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REVIEW ARTICLE
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Disease alerts and forecasting of zoonotic diseases: an overview

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Abstract

Epidemiologists are adopting new techniques by the use of Geographical Information System (GIS) to study a variety of animal and zoonotic diseases. Associations between satellite-derived environmental variables such as temperature, humidity, land cover type and vector density is used for disease prediction. Early warning systems rapidly detect the introduction or sudden increase in incidence of any disease of livestock which has the potential to develop into epidemic proportions and/or cause serious socioeconomic consequences or public health concerns. Early warning activities, mainly based on disease surveillance, reporting, and epidemiological analysis, are supported by information systems that enable integration, analysis and sharing of animal health data combined with relevant layers of information such as socioeconomic, production and climatic data. The convergence of factors such as the availability of multi-temporal satellite data and georeferenced epidemiological data, collaboration between scientists, biologists and the availability of sophisticated, statistical GIS creates a fertile research environment. In this paper, we review the Global Early Warning System (GLEWS) that formally brings together human and veterinary public health systems and application of environmental data for study of diseases like avian influenza and Rift valley fever which offers the capability to demonstrate vector-environment relationships and potentially forecast the risk of disease outbreaks or epidemics. An emphasis is also given on components of early warning system and its use for forecasting of animal and zoonotic diseases in India.

Key words: FAO, forecasting, global early warning system, geographical information system, OIE, WHO.

Introduction

The ability to detect outbreaks early is important to minimize morbidity and mortality through timely implementation of disease prevention and control measures. The World Trade Center and Anthrax terrorist attacks in 2001 [1] as well as the recent West Nile virus and SARS outbreaks, have motivated many public health authorities to develop early disease outbreak detection systems using non-diagnostic information, often derived from electronic data collected for other purposes [2, 3]. Emerging infectious diseases pose a growing threat to human population. Climatic changes like warmer temperatures and altered rainfall patterns are likely to increase the burden of vector-borne diseases resulting into emergence of zoonotic diseases, too. Many of the world's epidemics are known to be highly sensitive to changes in climate and short-term fluctuations in the weather [4, 5, 6]. “Forecasting” is the monitoring of specific risk parameters helping to predict situations that could lead to the occurrence of a given disease and its subsequent spread. The forecasting of disease helps to predict the course of disease, warn health care workers and adopt control measures to prevent disease outbreaks [7, 8].

Passive disease surveillance involves voluntary reporting by people who are ill enough to go to a treatment center; such centers are therefore only effective for detection and mitigation after a person has been infected. On the other hand, active disease surveillance, which involves "searching" for evidence of disease proactively through routine and continuous monitoring in endemic areas, could help to prevent an outbreak, or slow the rate of transmission at an earlier stage of an epidemic [9, 10]. The National Oceanic and Atmospheric Administration (NOAA) operate a series of weather satellites that collect operational data for weather forecasting and climate prediction. Besides NASA and NOAA, several European Union countries, Japan, Canada and India have remote sensing satellites that provide global observations to predict occurrence of disease [11, 12, 13]. The use of GIS to map vector species distribution and disease risks has evolved considerably during the past two decades [14]. The objectives of this review are to summarize developments in the application of disease surveillance system for studying animal and zoonotic disease pathogen biology and to identify opportunities for future research on forecasting of diseases.

Objectives of forecasting [7, 8]

The objectives employed for forecasting of the diseases include:

1. To study modes of transmission and to understand how to prevent spread of epidemic diseases
2. To monitor the effectiveness of disease control campaigns

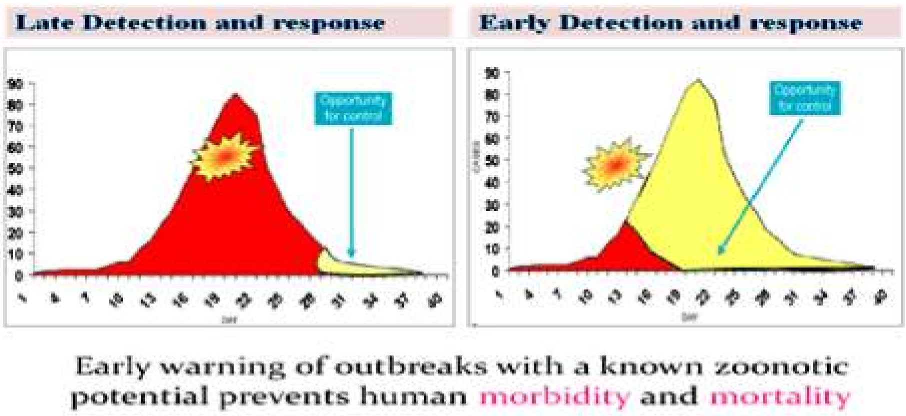

Figure-1. Early and late detection of disease and opportunity to control [15]

3. Emergency preparedness & disease management strategies
4. To demonstrate knowledge about the epidemiology of diseases
5. To study disease importance from a public health point of view

Advances in disease surveillance systems, epidemiological modelling combined with information technology have generated the expectation that early warning systems are not only feasible but necessary tools to combat the re-emergence and spread of infectious diseases [8].

What is early warning?

Early Warning is the provision of timely and effective response through the recognized institutions that allows individuals exposed to hazards to take actions to avoid or reduce risk and prepare for an effective response. [15]. Early Warning and Response (EWS) is based on the concept of dealing with a disease epidemic in its early stages. From a public health perspective, early warning of outbreaks with a known zoonotic potential of disease will enable control measures that can reduce human morbidity and mortality rates. The main uses of early warning system include education as an aid to understanding the crucial elements involved in early detection and response to environmental threats [15, 16].

Early warning initiatives

Several initiatives, at national and regional levels have already been developed in the field of early warning. At the international level FAO, OIE and WHO have each developed early warning and Response Systems that systematically collect, verify, analyze and respond to information from a wide variety of sources, including unofficial media reports and informal networks [17, 18].

International organizations and their initiative role in development of early warning system

Office International Des Epizooties (OIE)'S early warning system: OIE was established on 25th January 1924 in Paris. In May 2003 the Office became the World Organization for Animal Health but kept its historical acronym OIE. This organization has set up an animal health information search and verification system for the notification of emerging and reemerging diseases that have not yet been officially notified to the OIE. The framework was designed to empower countries and regional alliances in the fight against Transboundry animal Diseases (TADs). Emergency funds are rapidly mobilized for sending experts from OIE Reference Laboratories to assess the epidemiological situation in a country and define the actions required [19, 20].

World Animal Health Information Database (WAHID) Interface provides access to all data held within OIE's new World Animal Health Information System (WAHIS). It replaces and significantly extends the former web interface named Handistatus II System. A comprehensive range of information is available from immediate notifications and follow-up reports submitted by Country/Territory Members notifying exceptional epidemiological events current in their territory. A six-monthly reporting by member country on the absence or presence and evolution of diseases listed by the OIE and information of epidemiological significance to other countries [21].

Food and Agriculture Organisation: FAO was established on 16th October 1945, Canada then transferred to Rome, Italy. Achieving food security for all is the main goal at the heart of FAO. FAO, through its special EMPRES priority programme established in 1994, developed an early warning and response system [20]. EMPRES Global Animal Disease Information System (EMPRES-i) is a web-based application that has been designed to support veterinary services by facilitating regional and global disease information. Timely and reliable disease information enhances early warning and response to transboundary animal diseases (TADs) including emergent zoonoses, and supports their progressive control and elimination. EMPRES-i aims to clarify disease events worldwide that FAO receives from different sources: country or regional project reports, field mission reports, partner Non-Governmental Organizations (NGOs), cooperating institutions, government Ministries of Agriculture and Health. For verification purposes, EMPRES uses not just official, but also unofficial sources of information [22]. A major thrust of the EMPRES activity for early warning and early response has been the development of softwares such as Transboundary Animal Disease Information System (TAD info), Transboundary Animal Diseases Simulator (TAD simulator) and Good Emergency Management Practice (GEMP) [20, 22].

World Health Organisation: WHO was established on 7th April 1948, located at Geneva, Switzerland, concerned with international public health. WHO offers assistance to affected countries in the form of technical advice, supplies and by mounting coordinated international investigations [23]. The Global Outbreak Alert and Response Network (GOARN) is building on new and existing partnerships of national and international institutions and networks, to deal with the global threats of epidemic-prone and emerging diseases in humans and to prepare for rapid deployment and coordination of international resources in response to an outbreak of international importance [23,24]. GOARN aims at ensuring appropriate technical support to affected human populations quickly, assessing risks of rapidly emerging epidemic disease threats and sustaining containment and control of outbreaks by contributing to national outbreak preparedness [24,25]. WHO has developed a comprehensive "Event Management System" to manage critical information about outbreaks and ensure accurate and timely communications between key international public health professionals, including WHO Regional Offices, Country Offices, collaborating centers and partners in the Global Outbreak Alert and Response Network. This system generates a dynamic picture of Alert and Response Operations and provides information for action in a systematic way to enable both WHO and the Global Outbreak Alert and Response Network to prepare better, respond faster, and manage resources more effectively. The WHO event management system is being further strength-ened to support alert and response operational aspects of the revised International Health Regulations [26, 27].

Global early warning and response system (GLEWS)

GLEWS is a joint system that builds on added value of combining and coordinating the alert, response mechanisms developed by OIE, FAO and WHO [18]. The GLEWS assists in prediction, prevention and control of animal disease threats, including zoonoses through sharing of information, epidemiological analysis and joint field missions to assess and control the outbreak, whenever needed. The GLEWS initiative started with the voluntary participation of representatives of FAO, OIE and WHO, who share the common objective to enhance the early warning and response capacity for the benefit of the international community. Mutual benefit through collaboration has been identified throughout the Early Warning and Response process [28, 29].

Well defined GLEWS are available for highly pathogenic avian influenza (HPAI), Rift Valley fever (RVF) and other vector borne diseases and for rest of the diseases GLEWS is under development [29, 30].

The GLEWS Management Committee (GMC) is responsible for supervising the implementation of the GLEWS agreement, the strategic plan and provides general oversight of GLEWS. The GLEWS Management Committee guides and decides on the different tasks to be accomplished by the GLEWS Task Force which is co-chaired by FAO, OIE and WHO [18]. After being notified a rumor, suspicion or forecast regarding a disease outbreak the information gathered through the respective tracking and verification channels of each organization will be fed into a GLEWS electronic platform information will be further analyzed, monitored and/or sent out as Early Warning Messages. Specific analysis and modeling of trends will be carried out utilizing selected OIE and FAO collaborating centers, OIE and FAO laboratories and WHO collaborating centers. A GLEWS Emergency Response will only be necessary, if there is clear indication for a joint onsite assessment or intervention mission [23, 29].

Aims of GLEWS [18, 23, 28]:

1. Better international preparedness and rapid containment
2. Improve detection of exceptional epidemiological events at country level
3. Increase timeline and sensitivity of alerts and improve national surveillance and monitoring systems
4. Improve transparency among countries and compliance with reporting to OIE
5. Improve field animal health information quality and provide technical support
6. Strengthening the network between veterinary & medical laboratories
7. Provide rapid, efficient and coordinated assistance to the affected countries.

GLEWS joint risk analysis for emergent zoonotic diseases: Risk analysis is essential to assess and provide options to mitigate risks associated with the emergence or spread of animal pathogens at the animal/human/ecosystem interface. Risk analysis is one of the core areas that have been recently highlighted for increased collaboration between FAO, OIE and WHO to address emergence of pathogens, in particular on emergent zoonotic pathogens [26].

Joint risk assessment as planned will initially be performed in specific regions for priority zoonotic diseases, such as CCHF, RVF, H5N1 HPAI, Rabies and Brucellosis. In this framework, risk analysis and mapping methodologies will be developed and validated using data available on reported outbreaks, surveillance activities carried out by countries and combining this information with other datasets including land use, trade, livestock population, animal movement, etc. Risk mapping tools are essential to enhance accuracy and sensitivity of early warning activities. Early

Table-1. GLEWS has given the following list of diseases of common interest [31]

Zoonotic Diseases	Nonzoonotic Diseases
Anthrax	African Swine Fever (ASF)
Bovine Spongiform Encephalopathy (BSE)	Classical Swine Fever (CSF)
Brucellosis (B. melitensis)	Contagious Bovine Pleuropneumonia (CBPP)
Crimean Congo Hemorrhagic Fever	Black quarter
Ebola Virus	Haemorrhagic Septicemia
Food borne diseases	Foot and Mouth Disease (FMD)
Highly Pathogenic Avian Influenza (HPAI)	Peste des Petits Ruminants (PPR)
Japanese Encephalitis	
Marburg Hemorrhagic Fever	
New World Screwworm	
Nipah Virus	
Old World Screwworm	
Q Fever	
Rabies	
Rift Valley Fever (RVF)	
Sheep Pox/Goat Pox	
Tularemia	
Venezuelan Equine Encephalomyelitis	
West Nile Virus	

warning messages will be made available to the international community to serve effective response purposes and aid targeting disease surveillance and control activities at the animal-human-ecosystem interface [26, 27, 28].

GLEWS is supported by the following Regional/ National Networks: [32, 33]

1. FAO (191 Member Nations)
2. WHO (194 Member States)
3. OIE (178 Member Countries)
4. Regional Organizations: EC, SADC, ASEAN, CAN
5. International Reference Laboratories
6. National Authorities
7. Unofficial surveillance programs (PROMED, GPHIN)
8. Laboratory and Epidemiological networks
9. Other partners

GLEWS approach for Highly Pathogenic Avian Influenza (HPAI): In the aftermath of the avian influenza (AI) crisis triggered by the spread of the highly pathogenic avian influenza H5N1 (HPAI H5N1), the world has been on alert to curb the spread of the disease and to mitigate the risk of a potential human pandemic [10, 34].

The FAO Early Warning System for worldwide monitoring of avian influenza highlights the potential for better integration and exchange of information among key stakeholders, and better understanding of the disease [35]. Through EMPRES I disease tracking list is one example generation of disease information. All confirmed outbreaks, pending and foregoing investigations worldwide in domestic poultry and wild birds are listed. The Disease Tracking List (DTL) also displays the temporal evolution of daily incidence for a 1-yr period. This list is shared with national and regional field staff as well as key partner institutions, which are requested to verify and validate the unconfirmed events, and to follow up and search for reliable sources of information. Risk maps are made showing location of confirmed outbreak in poultry and in wild birds. EMPRES I linked with GIS to provide visual representation of disease outbreak and to understand epidemiological factors responsible for TADs emergence and spread [35, 36].

These examples show the importance of GIS to identify spatial or spatiotemporal patterns that can be used in developing more rigorous causal hypothesis tests. In conclusion, the ultimate goal of early warning systems is to make information and risk-assessment outcomes available to all relevant stakeholders and to provide the opportunity for timely reaction in the most cost-effective manner [10, 36].

GLEWS approach for Vector borne diseases; Rift Valley Fever (RVF): In parts of East Africa known to be prone to RVF epidemics, remotely-sensed rainfall and vegetation measurements have been integrated into regional and global early warning systems and are used to predict RVF before it reaches epidemic proportions. The ultimate goal of such systems is to safeguard sustained livestock production and have developing countries participate legitimately in local, regional and international trade [13, 35, 37].

Epidemics of RVF have occurred in southern and eastern Africa at irregular intervals. These epidemics have been associated with above average rainfall after a period of drought and the presence of susceptible exotic breeds of livestock [13, 35]. Data sets used in these predictions include satellite vegetation index and cold cloud duration (CCD) correlated with climatic changes [37]. Measurements from the Advanced Very High Resolution Radiometer sensor (AVHRR) on-board polar-orbiting satellite series operated by the NOAA are used to generate the normalized difference vegetation index (NDVI) [13, 37].

In East Africa, vegetation index maps have been used together with ground data in monitoring vector populations and RVF viral activity, establishing a correlation between these two parameters. Indeed a detailed analysis was made with virus isolation data over a 25-year period and NDVI records for the study area. As the water table rises to the point where flooding may occur, the NDVI ratio approaches 0.43 to 0.45 [38]. The main advantage of using remote sensing for prediction of RVF occurrence in East Africa is the relatively low cost of the system and its use may allow for preventive measures to be taken such as the vaccination of susceptible livestock and mosquito larval control methods [38, 39]. The technology has been used extensively by the FAO to warn countries facing an increased risk of the disease [40, 41].

The components of an Early Warning System (EWS): There are three components of EWS, *viz.*, routine surveillance of the targeted disease, modelling the disease risk based on historical surveillance and contemporary environmental data and forecasting future risk through the use of predictive models with continued epidemiological and environmental surveillance [8].

1. Disease surveillance: A sentinel network is an interactive disease surveillance system that involves the collection of health data on a routine basis, usually by health care professionals over a wide (usually at country level) area [41, 42, 43]. In most industrialized nations, notification of many infectious diseases is a statutory requirement. Rapid collection of data and assessment of regional and national statistics leads to early detection of changes in the incidence of infections [44, 45, 46]. The database also provides information for the planning and implementation of intervention [8, 46]. The growth of such sentinel systems, from independent national networks to co-ordinate international information systems, has generated a demand for health information systems capable of forecasting disease [47, 48].

The present understanding that a facility-based sentinel surveillance system can play an important role in providing information for monitoring communicable diseases, guiding further investigation, evaluating control measures and predicting epidemics [8, 40, 49].

2. Developing a model: Disease forecasting involves modelling, which may be based either on statistical relationships established between past case numbers and environmental predictors 'statistical approach' or an attempt to capture the biology of the transmission processes 'biological approach' [8]. Briefly, the statistical approach requires samples from as wide a range of environmental conditions as possible: predictions arising from this approach assume that the future will be the same as the past, i.e. that the relationships already established between case numbers and environmental variables will persist into the future [50].

The biological approach requires details on all the parameters and variables considered to be important in transmission. Predictions arising from this approach are in theory able to incorporate the effects of environmental changes, or interventions, as long as the impacts of each of these changes on the key transmission parameters are established. It should follow from the above that in the absence of full knowledge of all the transmission pathways for any particular diseases, only the statistical approach is possible. This explains why much of the early epidemiology of poorly-understood diseases such as cancer adopted the statistical route. Statistical models can be extremely powerful, but should be only a temporary substitute for the biological process-based models, whose development exposes our full ignorance of the systems we study. It is only by addressing this ignorance that real progress will be made [8, 50].

3: Disease forecasting and prediction: At the heart of early warning is a basic trade-off between the specificity of predictions and the lead times which those predictions can provide. In general, long-range forecasts give the least specific warnings, but have the advantage of providing planners with relatively long lead times. At the other extreme, systems based on early detection of cases provide highly specific information on the timing and location of outbreaks, but allow little time for implementing remedial measures. Any prediction of risk should include an estimate of its reliability [51, 52].

Epidemic prevention and control activities usually involve a chain of events and it is important to recognize the potential usefulness of a wide range of indicators, which may be combined to create an integrated prediction strategy. Such a hierarchical system has recently been proposed for tracking malaria epidemics in highland areas of Africa [52].

Geographical information system (GIS)

GIS is an automated system for the input, storage, analysis and output of spatial information. These data combined with population data and previous disease records for prediction of diseases [53].

Applications of GIS: [53, 54, 55]

1. Forecast epidemics
2. Identify gaps in immunizations
3. Monitor diseases and interventions over time
4. Study Geographical distribution and variation of diseases
5. Map populations at risk and stratify risk factors
6. Monitor Health centers, Routine health workers, equipments & supplies to service locations
7. Locate nearest Health facility

Forecasting of diseases in India

In India, the Project Directorate on Animal Disease Monitoring And Surveillance (PD_ADMAS) was established in 1987 by the ICAR to develop a system of disease monitoring and surveillance of economically important livestock diseases, with a goal to design strategic control measures. Although health care infrastructure has grown immensely over the years, disease surveillance system did not get the desired attention as the outbreaks of bird flu (2006), swine flu (2009), and Crimean-Congo hemorrhagic

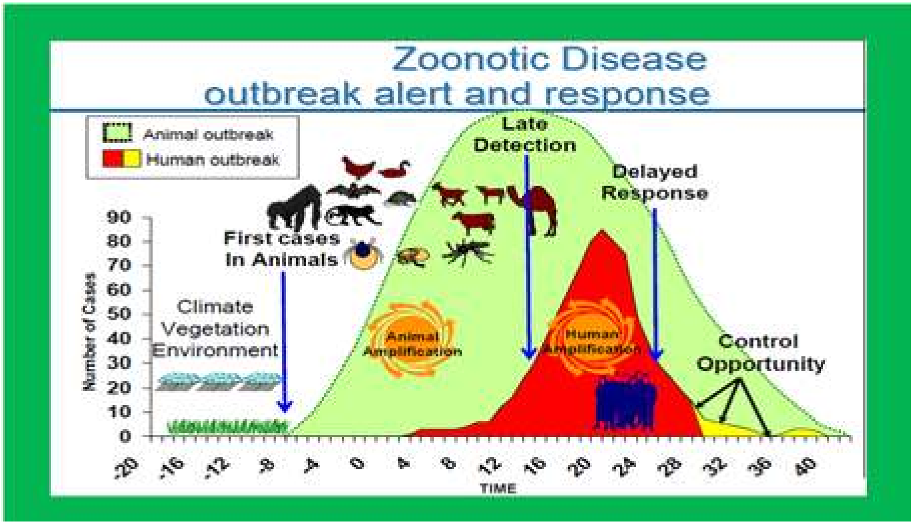

Figure-2. GIS-GLEWS approach for prediction of zoonotic Diseases [23]

fever (2011) in the country highlighted the weaknesses in the current surveillance system [56].

Animal disease surveillance network: At present, animal disease surveillance network in our country include data collection from diseased animal to veterinary doctor at Govt hospital/dispensary through clinical diagnosis- passed to Taluka / Block to District level then to the State Veterinary authorities. The disease information is shared from diagnostic laboratories District, State or Regional level. The State Governments share this information at National level mainly through Department of Animal Husbandry, Dairying and Fisheries (DADF), Ministry of Agriculture, Government of India. [57].

Centre for Animal Disease Research and Diagnosis (CADRAD): It is recognized as Central Disease Diagnostic Laboratory (CDDL) by the Department of Animal Husbandry & Dairying, Ministry of Agriculture (Govt. of India) since 2001-02 with specific mandate, technical programme and financial support. However, there are five Regional disease diagnosis laboratories located at Kolkata (Eastern), Pune (Western), Jallandhar (Northern), Bangalore (Southern) Guwahati (North-eastern). There are six Quarantine stations *viz.* Delhi, Mumbai, Chennai, Kolkata, Bangalore and Hyderabad [56, 57].

Disease surveillance and ICAR: [56, 57]

1. Project Directorate on Foot and Mouth Disease (PDFMD)
2. Project Directorate on Animal Disease Monitoring and Surveillance (PD_ADMAS)
3. High Security Animal Disease laboratory (HSADL, IVRI)

PDADMAS (Project Directorate on Animal Disease Monitoring and Surveillance) Bangalore: This is the agency working on surveillance of major economically important animal diseases including zoonoses. Advances in information technology provide adequate computing techniques to develop a National livestock disease information system which is the prime need of today.

1. “Epi- Info™ (Analysis Project On Livestock Disease Forecasting/Forewarning)”
2. “NADRES(National Animal Disease Referral Expert System)”

Epi- Info™ (Analysis Project on Livestock Disease Forecasting/Forewarning): PD_ADMAS has developed an innovative india. admas-Epitrak epidemiology software which is a dynamic and interactive livestock disease related database supported by GIS. This software addresses the needs of data collection, retrieval, analysis and critical reporting of disease events as and when they occur and is useful to students and vet colleges, field veterinarians, administrators and technocrats [57].

NADRES (National Animal Disease Referral Expert System): This is a component of National Agricultural Technology Program funded mission mode sub project on weather based animal disease forecasting and animal health information system through disease monitoring and surveillance [58].

Conclusions

Early detection and response provides better preparedness for effective control and containment of disease outbreaks. Animal Disease Surveillance is a key for improving disease analysis, early warning and prevents the spread of diseases. GLEWS strengthen early warning systems of OIE/ FAO/ WHO for the benefit of international community by using recent advances in communication & information technologies. GIS offers lot of scope in Veterinary Public Health research especially for surveillance, mapping and ecological analysis of emerging zoonoses. The well defined GLEWS are available for HPAI, RVF and some vector borne diseases, while for the rest diseases GLEWS is under development. PD_ADMAS and other surveillance and information networks are stand alone in India and there is a need for complete review of surveillance system for animal diseases which may guide important policy decisions. Successful implementation of EWS is dependent on efficacy of national disease surveillance program, degree of awareness among field veterinarians, technicians, extension specialists, and farmers about clinical and epidemiological features of diseases.

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