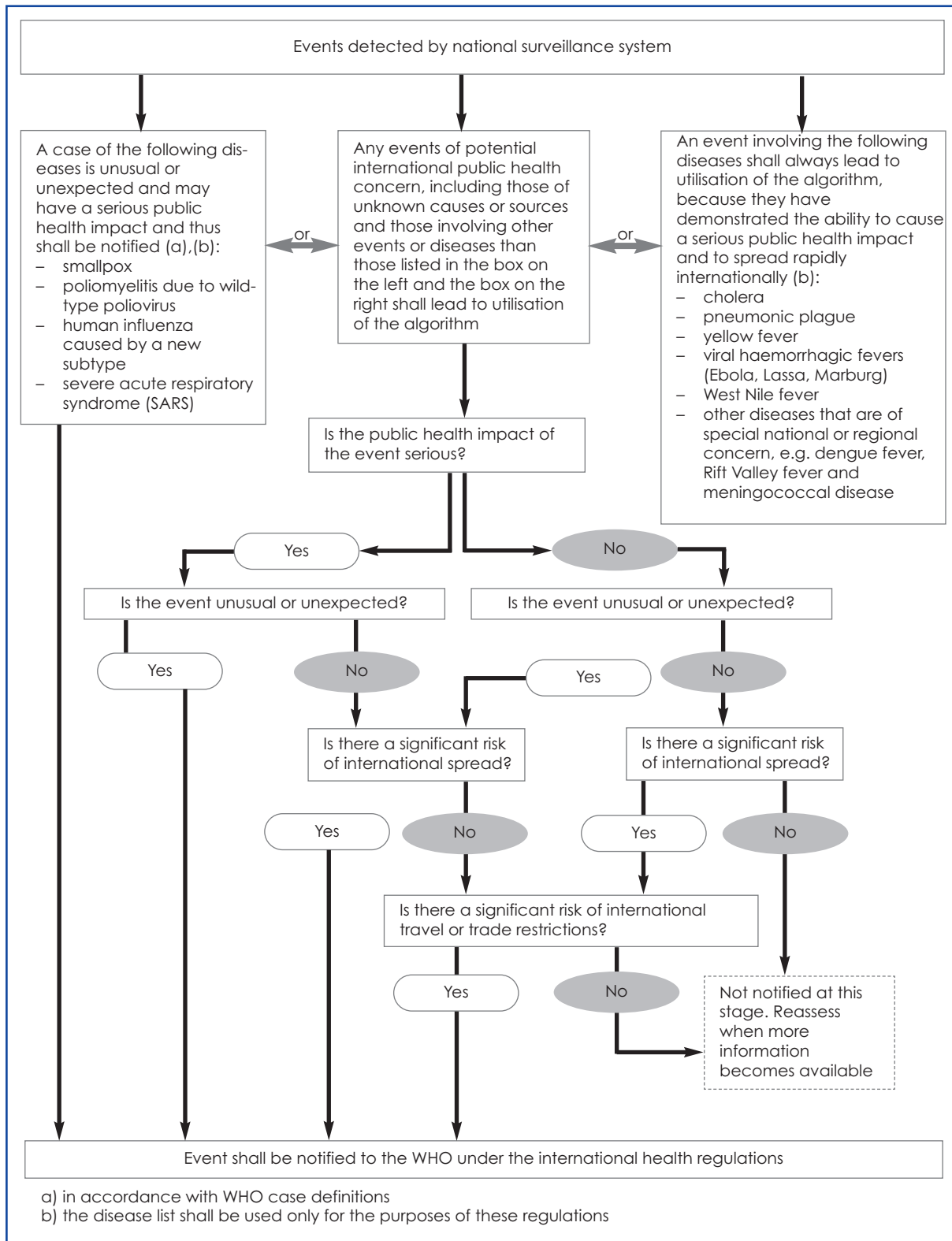


Figure 1 Decision instrument for the assessment and notification of events that may constitute a public health emergency of international concern

- the definition of the surveillance capacity requirements (in terms of usefulness, sensitivity, timeliness, stability, simplicity, flexibility, acceptability, data quality, positive predictive value, and representativeness) and of the minimal response required by the health system to health-related events (Fig. 2).

Animal health

In the animal health field, the evolution of disease reporting and surveillance has been strikingly similar to that observed in the human health sector. The only significant difference was a delay in the development and this was only observed during

the first phases of the development. In the veterinary field, similarly to human medicine, the first data collections and reports on disease frequency and mortality took the form of descriptive accounts left by the chroniclers. Virgil (70-18 BC), Ovid (43 BC-18 AD) and Vegetius (383-450 AD) described animal epidemics and Columella recognised bovine animals as carriers of contagious bovine pleuropneumonia (CBPP) (25).

Comprehensive information on disease distribution, occurrence, origin and control measures has only been available since the 18th century (i.e. two centuries after it was a common achievement for

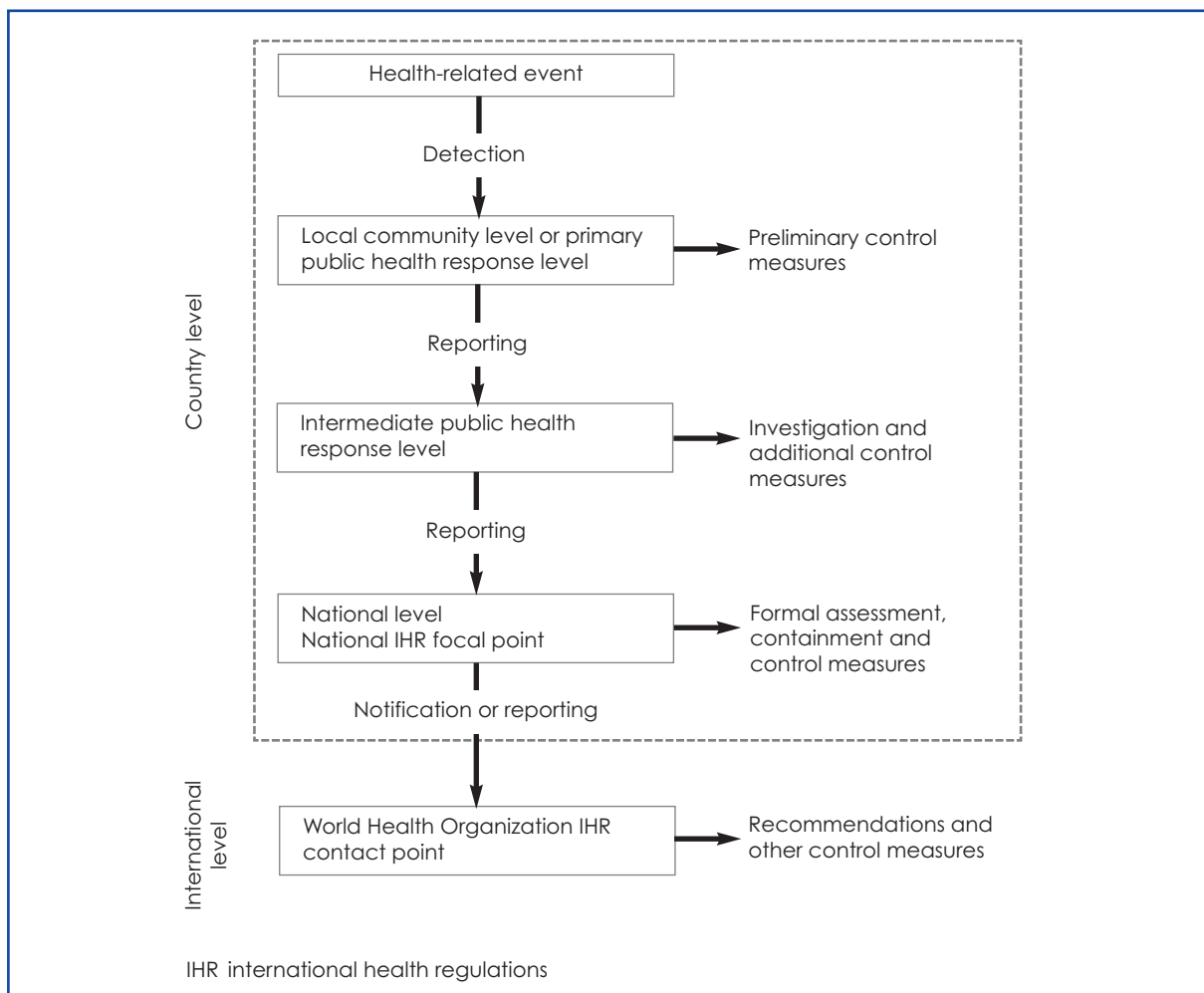


Figure 2
Public health surveillance structures and processes specified in international health regulations, 2005
Source: Baker and Fidler (3)

the human sector in northern Italy). In the second decade of the 18th century, a large epidemic of rinderpest swept across Italy and a comprehensive report on the epidemiological investigation was published by Borromeo in 1712 (9).

From the 19th century, the evolution of data gathering and use in veterinary medicine began to parallel that of public health. Veterinarians included in the local departments of public health, started to use the data collected to justify the execution of programmes aimed at preventing human diseases caused by food of animal origin (meat, milk, etc.). On the contrary, the collection of animal disease incidence data through disease notification, attempted by veterinarians working in the animal health departments, proved more difficult than for their public health counterparts. Therefore, veterinarians started quite early an active 'down the road' collection of data through herd visits and animal testing. One of the first examples of this type of data collection is within the CBPP eradication programme in the United States of America, performed by the Bureau of Animal Health. A similar approach was followed by several European countries for the eradication of rinderpest (36).

These first experiences show that, in the animal health sector, population surveillance and the tight association of surveillance with the management of control or eradication programmes started very early. The animal health officials in the mid-20th century were, therefore, culturally ready to accept the new approach developed by Alexander Langmuir and the development of this approach in the CDC coincided with the commencement of the principal mass disease control campaigns in Europe and in the United States, as follows:

- brucellosis and tuberculosis campaigns initiated in 1964 in Europe

- hog cholera (classical swine fever) campaign launched in 1963 in the USA
- most European countries started foot and mouth disease (FMD) mass vaccination campaigns in 1952
- the USA started in 1948 a cooperative programme with Mexico (and other Latin American countries) to control, eradicate and prevent FMD, thus protecting US livestock that was already FMD-free.

In the last decade of the past century, the globalisation of international trade and increased movements of human populations made it clear that the results of eradication campaigns were not the ideal method for every disease and that the segregation of animal and human populations, required to ensure the absence of risk of re-introduction of eradicated infections, was impossible to achieve in a globalised world. In the meanwhile, the policies of developed countries changed and led to the following:

- a decrease in public expenditure and intervention in health and food safety areas
- a transfer of responsibilities of the safety of food products to the producers (hazard analysis and critical control point or HACCP systems)
- the acknowledgement of the impossibility of any attempt to achieve a 'zero-risk' level and to the substitution of a 'zero-risk' policy with a policy of 'acceptable risk'.

Therefore, the animal and human health crises (FMD epidemics in the United Kingdom, severe acute respiratory syndrome [SARS], etc.) that occurred in the last decade of the 20th century and the first decade of the 21st century, together with the above-mentioned changes in disease control policies, required consistent changes in the paradigms of surveillance, in particular:

- criteria for international notification of animal diseases changed, emphasising the importance of (sudden) changes in the distribution of diseases (see chapter 1.1.2. Notification and epidemiological information in the *Terrestrial animal health code* and a similar change to that

- already described in the new IHR) (3, 32)
- early warning systems have been strengthened and globalised (6)
- surveillance activities have become more focused and risk-based (37).

Animal health surveillance

In the following sections, some essential characteristics of surveillance systems and the expected outputs of surveillance in relation to the three scenarios will be discussed.

Common characteristics and differences

In general, surveillance is aimed at demonstrating the absence of disease or infection or determining the occurrence or distribution of disease or infection, or detecting exotic or emerging diseases as early as possible. The type of surveillance applied depends on the desired outputs needed to support decision-making. Animal health surveillance is an essential component to detect diseases, monitor disease trends, control endemic and exotic diseases, support claims for freedom from disease or infection, provide data to support the risk analysis process for both animal health and/or public health purposes, and substantiate the rationale for sanitary measures. Surveillance data underpin the quality of disease status reports and should satisfy information requirements for accurate risk analysis, both for international trade and for national decision-making (32).

Depending on the objectives, resources and organisation infrastructure available, surveillance can be performed in a number of different ways. In particular, the surveillance:

- may be focused on a specific pathogen or any specific health problem
- may be based on an active or passive collection of data
- may collect data from the entire population under study or from a sample selected from the population
- in the case of a sample selected from the population, units for observation may or may not be randomly selected.

The method chosen will depend on the circumstances and more than one method may be used to monitor a disease situation. A very meaningful example of the effectiveness of various types of surveillance is the case of the CBPP epidemics in Italy. During that epidemic, surveillance prescribed by Italian law to detect outbreaks and eradicate infection was identical for dairy and fattening herds. During the epidemic, 94 outbreaks occurred between October 1990 and September 1993, when the infection was definitively eradicated. The methods of detection of the outbreaks were recorded for 76 of the outbreaks. Of these, 36 (47%) were detected using serology and 40 (53%) were detected using either post-mortem findings at the abattoir (30 outbreaks) or were clinically (10 outbreaks) detected (34). In other words, 47% of the outbreaks were detected using specific surveillance, or active collection of data, or using a sample extracted from the entire susceptible population; while 53% were detected using non-specific surveillance, or passive collection of data, or data collection from the entire population of interest (in the case of clinical detection), or a non-random sample of the susceptible population (abattoir detection). It is also worthy to note that most of the outbreaks in the dairy herds, where the method of detection was recorded (31 of the 47 or 66%), were detected using serology while almost all the outbreaks in beef herds (20 of 21 or 95%) were detected using non-specific methods. The difference is statistically significant (Fisher's exact test, $p=0.000002$). The effectiveness of detection methods characterised by low sensitivity when used at an individual

level, such as clinical examination or the necropsy at the abattoir, may produce a different behaviour of sensitivity at group level. The diagnosis at abattoir level of CBPP in Italy was based on two tests in series, both tests characterised by a low sensitivity at the individual level, as follows:

- the detection of typical CBPP lesions (lungs with marble lesions, sequestra, fibrinous pleuritis, etc.)
- bacteriological confirmation.

The sensitivity of isolation of *Mycoplasma mycoides* has been estimated at approximately 54% in natural outbreaks (4). In 11 CBPP-infected herds, in which data on the type of lesions and isolation were recorded at the moment of slaughter of all animals in the herds (4), 301 of 595 (51%) animals had pathological lesions or were positive for isolation of the agent from their tissues. Most of the 301 animals with lesions or successful isolation had chronic lesions (272/301, i.e. 90%). If we conservatively estimate that only 10% of animals with acute lesions and 20% of animals with chronic lesions are detected during the routine checks performed at the abattoir, the sensitivity of the entire diagnostic process (lesion detection and bacteriological confirmation) would be 10.3%. Sensitivity of the serological test (complement

fixation test) is 63.8% (4). The comparison of the two detection procedures is shown in Figure 3, where it is clearly evident that even with a sensitivity rate of 10% at the individual level (that of pathology with bacteriological confirmation), the sensitivity at group level quickly approaches that of the serological test. In particular, when more than 30 infected animals are slaughtered, the probability of detecting infection in at least one of the animals is greater than 96% (Fig. 3). The number of animals involved in the 94 outbreaks in Italy were 24 053 (34), with an average herd size of 256 animals, and the intra-herd prevalence was 51% (4). The decreased production of infected animals is conducive to their culling, therefore the number of animals tested quickly increases to a value offering a very high probability that infection will be detected; this explains why abattoir testing is an effective method for the detection of outbreaks.

Uses of surveillance

In this section, the three following main scenarios will be considered:

- absence of infection
- appearance of an exotic/emerging infection
- endemic infections.

Absence of infection

In a population free from an infection, surveillance is used mainly to protect the population from the introduction of the infective agent from other populations and to document the health status of the population for international trade purposes. The first of the two above-listed surveillance aims is mainly achieved through the use of early detection systems. There is now unanimous agreement on the importance of having an efficient national surveillance and monitoring system, for animal diseases and zoonoses in domestic and wild animals, that is capable of generating reliable information on the disease situation within the

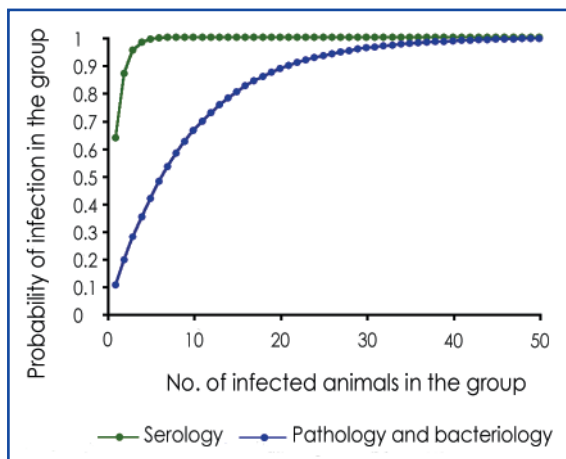


Figure 3
Sensitivity at group level of two detection methods

country and of rapidly detecting diseases introduced accidentally or deliberately. A long-term surveillance plan to maintain a high level of awareness against exotic diseases should be in place; however, it is not advisable to have an additional specific system to detect emerging diseases. Therefore, the routine disease surveillance and monitoring system should be able to detect animal health events whenever they occur. It is important to ensure that the system is able to detect and identify emerging phenomena or diseases, to enable a rapid evaluation of the situation and, if necessary, sound the alarm and trigger the appropriate measures to control the disease (6). The general characteristics that a national early detection system should include are clearly listed in the *Terrestrial animal health code* (32). According to the *Code*, an early detection system should be operated by the veterinary services and should include the following characteristics:

- representative coverage of target animal populations by field services
- the ability to undertake effective disease investigation and reporting
- access to laboratories capable of diagnosing and differentiating relevant diseases
- a training programme for detecting and reporting unusual animal health incidents should be provided to veterinarians, veterinary para-professionals and others involved in handling animals
- information on the legal obligations of private veterinarians in relation to the veterinary administration
- a timely reporting system of the event to veterinary services
- a description of the a national chain of command.

However, the existence of early detection systems at the national level is not sufficient to ensure that if an exotic disease is introduced into the country, it can be rapidly controlled with a minimum of

damage. Therefore, international early warning systems have been developed by international organisation such as the OIE, Food and Agriculture Organization (FAO) and WHO.

The OIE manages the international animal disease reporting system for the principal animal diseases, including zoonoses. Within this international animal disease reporting system, one component is the international early warning system, with an alert procedure to warn of exceptional epidemiological events, whether natural or intentional, that occur in member countries. Information is provided to decision-makers and other stakeholders to enable them to take the necessary preventive measures. Under this system, the occurrence of any exceptional epidemiological event must be reported as soon as possible to the OIE headquarters, which then redistributes the information through various channels. Follow-up reports are provided weekly to allow end-users to follow the epidemiological situation as it develops (6).

In 1994, the FAO established an emergency prevention system (EMPRES) for transboundary animal and plant pests and diseases to minimise the risk of such emergencies (16). Initial priority was given to two transboundary pest and diseases problems (2), as follows:

- major transboundary livestock diseases, including rinderpest and other epidemic animal diseases (CBPP, FMD, contagious caprine pleuropneumonia, peste de petit ruminants, Rift Valley fever and lumpy skin disease)
- the desert locust.

Early warning messages are posted on the internet and distributed via the EMPRES-livestock mailing list. More recently, EMPRES also included avian influenza among the transboundary animal diseases of interest, thus extending the system to a more global coverage than its initial scope (16).

For diseases of public health concern, the IHR of the WHO require member countries to notify the

WHO of any unexpected or unusual public health event (3).

In April 2000, the WHO launched the global outbreak alert and response network (GOARN), the objective of which is to gather epidemic intelligence from informal sources. It uses a multilingual application, which searches key websites, alert networks, newswire services and on-line media sites, public health email services, and websites of national governments, public health institutions, non-governmental organisations and specialised discussion groups to identify early warning information about epidemic threats and rumours of unusual disease events.

In 2004, to improve the efficiency of their early warning systems, the FAO, OIE and WHO embarked on the development of a global early warning system (GLEWS). The main objectives of GLEWS are as follows (6):

- to share the results of disease tracking systems between the three organisations
- to improve the information verification processes
- to develop a tool to assist in predicting livestock animal disease threats through epidemiological analysis and the examination of additional factors that might also have an impact on the occurrence and spread of such diseases (e.g. economic factors, civil unrest, and climate changes).

The other aim of surveillance in reference to diseases that are not present in a country is to document the free status. Documenting the free status of a country or zone facilitates the international trade of animals and animal products and supports the provisions of the *Terrestrial animal health code* and SPS Agreement.

The SPS Agreement (39) requires WTO members to base their sanitary measures on international standards, guidelines and recommendations, where they exist. The SPS Agreement recognises the OIE as the international organisation responsible

for the development and promotion of international standards, guidelines and recommendations for animal health and zoonoses. The relevant international standards for trade in live animals and animal products are the *Terrestrial animal health code* (for mammals, birds and bees) and the *Aquatic animal health code* (for fish, molluscs and crustaceans). According to both documents, recommendations for importing from a 'free country' are less demanding than those from non-free countries. Member countries of the WTO may also choose to adopt a higher level of protection than that provided by these texts if there is scientific justification or if the level of protection provided by measures prescribed in the relevant text are considered insufficient. In such circumstances, members are obliged to base such measures on a risk assessment and to adopt a consistent approach to risk management (29).

Whatever the path chosen by the trading countries (recognition of the free status by the OIE, available only for a few selected diseases, bilateral recognition of the free state, or adoption of a risk assessment), the definition of the status of a country or zone has to be based on factual data. Demonstrating freedom from infection involves providing sufficient evidence to demonstrate (to a level of confidence acceptable to member countries) that infection with a specified pathogen is not present in a population. In practice, it is not possible to prove (i.e., be 100% confident) that a population is free from infection (unless every member of the population is examined simultaneously with a perfect test offering 100% sensitivity and specificity). Instead, the aim is to provide adequate evidence (to an acceptable level of confidence), that infection, if present, is present in less than a specified proportion of the population (32).

Such evidence may be provided (32) either by structured population-based surveys (such as systematic sampling at slaughter or random

surveys) or by structured non-random surveillance activities. A wide variety of non-random surveillance sources may be available. These vary in their primary purpose and the type of surveillance information they are able to provide. Some surveillance systems are primarily established as early detection systems, but may also provide valuable information to demonstrate freedom from infection. Other systems provide cross-sectional information suitable for prevalence estimation, either once or repeatedly, while others provide continuous information, suitable for the estimate of incidence data (e.g. disease reporting systems, sentinel sites, testing schemes). Surveillance systems routinely use structured non-random data, either alone or in combination with surveys. Examples of non-random data sources that are useful when providing evidence of freedom from infection/disease are as follows: disease reporting/notifications, results of control programmes/health schemes, results of targeted testing/screening, ante-mortem and post-mortem inspections, results of laboratory investigations, field observations, testing of biological specimen banks, sentinel animal observation/testing and farm production records.

Surveillance information gathered from the same country, zone or compartment at different times may provide cumulative evidence of animal health status. Such evidence gathered over time may be combined to provide an overall level of confidence.

Appearance of an exotic/emerging infection

The aims of surveillance are different in the case of the occurrence of an exotic/emerging infection than in the case of the absence of infection.

When a new (i.e. by definition, an exotic) infection enters a country, additional information is required to predict its possible spread. The information needed for planning of control and eradication activities is very often missing. A paradigmatic

example of the lack of data, when there is a new incursion of a disease, is shown by what happened in Europe following the arrival of bluetongue (BT) in the early 2000s. In terms of both control actions and surveillance, neither the European Union (EU), nor the affected European countries were adequately prepared to cope with the problems posed by a vector-borne disease, such as BT, when it first appeared (18).

Prior to the 1998 outbreak in the Mediterranean, little information was available on the distribution of BT virus (BTV) vectors, i.e. of areas at risk of infection. In the early 1980s, *Culicoides imicola* had been identified in Spain, Portugal and on the Greek islands of Lesbos and Rhodes (7, 8, 26, 27). The presence of *C. imicola* had not been reported from the Balearic islands, Corsica, Sardinia, Sicily and Malta, nor was it found in the mainland territories of Greece and Italy (8). Further studies conducted in southern Italy, Sicily and the island of Pantelleria (Italy) in 1996 did not detect the presence of *C. imicola* (35). It was only in June 2000 that *C. imicola* was first identified in western Sicily (22). Even less was known regarding the distribution of other potential vectors of BTV, namely species of the *Obsoletus* and *Pulicaris* Complexes. Therefore, the Italian government decided to design a surveillance system that could delineate with precision the areas in which *C. imicola* might be present and where the virus might circulate (13). The predicted epidemiology of bluetongue, if introduced into southern Europe, was also unknown. Quantitative information was missing on the speed of spread, the possible risk posed by animal movement and transhumance and on the expected incidence of infection in the various susceptible species. Therefore, a number of serological surveys were initiated in the declining phase of the epidemic peak. Target populations and sampling design of the surveys varied in the various regions that were monitored. The design

depended on the behaviour of the epidemic and on the knowledge already accumulated (21). Results obtained from monitoring activities performed during the winter of 2000-2001 were used to plan the sentinel network in Italy, and as input data for a risk assessment aimed at deciding the control strategy to be adopted (21).

The implementation of the final surveillance system, that addressed the objectives of the Italian government and the requirements of the EU legislation, was logistically challenging. It required the gathering of vast quantities of data and very intensive field activities. It involved the regular clinical evaluation (in most cases fortnightly) of more than 30 000 sentinel animals and the placing of about 250 permanent insect traps throughout Italy.

Information and data produced by the surveillance system constitutes the information base of the early warning system for BT in Italy. The system has also accurately established the epidemiology of BTV infection and the distribution and dynamics of BT vectors (13, 23). In addition, it facilitated the monitoring of the spread of BTV infection (11, 19) and the evaluation of risk factors linked to the spread of vectors and animal movements. The surveillance systems implemented in the countries of southern Europe, and particularly in Italy where BTV had spread and persisted more than in any other EU country, produced information that was critical to the development of the flexibility that now characterises the European Union legislation on BT.

The data and knowledge obtained in these studies have also facilitated risk assessments to:

- define the optimal national BT control strategy
- define the risk arising from animal movements (for production or slaughter) from restricted zones based on the presence or absence of viral circulation and to population immunity from vaccination (20)
- define the minimum level of serological surveillance able to detect ongoing BTV infection with comparable sensitivity to the existing surveillance programme (10).

Endemic infections

This is the framework in which Langmuir expanded the scope of epidemiological surveillance to include the surveillance of populations and used the term 'surveillance' to refer to the collection, analysis and dissemination of data to those who need to know so that action can be taken.

The development of the new approach in the CDC coincided with the start of the main mass disease control campaigns in Europe (brucellosis and tuberculosis in 1964, FMD vaccination in 1952) and in the United States (hog cholera in 1963, a cooperative programme with Mexico to control FMD in 1948). To describe the use of surveillance as a tool to steer a control/eradication programme, the European brucellosis campaign will be used as example of the various phases of the programme and of the modification of the surveillance objectives and activities in relation to the development of the control programmes.

Usually, a campaign against a disease that is endemic in a given population, starts with a control phase that may be followed by an eradication phase and, if eradication is successful, by a prevention phase. The European brucellosis programme (from 1964 to date) followed the pathway described above (Figs 4 and 5), with obvious differences in the health status achieved by the various national (or in some cases regional) susceptible populations. Therefore, whilst some countries are now in the prevention phase, others are still in the first phases of the control programme. The European brucellosis control programme commenced in 1964 primarily as a voluntary programme of vaccination of pre-puberal replacement animals. During these initial steps of the control campaign, the tasks of surveillance

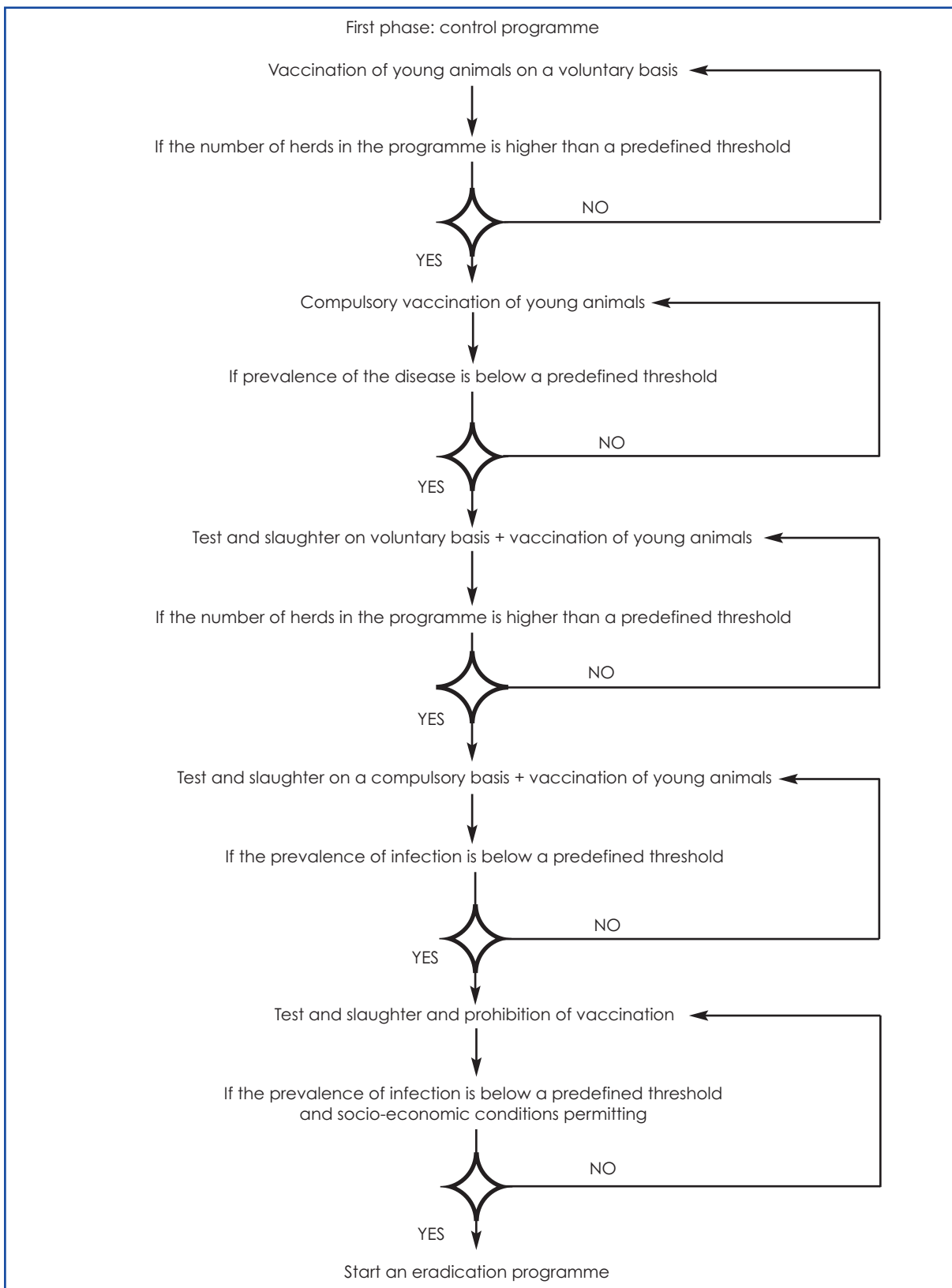


Figure 4
Brucellosis eradication phases in Europe (first phase)

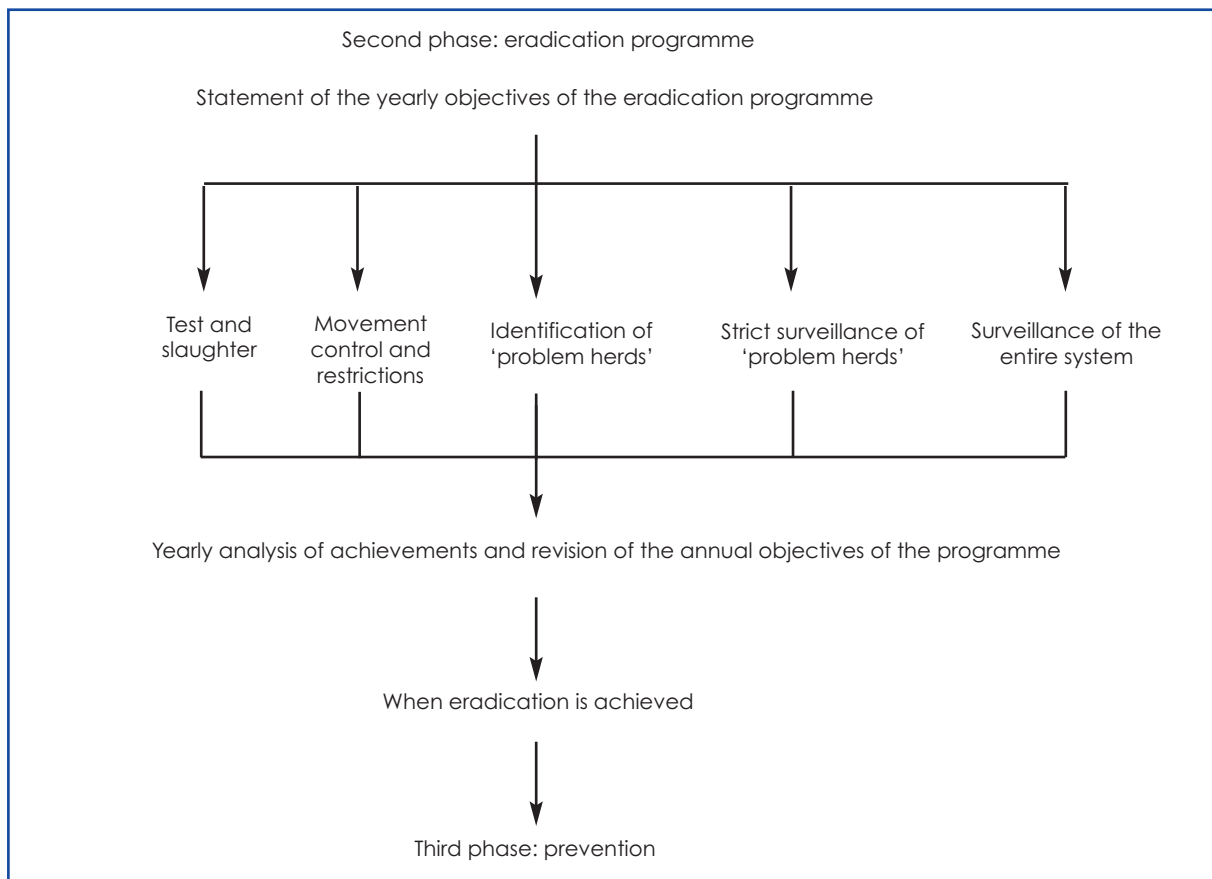


Figure 5
Brucellosis eradication phases in Europe (second phase)

were mainly the following:

- to trace back the cases of human infection to the infected herds or flocks responsible for the human cases
- to monitor the vaccination activities in terms of number of holdings participating in the programme and number of vaccinated animals.

The quantitative monitoring of the vaccination campaign was aimed at the planning of field activities and at detecting when the majority of herds/flocks participated in the programme. This information was used to decide when to modify the programme from a voluntary to compulsory one, applicable to all herds/flocks.

In the subsequent development of the programme,

there was first voluntary and then compulsory slaughter of infected animals, along with the vaccination of replacement animals (Fig. 4).

When the control programme was fully developed but before the launching of the eradication programme, the brucellosis control programme was based on the following:

- the qualification of holdings
- a compulsory annual serological testing of all reproductive stock in all national holdings
- the slaughter of reactors
- the re-testing of infected herds leading to their re-qualification.

Two main subpopulations of domestic ruminants resulted from this programme: one with a higher

health status composed of uninfected and unvaccinated holdings that had been tested periodically to ensure the absence of infection (qualified as 'officially brucellosis-free' holdings). The second subpopulation involved uninfected holdings where replacement animals were vaccinated and all adult animals were periodically tested ('brucellosis-free' holdings). The holdings with infected animals were submitted to clearing procedures aimed at achieving the 'officially brucellosis-free' or 'brucellosis-free' status, depending on a number of possible risk factors linked to each specific holding. This complex programme required a comparably complex monitoring and surveillance system to organise the field activities efficiently and to steer the programme itself (Fig. 6). Quarterly reports and an annual report were sent from the local veterinary services to the regional government and from the regional government to the central government. All cases of brucellosis in animals were notified by the local veterinary services to the local public health services. In regard to the public health sector, brucellosis is a notifiable disease, so each human case of brucellosis was reported by the local public health services to the regional government and to the local veterinary services. All outbreaks of brucellosis in humans were investigated by the local public health services to try to determine the source of infection and confirm the information reported.

When the prevalence of infection decreases below a stated value, the costs of vaccination campaigns exceed the benefits and an eradication policy may prove to provide more benefits in terms of cost. The threshold value for the change of policy depends on local conditions. However, the WHO suggests the change of policy when the prevalence of infected herds is between 1 and 5%. In Great Britain, in 1977, this threshold was set at 2% prevalence of infection in reproductive animals, which meant that herd prevalence rates were

higher than those suggested by the WHO.

Eradication is conceptually very different from control: it is neither a casual nor an automatic consequence of a control programme, no matter how well the control programme is organised or conducted. Eradication is based on sanitary measures and an organisation of activities that are completely different from those of a control programme (30). Crucial factors for the success of an eradication programme are the implementation of an effective surveillance system, together with the understanding and support of the eradication objective by the customers of the programme (i.e. the farmers).

In the final phases of a control programme and during eradication, 'problem herds' and cases of re-infection of already accredited herds become very important and may account for up to 50% of the total number of infections detected. Therefore, specific activities need to be planned to intensively monitor infected herds so as to identify the risk factors that could transform a herd into a 'problem herd' (30). In regard to the understanding and sharing of the eradication objective by the customers of the programme, during the planning phase of the programme, a detailed evaluation must be made of the socio-economic aspects that will affect the results of the programme. An analysis may be necessary to foresee the possible benefits and costs of the programme. Subsequent periodical evaluations of the real costs and benefits of the programme may be the way to gain the support required for the success of the eradication programme. In addition, the surveillance system must be capable of collecting and processing detailed information on the activities performed in order to establish a precise economic evaluation of the programme (30).

When eradication is complete, the subsequent phase of the programme is devoted to the prevention of the re-introduction of the infection in the free

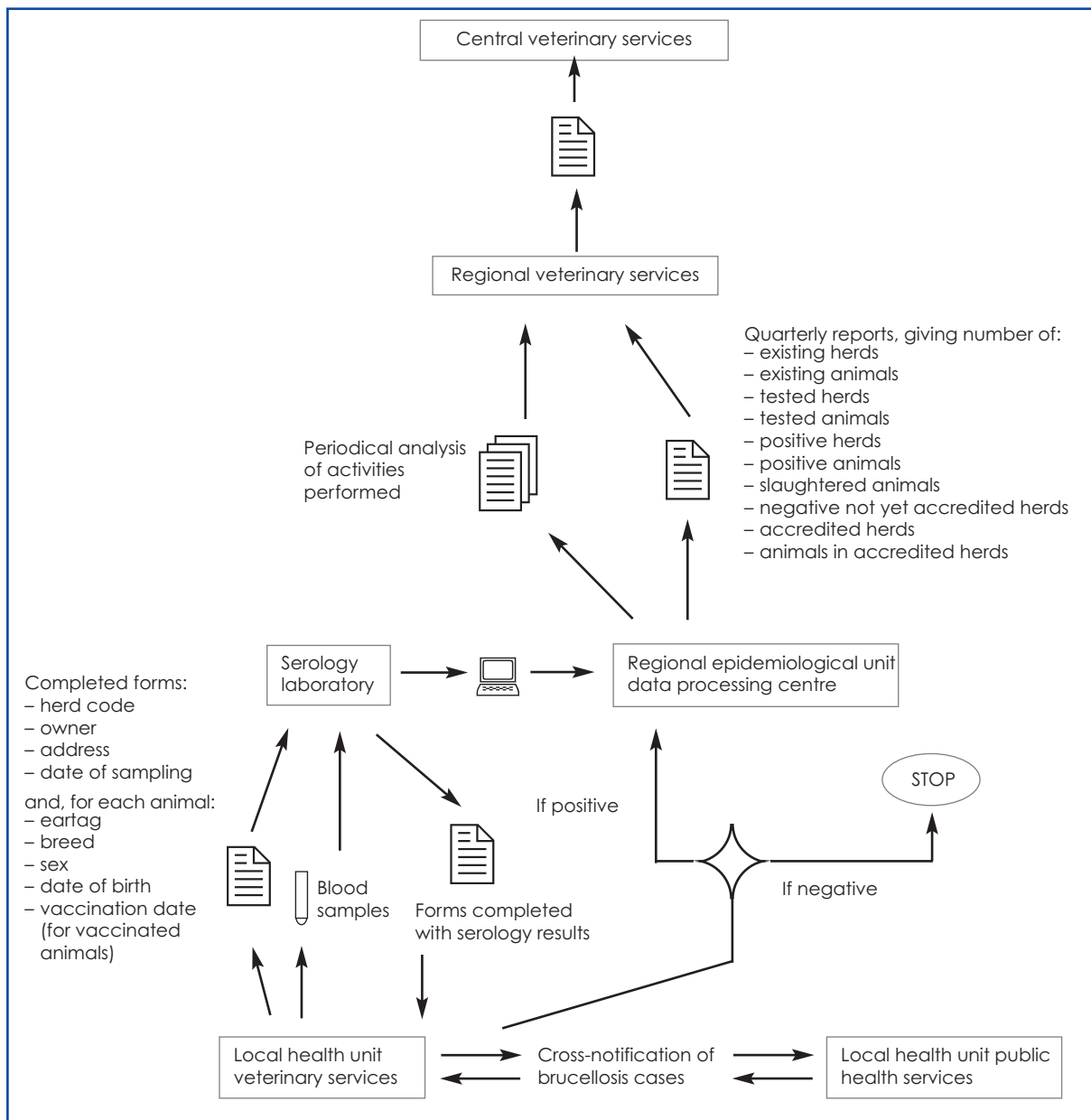


Figure 6 Information collected and data flow for veterinary component of the brucellosis control programme with reference to the Italian organisation of veterinary services

population. The role of surveillance in this situation has already been described (first scenario considered).

The use of surveillance for risk analysis

Animal health surveillance systems provide essential

inputs to conduct scientifically valid risk analyses. Animal health surveillance is so vital to risk analysis that in the past editions of the *Terrestrial animal health code*, the chapter on surveillance was part of the section on risk analysis. While a risk analysis inevitably includes elements of uncertainty, good quality

surveillance data is indeed the most reliable way of narrowing the range of uncertainty.

Surveillance data is required in all phases of a risk assessment process.

In the hazard identification phase, surveillance provides the information needed to develop a list of pathogens (i.e. hazards) that could be associated with the spread of disease or the movement of animals and animal products. Hazard identification requires information collected from existing disease control programmes or from investigations to demonstrate the absence of disease. This information is collected in both the exporting and importing countries; the quantity and quality of the data available will depend on whether or not the agent is notifiable in the exporting or in the importing country (29).

In the release assessment, the starting point is often to obtain an estimate of the prevalence of disease in the exporting country and neighbouring countries to assess the likelihood of introduction of disease from these countries either through natural means or through the movement of animals and animal products. Surveillance-based information essential for the release assessment refers mainly to the 'country factors' and concerns the evaluation of the veterinary service of the exporting country, and includes the following: the quality of the veterinary services, surveillance, eradication and control programmes, zoning systems, the existence of disease-free areas and areas of low disease prevalence, farming and husbandry practices and the consequent distribution of disease in different production systems (e.g. commercial and non-commercial operations), geographic and environmental characteristics, including rainfall and temperature, as well as the disease/infection status in (and likelihood of introduction from) neighbouring countries (29).

Concerning the exposure assessment, the central element is to identify the potential pathways for

exposure of animals in the country either through natural means or through the movement of animals and animal products. Surveillance systems may provide information on the characteristics of the susceptible populations and environmental factors in the importing country, including the animal and human (in case of zoonoses) demographics, farming and husbandry practices (in terms of type and distribution of herds, and animal densities), distribution of vectors (influenced by geographic and environmental characteristics, including rainfall and temperature), trade pathways in the importing country, including the existence and location of collecting centres and the effectiveness of the early detection system (29).

Consequence assessment involves estimating the biological and economic consequences of disease introduction. Surveillance systems (specially their international component in the case of import risk assessments) should be able to provide information on methods of spread, and morbidity and mortality in a newly infected population. This information is essential to estimate the likely number of affected herds/animals, the direct economic impact (mortality, impact on production) and the costs of control and eradication programmes.

Conclusions and future challenges

Human and animal health surveillance share strikingly similar evolutions and histories, despite the differing levels of sensitivity and awareness to disease and different expectations of public health and veterinary services, and despite the very different tools available to physicians and veterinarians for disease control.

The principal difference between human and animal health surveillance is the notification of single cases of disease in public health in comparison to the greater emphasis placed on population

surveillance in the veterinary sector. In public health, very rarely do disease notifications refer to outbreaks; usually these are single cases within a single outbreak. Outbreak notification in the human sector mainly refers to food-borne intoxications; other reports of disease outbreaks are mainly anecdotal or given in the context of scientific publications. In veterinary medicine, on the contrary, the reporting unit is usually the group of animals, so that even sporadic cases of disease are usually notified as outbreaks.

An interesting development in the approach to surveillance is that the concept of surveillance as a 'systematic collection, collation, and analysis of data, and the timely dissemination of information to those who need to know so that action can be taken'. The origin of this approach was in the public health sector, but it has been adopted rapidly by the veterinary sector. This adaptation is possibly in relation to the economic perspective that always underlies veterinary activities and to the mass prophylaxis campaigns that commenced shortly after the creation of the Epidemic Intelligence Service by Langmuir at the CDC.

The recent parallel development of surveillance in the human and animal sectors is also worthy of note, namely:

- the definition of health-related events under surveillance, that now include any unexpected or unusual health event (this is very similar in the OIE notification system and in the 2006 version of the IHR)
- the definition of the surveillance capacity requirements and of minimal response, now required by the new IHR, can be considered analogous to the concept of 'evaluation of veterinary services' described in the *Terrestrial animal health code* since the first half of the 1990s
- following the globalisation process, both animal and human surveillance place great emphasis on early warning systems and on

the international coordination of surveillance activities.

The major challenges that now face animal health surveillance professionals include the gathering of information from wild animal populations and the ability to evaluate equivalence between different surveillance systems based on structured non-random activities and random surveys.

Wildlife species are rarely the subject of surveillance activities for a number of practical reasons. Active sampling is difficult to perform because wild animals live in extensive areas, often in habitats that are difficult to access and usually with population densities that are much lower than those seen in domestic animals. Moreover, wild animal populations are often subject to a statute of protection that limits the tools available for the collection of samples. Therefore, surveillance in wildlife is mainly based on the passive collection of dead or moribund animals. In contrast to similar forms of surveillance in domestic animals, the intensity of such surveillance in wild animals is usually not related to the possible presence of disease in the target population. The main reason is that the direct effects of disease are difficult to detect in wild animals and often develop slowly at the population level. Sometimes the impact of pathogens is concealed at population level by other factors acting on the population dynamics of the host species (food availability, predation or hunting, etc.). Behavioural features of some wild animal populations may sometimes influence the population density (e.g. seasonal bird migrations, dispersal of cubs in case of foxes and wolves, etc.), and these features influence the observed mortality rate, and therefore the number of samples passively collected.

Another problem that makes surveillance in wildlife particularly difficult is the limited diagnostic tools available. For most serological tests, sensitivity and specificity are completely unknown when

the tests are applied to wild animals, while some serological tests are not applicable to wildlife due to a lack of specific reagents (e.g. indirect ELISA, due to the lack of conjugate for many wild species), skin tests requiring repeated captures of the animal are not applicable in free-living wild animals. Therefore, most diagnoses are performed using direct methods for the detection of the pathogens in the tissues of the dead or diseased animal. These methods are up to 25 times more expensive than serological tests and are more time-consuming. Therefore, according to the *Terrestrial animal health code*, for a country to be declared historically free from a disease or to declare freedom when the last occurrence has been between 10 and 25 years previously, it is required that 'infection is not known to be established in wildlife within the country or zone intended to be declared free. (A country or zone cannot apply for freedom if there is any evidence of infection in wildlife. However, specific surveillance in wildlife is not necessary)'. Similarly, according to the international standards, it is possible to declare a country free from highly pathogenic avian influenza or from classical swine fever in the domestic populations irrespective of the status of the wild populations, provided that appropriate biosecurity measures are taken to segregate and protect domestic from wild animals.

One of the main future challenges will be the development of techniques for data collection and diagnostic methods specifically tailored to the needs of wildlife disease surveillance. Better knowledge of the distribution of diseases in wild populations will be necessary both for the purpose of the conservation of wild animal populations and wild ecosystems and also to properly assess the risk to which the populations of domesticated animals are exposed in order to modulate the biosecurity measures to the actual risk. More comprehensive knowledge of the health state of

wildlife would be also necessary for public health reasons. Many emerging zoonoses (e.g. West Nile disease, Lyme disease, tick-borne encephalitis, avian influenza) and the worst public health emergencies of the last decades (e.g. human immunodeficiency virus, SARS, Ebola) have indeed originated from wild animals (5).

Another important future challenge is to be able to evaluate the equivalence between different surveillance systems based on structured non-random activities and random surveys. As clearly shown above, when discussing the effectiveness of abattoir surveillance in the detection of CBPP outbreaks, in many cases non-pathogen-specific non-random surveillance is more effective than pathogen-specific random surveys. The main drawback of non-pathogen-specific non-random surveillance is that the rate of reporting is always incomplete and that the overall sensitivity of the surveillance system is generally unknown. On the contrary, in the case of random surveys, it is possible to define either a maximum value of prevalence of infection that can be present and undetected in the target population or a confidence interval around the estimated value of prevalence, given the results of the survey. Therefore, it is usually impossible to compare the results of non-random surveillance with those of surveys and it is also impossible to evaluate the equivalence between the two approaches. Since surveillance systems are usually based on a mixture of random and non-random methods and the relative importance of either of them is related to the organisation structure of each country or region, the comparison of the results obtained is difficult and an exact determination of equivalence of different surveillance systems is not easy. The difficulties encountered are similar to those faced in the evaluation of veterinary services. The evaluation of a surveillance system (like the evaluation of a veterinary service) is always

subjective and is strongly conditioned by the entity performing the evaluation, by the organisation models referred to and by a subjective evaluation of the exporting country. Reciprocal trust between veterinary services worldwide is practically impossible unless fair and transparent evaluation methods are used (31).

The application of fair and transparent evaluation methods for both the veterinary services and the surveillance systems needs clear and detailed documentation of the procedures applied in performing the specified tasks by the veterinary services (together with the documentation of the results obtained) of the non-conformities detected in the application of procedures and of the corrective actions applied. In other words, for the application of fair and transparent evaluation methods, the veterinary service needs to operate in accordance with certified quality assurance procedures. This approach has already been adopted in the EU for the operation of laboratories involved in the testing of food and is progressively being adopted outside the EU and outside the food safety sector. Testing laboratories are required to be accredited and to operate according to the ISO 17025 standards. Similar requirements (perhaps based on the ISO 9000 series of standards) (31), will probably eventually be applied to the entire health system responsible for the certification of food production, including field veterinary services.

References

1. Anon. 2000. The role of name-based notification in public health and HIV surveillance. Joint United Nations Programme on HIV/AIDS (UNAIDS), Geneva, UNAIDS/00.28E, 47 pp (data.unaids.org/Publications/IRC-pub01/JC338-Name-based_en.pdf accessed on 31 August 2006).
2. Anon. 2006. Medieval demography. In Wikipedia, The free encyclopedia. (en.wikipedia.org/w/index.php?title=Medieval_demography&oldid=59019429 accessed on 28 June 2006).
3. Baker M.G. & Fidler D.P. 2006. Global public health surveillance under new international health regulations. *Emerg Infect Dis*, **12** (7), 1058-1065. (www.cdc.gov/ncidod/EID/vol12no07/05-1497.htm accessed on 29 June 2006).
4. Bellini S., Giovannini A., Di Francesco C., Tittarelli M. & Caporale V. 1998. Sensitivity and specificity of serological and bacteriological tests for contagious bovine pleuropneumonia. *Rev Sci Tech*, **17** (3), 654-659.
5. Bengis R.G., Leighton F.A., Fischer J.R., Artois M., Mörner T. & Tate C.M. 2004. The role of wildlife in emerging and re-emerging zoonoses. *Rev Sci Tech*, **23** (2), 497-511.
6. Ben Jebara K. 2004. Surveillance, detection and response: managing emerging diseases at national and international levels. *Rev Sci Tech*, **23**, 709-715.
7. Boorman J. 1986. Presence of bluetongue virus vectors on Rhodes. *Vet Rec*, **118**, 21.
8. Boorman J., Jennings M., Mellor P. & Wilkinson P. 1985. Further data on the distribution of midges in southern Europe and the Mediterranean area, with special reference to *Culicoides imicola*. In *Bluetongue and related orbiviruses* (T.L. Barber, M.M. Jochim and B.I. Osburn, eds). Proc. First International Symposium, 16-20 January 1984, Monterey, California. A.R. Liss, New York. *Progr Clin Biol Res*, **178**, 187-190.
9. Borromeo A.M. 1712. Relazione dell'epidemia de' buoj succeduta nel Padovano l'anno MDCCXI. In: Anon. *Istoria dell'epidemia de' buoj accaduta nel Padovano l'anno mdccxi*. Felice Mosca, Naples, 1-42.
10. Calistri P., Giovannini A., Conte A. & Caporale V. 2004. Use of a Montecarlo simulation

- model for the re-planning of bluetongue surveillance in Italy. *In* Bluetongue, Part I (N.J. MacLachlan & J.E. Pearson, eds). Proc. Third International Symposium, 26-29 October 2003, Taormina. *Vet Ital*, **40** (3), 360-364.
11. Calistri P., Giovannini A., Conte A., Nannini D., Santucci U., Patta C., Rolesu S. & Caporale V. 2004. Bluetongue in Italy, Part I. *In* Bluetongue, Part I (N.J. MacLachlan & J.E. Pearson, eds). Proc. Third International Symposium, 26-29 October 2003, Taormina. *Vet Ital*, **40** (3), 243-251.
 12. Cipolla C.M. 1992. Il burocrate e il marinaio. La "Sanità" toscana e le tribolazioni degli inglesi a Livorno nel xvii secolo. Il Mulino, Bologna.
 13. 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 B*, **50** (3), 139-147.
 14. Cosmacini G. 1997. L'arte lunga. Storia della medicina dall'antichità a oggi. Giuseppe Laterza e Figli, Bari.
 15. Declich S. & Carter A.O. 1994. Public health surveillance: Historical origins, methods and evaluation. *Bull World Health Org*, **72**, 285-304.
 16. Food and Agriculture Organization (FAO) 2004. FAO EMPRES emerging prevention system. FAO, Rome (www.fao.org/ag/againfo/programmes/en/empres/home.asp accessed on 14 July 2006).
 17. Giarelli E. & Jacobs L. 2003. Surveillance for care and control. Part 2: Public health and epidemiology. *Prev/Early Detec SIG News*, **13**(3), 4-8. (onsopcontent.ons.org/Publications/SIGNewsletters/prev/prev13.3.html#story4 accessed on 28 June 2006).
 18. Giovannini A., Calistri P., Conte A., Savini L., Nannini D., Patta C., Santucci U. & Caporale V. 2004. BTV surveillance in an emerging area. *In* Bluetongue, Part I (N.J. MacLachlan & J.E. Pearson, eds). Proc. Third International Symposium, 26-29 October 2003, Taormina. *Vet Ital*, **40** (3), 188-197.
 19. Giovannini A., Calistri P., Nannini D., Paladini C., Santucci U. & Caporale V. 2004. Bluetongue in Italy, Part II. *In* Bluetongue, Part I (N.J. MacLachlan & J.E. Pearson, eds). Proc. Third International Symposium, 26-29 October 2003, Taormina. *Vet Ital*, **40** (3), 252-259.
 20. Giovannini A., Conte A., Calistri P., Di Francesco C.E. & Caporale V. 2004. Risk analysis on the introduction into free territories of vaccinated animals from restricted zones. *In* Bluetongue, Part II (N.J. MacLachlan & J.E. Pearson, eds). Proc. Third International Symposium, 26-29 October 2003, Taormina. *Vet Ital*, **40** (3), 697-702.
 21. Giovannini A., MacDiarmid S., Calistri P., Conte A., Savini L., Nannini D. & Weber S. 2004. The use of risk assessment to decide the control strategy for bluetongue in Italian ruminant populations. *J Risk Anal*, **24** (6), 1737-1753.
 22. Goffredo M., Satta G., Torina A., Federico G., Scaramozzino M., Cafiero M.A., Lelli R. & Meiswinkel R. 2001. The 2000 bluetongue virus (BTV) outbreak in Italy: distribution and abundance of the principal vector *Culicoides imicola* Kieffer. *In* Proc. 10th International Symposium of the American Association of Veterinary Laboratory Diagnosticians (AAVLD) and OIE Seminar on biotechnology, 4-7 July, Salsomaggiore, Parma. AAVLD, Ames, 308-309.
 23. Goffredo M., Conte A.M., Coccicolito R. & Meiswinkel R. 2003. Distribuzione e abbondanza di *Culicoides imicola* in Italia. *Vet Ital*, **39**, 22-32.
 24. Graunt J. 1662. Observations on the bills of mortality, 1st Ed. (www.ac.wvu.edu/~stephan/Graunt/bills.html accessed on 29 June 2006).
 25. Mantovani A., Macrì A., Prosperi S., Lasagna E. & Marvasi L. 2006. Veterinary epidemiology in Italy. *Hist Med Vet* (in press).
 26. Mellor P.S., Boorman J.P.T., Wilkinson P.J. &

- Martinez-Gomez F. 1983. Potential vectors of bluetongue and African horse sickness viruses in Spain. *Vet Rec*, **112**, 229-230.
27. Mellor P.S., Jennings D.M., Wilkinson P.J. & Boorman J.P.T. 1985. *Culicoides imicola*: a bluetongue virus vector in Spain and Portugal. *Vet Rec*, **116**, 589-590.
28. Moro M.L. & McCormick A. 1988. Surveillance for communicable disease. In *Surveillance in health and disease* (W.J. Eylesbosch & N.D. Noah, eds). Oxford University Press, Oxford, 166-820.
29. Murray N., MacDiarmid S.C., Wooldridge M., Gummow B., Morley R.S., Weber S.E., Giovannini A. & Wilson D. 2004. Handbook on import risk analysis for animals and animal products. Volume 1. Introduction and qualitative risk analysis. Office International des Épizooties, Paris, 59 pp.
30. Nannini D., Giovannini A. & Caporale V. 1992. Riflessioni sul controllo e l'eradicazione della brucellosi bovina. *Vet Ital*, **28** (6), 26-37.
31. Nannini D., Giovannini A., Fiore G.L., Marabelli R. & Caporale V. 1999. Quality assurance of veterinary services at the international level: a proposed approach. *Rev Sci Tech*, **18** (3), 571-584.
32. Office International des Épizooties (OIE). 2005. Terrestrial animal health code, 14th Ed. OIE, Paris (www.oie.int/eng/normes/mcode/en_sommaire.htm accessed on 31 March 2006).
33. Popper K.R. 1983. Realism and the aim of science. From the postscript to the logic of scientific discovery (W.W. Bartley III, ed). Routledge, Taylor and Francis Group, London, 262-263.
34. Regalla J., Caporale V., Giovannini A., Santini F., Martel J.L. & Penha Gonçalves A. 1996. Manifestation and epidemiology of contagious bovine pleuropneumonia in Europe. *Rev Sci Tech*, **15** (4), 1309-1330.
35. Scaramozzino P., Boorman J., Semproni G., Vitale F., Mellor P. & Caracappa S. 1996. Entomological survey on *Ceratopogonidae* in central-southern Italy. In *European Multicolloquial on Parasitology*. *Parassitologia*, **38**, 124.
36. Schwabe C.W., Riemann H.P. & Franti C.E. 1977. *Epidemiology in veterinary practice*. Lea and Febiger, Philadelphia, 303 pp.
37. Stärk K.D.C., Regula G., Hernandez J., Knopf L., Fuchs K., Morris R.S. & Davies P. 2006. Concepts for risk-based surveillance in the field of veterinary medicine and veterinary public health: Review of current approaches. *BMC Health Services Research*, **6**, 20. (www.biomedcentral.com/content/pdf/1472-6963-6-20.pdf accessed on 3 July 2006).
38. Thucydides 431 BC. The history of the Peloponnesian war (translated by R. Crawley), 10th Ed., December, 2004. Project Gutenberg Ebook #7142. Book II, Chapter VII (www.gutenberg.org/dirs/etext04/plpwr10.txt accessed on 28 June 2006).
39. World Trade Organization (WTO) 1994. Agreement on the application of sanitary and phytosanitary measures. The results of the Uruguay Round of the multilateral trade negotiations. The legal texts. WTO, Geneva, 69-84.