



Surveillance and risk assessment for early detection of emerging infectious diseases in livestock

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Summary

Those who work in the area of surveillance and prevention of emerging infectious diseases (EIDs) face a challenge in accurately predicting where infection will occur and who (or what) it will affect. Establishing surveillance and control programmes for EIDs requires substantial and long-term commitment of resources that are limited in nature. This contrasts with the unquantifiable number of possible zoonotic and non-zoonotic infectious diseases that may emerge, even when the focus is restricted to diseases involving livestock. Such diseases may emerge from many combinations of, and changes in, host species, production systems, environments/habitats and pathogen types. Given these multiple elements, risk prioritisation frameworks should be used more widely to support decision-making and resource allocation for surveillance. In this paper, the authors use recent examples of EID events in livestock to review surveillance approaches for the early detection of EIDs, and highlight the need for surveillance programmes to be informed and prioritised by regularly updated risk assessment frameworks. They conclude by discussing some unmet needs in risk assessment practices for EIDs, and the need for improved coordination in global infectious disease surveillance.

Keywords

Control – Early detection – Emerging infectious disease – Epidemiology – Hazard – Livestock – Pathogen – Prevention – Production systems – Risk assessment.

Introduction

In recent years many infectious diseases have emerged in animals that have huge health and economic implications. Such emerging infectious diseases (EIDs) are usually defined as those that have either newly appeared in a population or have existed previously but are rapidly increasing in incidence or geographic range [1]. Importantly, this means that the same disease (or infection or pathogen) may be:

- newly present in a region in which it has not previously been found
- endemic in another location where it might be rapidly spreading geographically

- causing an outbreak in another location by rapidly increasing in incidence within that population.

Such EIDs may or may not be zoonotic. Finally, EIDs may be truly new infections, or they may be first detections of pathogens that are present but have hitherto gone undetected. The definition also encompasses pathogens known to science – i.e. a previously described and named pathogen – and those unknown to science, such as one of the potential millions of yet-to-be-discovered pathogens [1].

The implications of all this are that approaches to disease surveillance and control should carefully consider the

local context, species affected and current epidemiological dynamics of each EID.

The pathways for disease emergence are determined by a complex array of interactions between hosts, pathogens, production systems (when considering the livestock farming environment) and environmental factors, which have been the focus of extensive reviews [2, 3, 4, 5, 6, 7, 8, 9]. Factors involved in disease emergence are related to the invasiveness of the pathogen and the vulnerability of the host, which, in turn, is affected by its environment [6].

In this paper, the authors focus on recent emerging diseases affecting livestock to exemplify some current approaches to and gaps in surveillance and risk assessment for EIDs. They apply the World Organisation for Animal Health (WOAH) definition of surveillance, which is ‘the systematic ongoing collection, collation, and analysis of information related to animal health and the timely dissemination of information so that action can be taken’ [10].

The role of livestock production systems in disease emergence

A key characteristic that has to date often been overlooked is the role of different livestock production systems in the emergence of novel pathogens. Today, there is considerable diversity among production systems, each generating its own type of disease emergence risk, and some are more obvious than others. Intensive production systems working under high biosecurity (such as controlled-environment farms or those located in isolated areas) have minimal contact with wildlife and humans, and hence chances for exposure to other exogenous pathogens should be minimised. However, any new pathogen that does get in can have greater impact on the farm given the higher contact rate of the animals. It has been reported that some large-scale farm operations have a higher risk of pathogen incursions, such as highly pathogenic avian influenza A H5N1 outbreaks, than small-scale farms [3].

Disease emergence in these systems may also come about through transformation of animals’ natural flora or endemic pathogens. This can be facilitated by fast production cycles and the fact that these systems tend to be associated with large global value chains. A clear example is the emergence of the new virulent strains of porcine circovirus type 2 (PCV2) in the 1990s and 2000s. Retrospective analysis found that PCV2 viruses had been circulating in the pig population since the 1960s, until a genotype shift occurred [11]. The causes of this shift are unknown, but the new strain was first reported in a 600 sow ‘farrow-to-finish’ pig farm in Canada [12]. Trade movements caused the fast spread of this pathogen around the globe [13]. New genotypes are still emerging (PCV2 now has eight distinct genotypes) and rapidly spreading throughout the world [14], including in those high-biosecurity farms,

generating concerns about the possible loss of future vaccine effectiveness.

The combination of intensive production with low biosecurity and mixing of species represents another risk for disease emergence. In many low-income countries, it is common for cattle, pigs and poultry to be raised on the same farm. This is to benefit from synergies – for example, using poultry litter as cattle feed – and increase resilience, for example, in the event of an epidemic. An influenza pandemic reportedly occurred following a triple reassortment of swine, avian and human influenza viruses in 1998, which became established in the pig population and evolved to the H1N1 influenza virus responsible for the 2009 pandemic [15].

Intensive systems with low biosecurity, particularly in areas with a high population density of humans, weak infrastructure and low investment capacity, typically use large quantities of antimicrobials as prophylactics and growth promoters for the successful production of livestock, creating a favourable environment for new antimicrobial-resistant genes to emerge [16]. In addition, these systems may provide opportunities for livestock to interact with wildlife, which may be acting as vectors or carriers of EIDs. Wild boar were blamed for introducing African swine fever to Russia [17], while avian influenza outbreaks have emerged in poultry farms after contact with wild birds [18]. In such situations, the reason for the outbreak was not the wildlife (many viruses live in undisturbed wild hosts without causing a problem) but rather the farming methods that allowed livestock to be exposed to the presence of pathogens in wildlife populations.

Frameworks for the surveillance of emerging infectious diseases

Early detection of emergence events is crucial if diseases are to be controlled quickly, and effective surveillance is the cornerstone of this. Infectious disease surveillance should be designed and implemented to pursue specific objectives, which will vary depending on whether the disease is present or absent [19]. The most essential objective for emerging disease surveillance is prompt detection of outbreaks, and of instances of the emergence and re-emergence of known and unknown pathogens, to enable early response. This should allow the rapid implementation of control measures and consequently reduce the impact of EIDs.

Risk-based surveillance involves targeting surveillance activities on those species, sub-populations, production systems or demographic groups that are at higher risk of infection [20]. A risk-based approach may be used at several levels, and may include hazard prioritisation at the national or international strategic level; risk-based selection of sub-populations (strata) for sampling; and risk-based, sample-size calculations for repeated surveys, which take previous test results and local disease knowledge into account [19, 20].

For example, risk-based surveillance has been used to select locations for bluetongue surveillance in cattle in England, based on the risk of incursion of the pathogen obtained from atmospheric dispersion modelling [21]. Network analysis of the connections between different types of pig farms in Italy has been used to identify the riskiest seasons and nodes where surveillance should be focused to minimise the impact of infectious disease spread [22].

Both these examples are of known diseases, but they show that risk-based surveillance can be an effective way of increasing the efficiency of surveillance. It could, in theory, provide a cost-effective early warning system for disease emergence [20]. The establishment of such risk-based systems does, however, require knowledge of the factors that increase the risk of infection (such as age, breed, location) and the distribution of these factors in the population or in geographical space. Ideally, knowledge of the determinants of the infection's impact, if emergence does occur, would also be available. In the case of EIDs, such knowledge is usually limited and often absent. In these cases, syndromic surveillance is likely to be more appropriate.

Syndromic surveillance focuses on detecting health indicators (proxies for infection) that are discernible before confirmatory diagnosis [23]. Early approaches tended to focus on detecting variations of these proxies within single time series [24]. More recently, complex systems approaches are being developed that can integrate multiple data streams and cope with highly variable data [25]. Syndromic surveillance systems can therefore be established to enable early detection of emerging and not-yet-known pathogens. These may use online forums such as ProMED (Program for Monitoring Emerging Diseases) and other unstructured data sources and case reports in the veterinary press to enable the first cases of an emerging disease to be identified. Syndromic surveillance for unknown pathogens involves the ongoing collection and analysis of data on disease events (or patterns that might suggest disease) [24]. Ideally, it should utilise information from different data sources that are simultaneously assessed and combined [26]. These so-called multivariate syndromic systems, although not yet common in the field of animal health, have proved their potential for early detection of livestock diseases when applied to simulated animal epidemics [26].

As a larger spectrum of data becomes readily available for continuing analysis, there is increasing potential to apply syndromic surveillance to detect emerging pathogens more rapidly. Analyses of this type of data are useful for understanding more about the submissions and identifying trends of concern [27, 28]. For example, a recent study from Spain has shown the potential of bovine mortality data and time-series analysis to enhance a syndromic

surveillance system in cattle [29]. International agencies may want to consider establishing a forum for reporting syndromic surveillance and also to encourage consistency in the reporting of clinical signs and data structures. The high heterogeneity in EIDs means that there is no single best strategy for their surveillance and control. It seems reasonable to assume that a combination of multiple complementary approaches is more likely to achieve early detection and cost-effective control [30].

Frameworks for assessing the risk of emerging infectious diseases

Risk assessment for EIDs may focus on the risk of introduction (entry) of a hazard to a specified region, or on the risk of dissemination (exposure and consequence) following hazard importation, or on all of these steps [19]. A recent report found very few examples of comprehensive risk assessment frameworks that can be applied after the early detection of EIDs [30]. This is surprising, given their potential value for informing surveillance and preparedness and the potential for serious consequences if an EID spreads.

One example of a useful systematic approach is the recently published assessment of the risk of emergence of coronaviruses in the United States of America (USA) in wild and domestic pigs [31]. This study highlighted the need for risk-based surveillance strategies to be rooted in the fundamental mechanisms of disease emergence theory, and demonstrated that such strategies should be flexible enough to be developed as needed. In this way, disease emergence can be seen as a series of sequential steps, in which the relationship between risk factors and the probability of each step occurring is defined. In the example from the USA, this allowed the production of risk maps for coronavirus emergence at the interface between wild pigs, domestic pigs and humans that could be updated as more data became available [31]. While this study focused on a single country, a single group of viruses and a single species (which was necessary if the required level of detail was to be captured), the authors acknowledged that they did not consider temporal variation in several parameters that could have had an essential role in transmission risk [31]. The level of detail required in this single study emphasises how exercises aiming to 'predict' or even forecast the emergence of multiple known (or unknown) pathogens are likely to be highly uncertain and extremely speculative, and therefore may be insufficient for risk managers to act on, but could provide insight.

Many of the risk assessment frameworks in use in Europe today were developed from one originally described by Palmer *et al.* in 2005 [32]. An updated version of this assessment algorithm is used by the United Kingdom Human Animal Infections and Risk Surveillance group, a cross-government body that acts as a forum to identify and discuss infections with potential for interspecies transfer (particularly zoonotic infections) [33]. The approach involves horizon scanning

and high-level overviews of probable risk rather than empirical sampling or data collection. It uses a fast, simple, iterative process that is documented and reported openly. Given the time-critical nature of applying these frameworks, they are often qualitative or there may be an existing model that can be adapted. The quality of evidence used to estimate risk and confidence in the assessment output is classified into one of three simple categories (good, satisfactory, unsatisfactory) that are clearly defined [34]. Risk management options are suggested for each level of assessed risk. This framework is used regularly and the results are openly reported online [33]. It represents one of the clearest examples of an integrated risk assessment process spanning health surveillance in humans, livestock and wildlife.

A limitation of several risk assessment frameworks is that they only focus on a single pathogen and limited possible pathways of emergence, meaning that they may be unable to identify which type of scenario (pathogen, livestock species or production system) poses the highest risks to health. This has been partly overcome by the recent development of generic risk assessment tools [35]. These can be applied to assess the incursion risk of multiple infectious animal diseases, allowing for a rapid response to a variety of newly emerging or re-emerging diseases [36]. Frameworks that focus on pathogens may miss key factors relating to hosts or production systems, and do not normally account for the large diversity of value chains within the food system. For example, a recent expert-opinion-based risk assessment to rank viruses in terms of their zoonotic spillover potential [37] focused on viral origins in wildlife and hence neglected to consider the riskiest livestock farming systems. This means that not all risk assessments are useful for determining risks from livestock, and care needs to be taken when selecting an appropriate tool.

For any risk assessment there will always be uncertainty and this needs to be clearly communicated so that areas for further scientific study can be identified and decisions by risk managers can take such uncertainty into account [38]. Uncertainty represents the limits of our knowledge, and so, when considering the ability to detect pathogens and assess risk, it is inevitably very much higher for an unknown emerging disease. Even for a known disease there may still be considerable uncertainty in the evidence needed to estimate the risk (e.g. how widespread the disease is, virulence/survival of the aetiological agent, potential hosts). In this case, experts are frequently consulted to provide additional insights to the available data (or a plausible scenario when data are not available), and this information is integrated into the risk assessment template or tool. For example, the French Epidemic Intelligence System and the World Health Organization (WHO) Tool for Influenza Pandemic Risk Assessment both heavily rely on inputs from experts [39, 40]. When using such approaches, it is important that the right experts are selected, ensuring that the multiple factors that

influence disease emergence across a wider system are considered and that the expert's contribution is unbiased [38].

Unmet needs in surveillance and assessment of emerging infectious disease risks

The drivers of disease emergence are broad and multifactorial [41]. Drivers often reflect changes in systems that may affect the risk of disease emergence: this is a challenging thing to capture within any risk assessment framework. In addition, as there is high connectivity across the globe, any such drivers and the corresponding data need to be considered at an international or global level. This therefore places the emphasis on organisations such as WOAAH, the Food and Agriculture Organization of the United Nations and WHO to facilitate countries working together in their collection of data and subsequent assessment of the risks.

The paper published in this issue of the *Scientific and Technical Review* written by Horigan *et al.* describes different types of data that could be used within a risk assessment and assesses the quality of available data, including non-traditional data types such as those from social media or citizen-science projects [42]. Data such as demographic data (on human/animal populations), environmental data, trade data and movement data ideally need to be readily available and of adequate quality. Indeed, many of the international institutes provide data on the occurrence of disease, but there is no international central data repository or catalogue that signposts where many of the data sets required to develop a risk assessment can be found. The development of such a library that is constantly updated would be extremely beneficial. With the available data, generic risk assessment frameworks could then be further developed and readily deployed for future EID events [36, 43].

Conclusions

The sequence of events leading to the emergence of a disease that affects livestock depends on factors involving one or more hosts, production systems, environments/habitats and hazards. Together, these determine an ever-changing probability of disease emergence as well as influencing the overall uncertainty associated with the risk estimate. Given the plethora of potential EIDs that might affect animals and humans, prompt identification and timely control depend on an effective surveillance system. This, in turn, should be informed and improved by up-to-date risk assessments.

The efficacy of syndromic surveillance is dependent upon continuous, consistent and coordinated international efforts for collection and timely reporting of accurate data on (possible) disease events in animals and humans, a process that is presently deficient. Organisations such as WOAAH, with a widespread and readily available international network and

systems for real-time processing of health data, are ideally positioned to coordinate international reporting. While surveillance should be designed with knowledge of the local context, it must also be informed by the broader picture (e.g. early warning of disease events in neighbouring countries).

Surveillance for EID events involving known pathogens should be risk based and therefore needs to be informed by risk assessment frameworks that are fit for purpose. This means being capable of providing risk estimates of a quality that is adequate for the scale of the decision that needs to be made. This is particularly important if the risk assessment is intended to provide a risk comparison and ranking for the purpose of resource allocation. The availability of good quality data for risk assessments is key but challenging in the context of emerging diseases and particularly new pathogens where, often, the risk

pathways themselves can be highly uncertain. Data availability is one of the major considerations for selecting a specific approach. However, regardless of the risk assessment framework chosen, transparent characterisation and communication of uncertainties in the events along the risk pathways, and how these uncertainties relate to and affect the conclusions being drawn, are essential for decision-making.

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La surveillance et l'évaluation du risque pour une détection précoce des maladies infectieuses émergentes affectant les animaux d'élevage

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Résumé

Les personnes travaillant dans le domaine de la surveillance et de la prévention des maladies infectieuses émergentes (MIE) sont confrontées à la difficulté de prédire avec exactitude le lieu d'émergence d'une maladie, ainsi que l'espèce, le système ou le site affectés. La mise en place de programmes de surveillance et de lutte contre les MIE exige une mobilisation conséquente et durable de ressources nécessairement limitées. Par contraste, le nombre de maladies infectieuses zoonotiques et non zoonotiques pouvant se déclarer est impossible à quantifier, même si l'on s'en tient aux seules maladies affectant les animaux d'élevage. Ces maladies surviennent à la faveur des nombreuses et diverses configurations, associations ou modifications qui peuvent se produire parmi les espèces hôtes, les systèmes de production, les environnements ou habitats et les types d'agents pathogènes. Compte tenu de la multiplicité de ces éléments, il devrait être fait plus largement appel à des cadres de priorisation du risque afin de soutenir les processus de prise de décision et d'allocation des ressources en matière de surveillance. Les auteurs s'appuient sur des exemples récents d'événements liés à des MIE pour faire le point sur les méthodes de surveillance appliquées pour la détection précoce de ces maladies et soulignent l'importance de documenter et de prioriser les programmes de surveillance en procédant à des mises à jour régulières des cadres utilisés pour l'évaluation du risque. Ils concluent en évoquant certains aspects importants que les pratiques actuelles d'évaluation du risque ne permettent pas de couvrir lorsqu'il s'agit de MIE, ainsi que l'importance d'améliorer la coordination de la surveillance des maladies infectieuses au niveau mondial.

Mots-clés

Agent pathogène – Animal d'élevage – Contrôle – Danger – Détection précoce – Épidémiologie – Évaluation du risque – Maladie infectieuse émergente – Prévention – Système de production.

Vigilancia y determinación del riesgo para la detección temprana de enfermedades infecciosas emergentes en el ganado

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Resumen

Cuanto trabajan en el ámbito de la vigilancia y la prevención de enfermedades infecciosas emergentes (EIE) tienen dificultades para predecir con precisión dónde va a surgir y a quién (o qué) afectará una infección. La instauración de programas de vigilancia y control de EIE exige una inversión sustancial y duradera de recursos que por definición son escasos, sobre todo teniendo en cuenta el número incalculable de enfermedades infecciosas zoonóticas y no zoonóticas que pueden aparecer, aun considerando solo aquellas que afectan al ganado. Este tipo de enfermedades pueden surgir como resultado de muchas combinaciones distintas de especie hospedadora, sistema productivo, medio/hábitat y tipo de patógeno o por efecto de cambios que se den en cualquiera de estos elementos. En vista de la multiplicidad de factores que concurren, convendría emplear de modo más generalizado un sistema de jerarquización de los riesgos en el cual fundamentar las decisiones de vigilancia y la distribución de los recursos destinados a ella. Los autores, valiéndose de ejemplos recientes de episodios infecciosos emergentes que afectaron al ganado, pasan revista a distintos métodos de vigilancia para la detección temprana de EIE y recalcan que los programas de vigilancia deben reposar en procedimientos de determinación del riesgo periódicamente actualizados y en las prioridades fijadas a partir de estos procedimientos. Por último, los autores se detienen en algunas necesidades desatendidas en la praxis de la determinación del riesgo de EIE y en la necesidad de una mejor coordinación de la vigilancia mundial de las enfermedades infecciosas.

Palabras clave

Control – Detección temprana – Determinación del riesgo – Enfermedad infecciosa emergente – Epidemiología – Ganado – Patógeno – Peligro – Prevención – Sistemas productivos.

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