Review article

The use of animals as a surveillance tool for monitoring environmental health hazards, human health hazards and bioterrorism

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A B S T R A C T

This review discusses the utilization of wild or domestic animals as surveillance tools for monitoring naturally occurring environmental and human health hazards. Besides providing early warning to natural hazards, animals can also provide early warning to societal hazards like bioterrorism. Animals are ideal surveillance tools to humans because they share the same environment as humans and spend more time outdoors than humans, increasing their exposure risk. Furthermore, the biologically compressed lifespans of some animals may allow them to develop clinical signs more rapidly after exposure to specific pathogens. Animals are an excellent channel for monitoring novel and known pathogens with outbreak potential given that more than 60 % of emerging infectious diseases in humans originate as zoonoses. This review attempts to highlight animal illnesses, deaths, biomarkers or sentinel events, to remind human and veterinary public health programs that animal health can be used to discover, monitor or predict environmental health hazards, human health hazards, or bioterrorism. Lastly, we hope that this review will encourage the implementation of animals as a surveillance tool by clinicians, veterinarians, ecosystem health professionals, researchers and governments.

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1. Introduction

Zoonosis is derived from the Greek words "zoon" (animals) and "nosos" (disease), referring to any infectious diseases transmitted from animals to humans, either directly or indirectly (World Health Organization, 2016). As the global human population increases, so will anthropogenic pressures on wildlife and the environment, augmenting the likelihood of zoonotic pathogen spillover from animal to human populations. The World Health Organization (WHO) identifies zoonoses as emerging threats and describe them as previously occurring phenomena that have an increasing trend and expansion in geographical, host or vector range. More than 60 % of all emerging infectious diseases are from zoonoses (Mackenzie and Jeggo, 2013). Despite acting as the main reservoir for only 3 % of the known zoonoses, humans are the main source of identification for disease outbreaks (Frank, 2008). As such, epidemiological relationships

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between animal and human outbreaks can be exploited to strengthen veterinary and public health response efficiencies via the integration of animal and human surveillance systems (Stone and Hautala, 2008).

Animals are ideal surveillance tools to humans, because they not only share the same environment as humans, but they also spend more time outdoors than humans, hence increasing their exposure risk (Rabinowitz et al., 2010). They frequently respond to

Table 1
Websites for Information Related to the Use of Animals for Surveillance.

Website Address	Maintained by	Description
http://canarydatabase.org/	Yale University School of Medicine, New Haven, Connecticut, U.S.[1]	The Canary Database is a compilation of curated peer-reviewed research articles related to the use of animals as sentinels of human health hazards
http://www.oie.int/	The World Organization for Animal Health	The OIE[2] is an intergovernmental organization responsible for improving animal health worldwide.
http://www.cdc.gov/	CDC[3]	CDC works to keep the U.S. safe from health, safety and security threats, both foreign and domestic.
http://www.cdc.gov/nceh/lead/default.htm	CDC	Aims to eliminate childhood lead poisoning in the U.S.
http://www.cdc.gov/flu/index.htm	CDC	Provides information, useful links and updates on seasonal influenza and vaccinations.
http://www.cdc.gov/healthypets/	CDC	Provides information and updates on companion animals and wild animals, and the diseases they can carry.
http://www.cdc.gov/ncezid/index.html	CDC	Aims to protect people at home and around the world from emerging and zoonotic infectious disease.
http://www.cdc.gov/ncidod/dvbid/westnile/index.htm	CDC	Provides information and updates on WNV[4] epidemiology and prevention.
http://www.bt.cdc.gov/bioterrorism/	CDC	Provides information and updates on bioterrorism.
http://www.bt.cdc.gov/chemical/	CDC	Provides information and updates on chemical agents and emergencies.
https://www.cdc.gov/coronavirus/mers/	CDC	Provides information and updates on MERS-CoV[5] including symptoms and complications, how it spreads, prevention and treatment.
http://www.cdc.gov/zika/index.html	CDC	Provides information and updates on ZIKV.[6]
http://www.who.int/zoonoses/en/	WHO[7]	Provides information and updates on zoonoses and the human-animal ecosystems interface.
http://www.who.int/phe/en/	WHO	Provides information and updates on public health, environmental and social determinants of health.
http://www.who.int/quantifying_ehimpacts/en/	WHO	Provides information and updates on quantifying environmental health impacts.
http://www.who.int/csr/resources/publications/AnthraxGuidelines2008/en/index.html	WHO	Provides information on anthrax in humans and animals.
http://www.who.int/influenza/human_animal_interface/en/	WHO	Provides information and updates on influenza at the human-animal interface.
http://coastalscience.noaa.gov/about/centers/ccma	National Oceanic and Atmospheric Administration	The Center for Coastal Monitoring and Assessment carries out field research and data analysis to support marine resource management at local, regional and national levels.
http://www.promedmail.org/	Program for Monitoring Emerging Diseases	An internet-based reporting system dedicated to rapid global dissemination of information on outbreaks of infectious diseases and acute exposures to toxins that affect human health, including those in animals and in plants grown for food or animal feed.
http://www.onehealthcommission.org/	One Health Commission	A globally focused organization dedicated to promoting improved health of people, domestic animals, wildlife, plants and the environment.
http://www.onehealthinitiative.com/	One Health Initiative	A worldwide strategy for expanding interdisciplinary collaborations and communications in all aspects of health care for humans, animals and the environment.
http://www.onemedicine.org.uk/	Comparative Clinical Science Foundation	Promotes research aimed at achieving a fundamental understanding of the major killer diseases in humans and animals, bringing together medical and veterinary researchers, with the ultimate goal of identifying better treatments and cures for diseases such as cancer and genetic disorders for the benefit of both people and animals.
https://www.avma.org/Pages/home.aspx	American Veterinary Medical Association	A collective voice representing more than 86,500 veterinarians to advance the science and practice of veterinary medicine to improve animal and human health.
http://ec.europa.eu/food/index_en.htm	European Commission	Aims to assure a high level of food safety, animal health, animal welfare and plant health within the European Union through coherent farm-to-table measures and adequate monitoring, while ensuring the effective functioning of the internal market.
http://www.fao.org/avianflu/en/index.html	Food and Agriculture Organization of the United Nations	Provides information and updates on avian influenza.
http://www.usgs.gov/	U.S. Geological Survey	Provides information and updates on the health of our ecosystems and environment, the natural hazards that threaten us, the natural resources we rely on, the impacts of climate and land-use change, and the core science systems that help us provide timely, relevant, and useable information.
http://www.flu.gov/index.html	U.S. Department of Health & Human Services	Provides information and updates on flu.
http://www.istm.org/geosentinel	GeoSentinel	A worldwide communication and data collection network for the surveillance of travel related morbidity.

[1] U.S., United States.
[2] OIE, World Organization for Animal Health.
[3] CDC, Centers for Disease Control and Prevention.
[4] WNV, West Nile virus.
[5] MERS-CoV, Middle East respiratory syndrome coronavirus.
[6] ZIKV, Zika virus.
[7] WHO, World Health Organization.

agents in an analogous manner to humans and manifest similar disease symptoms. Some animals have biologically compressed lifespans, consequently developing clinical signs more rapidly after exposure to specific pathogens. Furthermore, they may be more susceptible to contaminants than humans and they do not share some human behaviors that may confound investigation results (e.g. smoking). Table 1 provides a list of websites containing information related to the use of animals for surveillance. Proper utilization of animals for surveillance may allow the early identification of epidemics, which facilitates mitigation of its magnitude, or prevention of its occurrence (Chomel, 2003; Kahn, 2006). This is due to the ability of animals to: 1) exhibit changes in the occurrence or prevalence of a pathogen or disease with time, 2) serve as markers for on-going exposure risk, 3) allow examination of hypotheses on the ecology of pathogens, and 4) provide information on the efficiency of disease control measures (McCluskey, 2003).

This review attempts to highlight animal illnesses, deaths, biomarkers or sentinel events, to remind human and veterinary public health programs that animal health can be used to discover, monitor or predict environmental and human health hazards, or bioterrorism.

Animals useful for surveillance mostly exist in the environment as hosts of naturally cycling pathogens. They can be utilized in passive, active or sentinel surveillance programs. Passive (reactive) surveillance involves the spontaneous reporting of disease data from the animal sector to veterinary authorities (Hoinville et al., 2013). Data reported can include illnesses or deaths in animals, or notifiable diseases that must be reported by law. The data is then analyzed to observe disease trends and identify potential outbreaks. Active (proactive) surveillance on the other hand involves calling on animal facilities to interview workers and to review animal health records to identify diseases under surveillance. It also involves actively monitoring domestic or wild animals for biomarkers.

The choice of surveillance type depends on the characteristics of a pathogen and the objective of the program. Passive surveillance is best employed when the objective of the program is targeted towards early detection of outbreaks or monitoring the extent of disease for making decisions on control strategies; whereas, active surveillance is best employed when a disease is targeted for elimination. Passive surveillance is the least time consuming, labor intensive and expensive of the three forms of surveillance, and covers an extensive range. However, because it relies heavily on reports from veterinarians who receive little incentive for reporting, the data reported is frequently incomplete and delayed. Underreporting of disease suspicions is also known to be a major cause of disease control failure (FAO, 2011) and multiple studies have been conducted to better comprehend the decision-making processes behind underreporting so as to develop recommendations for improved passive surveillance (Bronner et al., 2014; Delabouglise et al., 2016; Paul et al., 2013; Sawford et al., 2012; Thompson et al., 2016). In contrast, active surveillance demands more time and resources and is thus less commonly employed. However, it provides more complete and accurate data than passive surveillance. A study comparing active and passive animal surveillance in Chad concluded that for monitoring of existing diseases, the less expensive passive surveillance is better

Table 2
Examples of Events Involving Animal Surveillance.

Date	Event	Description
323 BCE	West Nile virus	Alexander the Great is believed to have died following a 2 week febrile illness in 323 BCE, due to viral encephalitis from WNV[8] (Marr and Calisher, 2003). Historian Plutarch mentioned that flock of ravens displayed unusual behavior and died subsequently as Alexander entered Babylon.
1878	Several hundred livestock deaths	Death of several hundred livestock in lake Alexandrina, Australia allowed the identification of cyanobacteria Nodularia spumigena in water. Despite warnings issued, there was undescribed illness was reported in one individual after consuming contaminated water (Codd et al., 1994).
20th century	Canaries in coal mines	Coal miners in the U.K.[9] and the U.S.[10] brought canaries into coalmines as an early-warning signal for toxic gases including methane and carbon monoxide. The birds, being more sensitive, would become sick before the miners, who would then have a chance to escape or put on protective respirators (Burrell and Seibert, 1914).
1956	Minamata disease	Cats from a fishing village, Minamata developed a neurological disease. People of Minamata later displayed similar symptoms. Investigations later found that effluent from a factory had polluted surrounding waters resulting in accumulation of mercury in fish (Takeuchi et al., 1977).
1962	Chicken sentinels	Chickens as sentinels for surveillance of arboviruses like WNV, WEE[11] and SLE[12] viruses (Rainey et al., 1962).
Until 1969	Rabbits warn of nerve gases during transportation	Rabbits were placed in small cages in railcars during transportation of nerve gases and sudden animal mortality would warn of gas release (Brankowitz, 1987).
April 1979	Sverdlovsky Anthrax release	Anthrax was accidentally released from a Soviet military microbiology facility. Livestock died at a greater distance of 60 km from the plant, compared to human cases which occurred within a narrow 4 km zone downwind of the facility (Meselson et al., 1994).
20 March 1995	Tokyo sarin gas release	Japanese policemen carried canaries in cages with them during raids to warn of the presence of toxic gases (National Research Council of the National Academies, 2005).
June 1999 and 2007	West Nile virus	WNV was reintroduced into the U.S., where it caused the ongoing epizootic in birds with a spillover of infections to humans and equines (Chancey et al., 2015).
2003	Chickens on alert in Kuwait	U.S. Marine Corps employed chickens for the detection of nerve and blister agents. They were meant to act as a backup to false alarms the automated detectors were notorious for (Ember, 2003).
2004	Dog, livestock, wildlife deaths	Death of dogs, livestock and wildlife in the Buccaneer Bay Lake, Eastern Nebraska, U.S. allowed identification of cyanobacteria Anabaena, Microcystis, Oscillatoria and Aphanizo-menon in water. >50 incidences of skin lesions, rash, gastroenteritis and/or headache were reported in humans. Warnings were issued (Walker et al., 2008).
2005	Plague cases in Yulong county of the Yunnan province, China	Serologic survey found antibodies against the F1 antigen from domestic dogs around the affected county, demonstrating that domestic dogs could serve as animals for plague surveillance (Li et al., 2008).
Late 2006	Windblown lead carbonate in Esperance, Western Australia	Windblown lead carbonate causing huge number of bird deaths in Esperance, Western Australia, prevents lead exposure to Esperance community (Gulson et al., 2009).

[8] WNV, West Nile virus.
[9] U.K., United Kingdom.
[10] U.S., United States.
[11] WEE, Western equine encephalomyelitis.
[12] SLE, St. Louis encephalitis.

suited for Chad's conditions. Whereas, for monitoring of rare diseases, active surveillance of animal herds is required to complete passive surveillance (Ouagal et al., 2010).

Occasionally, when high-quality data about a specific disease is required, animal sentinels are intentionally deployed for surveillance. These animals receive greater attention than would be possible with active or passive surveillance. Sentinel surveillance is less extensive in terms of range and personnel involved compared to passive surveillance, but often yields more detailed data. It is best employed when thorough investigation of each animal or site is necessary, however it may not be as effective for detecting diseases outside the demarcated limits of the sentinel sites.

Examples of events involving the various forms of animal surveillance spanning 323 BCE and the 21st century can be found in Table 2. The review concludes with the One Health approach.

2. Animal as sentinels for surveillance

A sentinel is a naïve animal which is intentionally placed in an environment of potential infection that is monitored at short time intervals to detect infection. If the sentinel is deployed close to human populations, the sentinel should react to the infectious agent (but not become infectious), thereby providing early warning of human health hazards in the environment (van der Schalie et al., 1999). A classic example of an animal sentinel system is the well-known canary in the coalmine (Burrell and Seibert, 1914). Canaries are sensitive to the effects of poisonous gases, particularly carbon monoxide, and were routinely taken into the mines to warn of dangers. Its inclination to sing much of the time, coupled with its brightly colored plumage offered both "audio and visual" cues to the miners. If the canary stopped singing and/or fell from its perch, this was the signal for the miners to don their respirators or evacuate. Many miners owe their existence and livelihood to this historic animal sentinel.

Besides canaries, other animal species have also been used as sentinels of toxic chemical exposure. For example, birds, horses, cats, guinea pigs, rats, mice and rabbits were employed as sentinels for chemical agent exposure during World War I (WWI) and WWII. Until 1969, rabbits were placed in small cages in railcars during the transportation of nerve gases and sudden animal mortality would warn of gas release (Brankowitz, 1987).

Although technological advancements have since resulted in the more widespread use of electronic detectors for detecting toxic chemicals, animal sentinels are still superior because of the complexity and likeness of the animal and human physiology. This is evidenced by more recent uses of animals, in particular avian species, as sentinels of toxic chemical exposure. For example, on March 20, 1995, the Tokyo underground trains were hit by synchronized chemical terrorist attacks (National Research Council of the National Academies, 2005). The Aum Shinrikyo religious sect dispensed a concoction of military nerve agent, Sarin, killing twelve and injuring thousands. As a precaution, the Japanese policemen carried canaries — the very primitive animal sentinel — in cages with them to warn of the presence of toxic gases during raids. Another recent example of the use of avian species as sentinels of toxic chemical exposures was in 2003, when U.S. Marine Corps employed chicken sentinels at the Kuwaiti staging area despite the deployment of automated detectors (Ember, 2003). The chickens were employed to complement the M22 ion-mobility spectrometer, which was used to tag nerve and blister agents. They were meant to act as a backup to false alarms the automated detectors were notorious for.

Other than as sentinels of toxic chemical exposure, the avian species has also proven itself to be a valuable sentinel of disease outbreaks. For example, chickens have been used as sentinels for the surveillance of arboviruses like West Nile Virus (WNV),

western equine encephalomyelitis (WEE) and St. Louis encephalitis (SLE) viruses (Moore et al., 1993). They are amenable to and can tolerate arboviral infections with little or no symptoms, developing antibodies within a week of being bitten by an infected mosquito. They produce low tittered viremia, are cheap to purchase, robust and easily bled (biweekly or monthly during the peak season from June to October), making them excellent sentinel animals of arboviruses. Despite providing accurate spatiotemporal information on virus transmission, the relationship between mosquito transmission and percentage of bird and mosquito infections in a particular region still needs to be determined in order to precisely evaluate human risk. In order to improve their use as sentinels, chicken interferon-α can be administered perorally in drinking water, where it acts as an adjuvant, inducing rapid seroconversion in chickens after infection by low pathogenic avian influenza (LPAI). These chickens are called 'super-sentinels' since they are able to detect clinically inapparent LPAI (Marcus et al., 2007). LPAI strains are the most widespread, and can mutate into highly pathogenic avian influenza (HPAI) strains, which can lead to human transmission and potential fatalities. Thus, by placing super-sentinel chickens in locations prone to bird flu outbreaks, for example live-bird markets, this would allow early detection of LPAI, thereby buying time for its control.

In spite of the value of animal sentinels in monitoring the presence of pathogens or chemicals in the surroundings, there are ethical concerns regarding the deliberate exposure of animals to danger by placing them at sites of suspected contamination. Consequently, the surveillance of extant animals in their natural habitats could act as an alternative means to warn of human, veterinary or environmental health hazards.

3. Animals as a surveillance tool for monitoring environmental health hazards

Animals in many habitats can be studied to monitor health hazards in the environment (Reif, 2011). Environmental health hazards refer to both natural and unnatural contaminants in air, water, soil or food, which can potentially lead to acute or chronic health issues in humans (National Research Council (U.S.) and Committee on Animals as Monitors of Environmental Hazards, 1991).

A variety of marine species are excellent surveillance tools of environmental stress and potential health threats for humans. For example, the Mussel Watch Program actively analyzes sediment and bivalve tissue chemistry for a suite of organic contaminants and trace metals to identify trends at over 300 selected U.S. coastal sites from 1986 to today. It is designed to identify deleterious changes in the marine habitat and indicate potential human health concerns (Kim et al., 2008). *Anomalocardia brasiliana* is also a good surveillance tool for actively monitoring contamination levels of coliforms in shellfish harvesting regions in Brazil's northeast coast (Lima-Filho et al., 2015). Mussels, clams and oysters are particularly suitable for us as surveillance tools because they are able to bioaccumulate many chemicals (O'Connor and Lauenstein, 2006), as well as concentrate microbial organisms and pathogens (Kueh and Chan, 1985) to concentrations in excess of 1000 fold (Grodzki et al., 2014). Thus, the high concentrations of chemical and pathogens make it easier to detect environmental and health threats in these organisms. Moreover, improved sequencing technologies have led to the monitoring of bivalves via genomics, epigenomics, transcriptomics, proteomics and metabolomics (Suarez-Ulloa et al., 2013). Such integrative omic studies will make powerful tools in the biomonitoring of marine pollution.

Besides marine species, cats can be potentially used as a passive surveillance tool for monitoring toxic chemicals in the aquatic ecosystem. In 1956, Japanese veterinarians discovered a

neurological disease in cats in the Minamata fishing village (Takeuchi et al., 1977). It was called "dancing cat fever" because the cats displayed convulsions and involuntary jumping movements. However, this disease was not investigated rigorously until similar symptoms also manifested in the people of Minamata. As a result of subsequent epidemiologic studies in Minamata, researchers realised that effluent from a factory had polluted surrounding waters resulting in the accumulation of mercury in fish. Subsequent consumption of contaminated fish by fishermen and their families resulted in high mercury concentrations in their brains, kidneys and livers. Had the authorities paid more attention to the cats' disease symptoms, this could have been prevented. Nevertheless, this episode raised the awareness of cats as a surveillance tool for monitoring mercury poisoning, food safety and public health throughout the world. Besides mercury poisoning, there have been increasing numbers of reports of human or animal illnesses or deaths associated with harmful cyanobacteria blooms in freshwater systems. Hence, in a similar way, the surveillance of fish, dogs or livestock can provide important early warnings of cyanobacteria-associated environmental hazards (Hilborn and Beasley, 2015).

More recently in 2006, the "birds dropping from the sky" phenomenon demonstrated how passive monitoring of bird die-offs alerted the community of Esperance, Western Australia to a case of lead poisoning in the environment (Gulson et al., 2009). During that period, the community was alarmed by the sudden death of more than 9000 birds. This sparked an urgent investigation which eventually revealed that the birds had died of lead poisoning. The lead ore concentrate had originated from the handling of lead carbonate concentrate at the Megallan mine 600 km north of Esperance. The Western Australia Department of Health and Local Shire Council measured lead concentrations in rainwater from household tanks (the main source of drinking water) and discovered that 10% of households had lead concentrations exceeding WHO guidelines of 10 µg/L. Although the death of numerous native bird species was tragic, it triggered the investigation, which ultimately prevented the catastrophic exposure of lead to the community.

4. Animals as a surveillance tool for monitoring human health hazards

The clear and present dangers of emerging infectious diseases have propelled world governments to enhance animal surveillance activities (Gubernot et al., 2008). Due to the zoonotic origin of most human health hazards, it is thought that animals may have a greater susceptibility to zoonotic pathogens, thereby justifying their use as surveillance tools for monitoring human health hazards.

For example, in 1999, death and illness in multiple avian species aided investigators in identifying WNV as the root of the encephalitis outbreak in humans in New York. During those periods, the unusually high numbers of encephalitis cases in humans was concurrent with a surge in dying crows with neurological symptoms similar to encephalitis patients (Eidson et al., 2001). This prompted investigations, which identified WNV as the cause of the outbreak, and demarcated its geographical limits since the crows were amplification hosts for viral transmission. The CDC, U.S. Geological Survey National Wildlife Health Centre and U.S. Department of Agriculture have since been involved in the battle against WNV. Strategies are currently in place to consolidate data on human, mosquito, bird, chicken and veterinary cases of West Nile infection in the Arbonet system (U.S. Geological Survey and CDC, 2016). Other than birds, dogs could also act as surveillance tools for monitoring WNV circulation. Seroconversion was detected in juvenile dogs 6 weeks before WNV appeared in humans in Houston, Texas (Resnick et al., 2008).

Hence, active surveillance of WNV seroprevalence in birds and dogs can be used for monitoring WNV activity.

Additionally, the active surveillance of swine and live bird markets or supply abattoirs at the human-animal interface could be used to monitor the risk of HPAI to human and animal populations. In 2009 and 2010, the H1N1 swine flu pandemic claimed more than 18,138 lives. This new strain resulted when a triple reassortment of Northern American swine, bird and human flu viruses further combined with a Eurasian pig flu virus (Trifonov et al., 2009). Also in 2009 was the H5N1 avian influenza outbreak which led to the intense surveillance of wild ducks for avian flu viruses in Europe (Globig et al., 2009). In Eastern Asia, wild swans are an ideal surveillance species as there is vast geographical overlap between whooper swan distributions and H5N1 outbreak areas (Newman et al., 2009). Other hosts of HPAI include cats and dogs (Cleaveland et al., 2006; Kuiken et al., 2005). These studies show that active surveillance of suitable animal species through serosurveys could provide early warnings of HPAI foci, accelerating public health investigation and action.

Bats are also important animals from a surveillance perspective. They have long life spans, are highly mobile and are increasingly well adapted to human environments due to habitat loss as a result of land use changes. They live in close proximity to humans, and interact with livestock and domestic animals that are potential intermediate hosts for pathogens. Bats are the natural reservoir of Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) (Lau et al., 2005; Li et al., 2005), which was responsible for the SARS-CoV outbreak in 2003, with 8422 known infected cases and 916 confirmed human deaths worldwide (WHO, 2003). Besides SARS-CoV, bats are also reservoir hosts to filoviruses like Ebola (Leroy et al., 2009) and Marburg (Towner et al., 2007) viruses; paramyxoviruses like Hendra (Halpin et al., 2000) and Nipah (Yob et al., 2001) viruses; rubulaviruses like Tioman (Chua et al., 2001) and Menangle (Philbey et al., 1998) viruses; and the Australian fruit bat lyssavirus (Fraser et al., 1996).

There are however various challenges associated with the active surveillance of bats. Firstly, the collection of blood and fluid samples from bats is dangerous given their highly infectious nature. Secondly, the collection of bat specimens is difficult in remote areas. Thirdly, bats are sensitive to disturbances and may migrate as a consequence of investigations, making it difficult to locate bat colonies. Hotspots with high human and bat population density have thus been identified to focus bat surveillance efforts on areas with the highest probability of the emergence of zoonoses (Jones et al., 2008).

Dromedaries may also be potentially useful as surveillance tools. In particular, active surveillance of dromedaries in herds and large abattoirs could potentially reveal the prevalence of Middle East Respiratory Syndrome Coronavirus (MERS-CoV) infection. In 2012, MERS-CoV was first detected in humans in Saudi Arabia. Sera from dromedary camels across and beyond the Arabian Peninsula were found to harbor high levels of antibodies against MERS-CoV (Reusken et al., 2013). Indeed, viral sequencing revealed nucleotide polymorphism signatures, indicative of cross-species transmission (Chu et al., 2014; Memish et al., 2014). This suggests that human MERS-CoV infections could have been zoonotically acquired from camels and that their surveillance could reveal MERS-CoV foci.

Mosquitoes, *Aedes aegypti* and potentially *Aedes albopictus*, transmit Brazilian Zika virus (ZIKV) among humans. In 2015, the first ZIKV infection was confirmed, and within a few months it was declared by the WHO to be a public health emergency of international concern (Aziz et al., 2016). Health authorities have found ZIKV disease to be associated with auto-immune and neurological complications, and microcephaly in babies. Transmission has been rampant in various regions and ZIKV is expected to spread to new territories. Hence, the active surveillance of

mosquitoes could enable the evaluation of vector control measures to determine the efficacy of ZIKV outbreak interventions.

5. Animals as a surveillance tool for monitoring bioterrorism

Bioterrorism is the intentional release of microorganisms or biological agents to cause disease or death in humans, animals or plants to influence government conduct or threaten civilian population (CDC, 2007). Since more than 80 % of bioweapons are zoonoses, animals are likely to be at high risk (Ryan, 2008) and thus the surveillance of animals may provide early warning of a bioterrorist attack (Rabinowitz et al., 2006).

Farm animals like sheep and cows are potentially valuable surveillance tools for passively monitoring the production or release of bioterrorism weapons in rural areas. *Bacillus anthracis*, the causative agent of anthrax, which has fatality rates of near 100 % in both humans and animals, has been identified by CDC as one of the most likely biological agents to be used (CDC, 2016). Moreover, anthrax can form resilient spores that persist for decades in soil. During WWII, the British government was experimenting the use of anthrax on Gruinard Island. Despite efforts to decontaminate the island, the long-lasting contamination of the soil by anthrax spores put the island under quarantine for 48 years before it was considered safe for human use ("Britain's Anthrax Island," 2001). This highlights the importance of passively monitoring random cases in animals to identify anthrax hot spots. In 1979, *B. anthracis* spores were inadvertently released from a Soviet military microbiology facility in Sverdlovsky (Meselson et al., 1994). Livestock 60 km away from the plant died, whereas human cases occurred within 4 km downwind of the facility. Analysis showed that the dosage of *B. anthracis* at which sheep and cows became ill was more than an order of magnitude lower than the dosage required to affect humans. This analysis therefore suggests that livestock are much more susceptible than humans to *B. anthracis* and would be ideal for use as surveillance tools for *B. anthracis* since lower dosages at greater distances from the source were sufficient to affect the animals.

Furthermore, animals like domestic dogs and rodents spend more time outdoors and have greater exposure to the environment than humans, making them great surveillance tools for monitoring plague. *Yersinia pestis*, the etiological agent of plague, has also been identified by CDC as a bioterrorism agent (CDC, 2016). It appeared in humans in the U.S. in the 1900s (Link, 1955; Lipson, 1972), and became established enzootically in wild rodents by the mid-1940s. It is hypothesized that plague is maintained by reservoir species like rodents, and that carnivores become ill following the ingestion of plague-infected rodents. In 2005, 5 plague cases were confirmed in the Yulong County of the Yunnan Province, China (Li et al., 2008). A survey of serum samples of domestic dogs in and around the affected county confirmed that they could be used for active plague surveillance.

6. Framework for evaluating animals as sentinels for surveillance

The dynamics of infectious diseases are highly variable. They are determined by infecting dose, pathogen characteristics, host susceptibility and transmission routes. It is therefore important to have a framework for the proper evaluation of animals to determine if they are suitable for use as sentinels for surveillance. To this end, the Halliday et al. (2007) conceptual framework effectively evaluates animals as sentinel populations for various surveillance aims and ecological settings (Halliday et al., 2007). There are three fundamental components of the sentinel framework: the pathogen under surveillance, the target population, and the sentinel population. The sentinel framework produces a sentinel response which could take

the form of seroconversion, current infection, morbidity, mortality and changes in morphology or behavior. In addition to the sentinel response, other sentinel practical factors and host factors also influence the detectability of the sentinel response, which eventually determines the utility of the sentinel. As alluded to earlier, although there are numerous benefits in using animal sentinels, its use is associated with ethical concerns which might be alleviated by the surveillance of existing animals in their natural habitats.

7. The one health approach

In spite of the obvious potential of animals as a surveillance tool for monitoring environmental damage, risks to human health and bioterrorism, animals currently appear to be underutilized as surveillance tools. A likely reason is that human and animal health surveillance efforts mostly stem from disparate initiatives, resulting in data being kept in entirely separate databases (Scotch et al., 2009). There is thus an increasing need for interdisciplinary integration between human and veterinary medicine, and communication before we can completely exploit the benefits of animals for surveillance (Bisdorff et al., 2016; Wendt et al., 2015). To this end, committees have been established to increase awareness of the mutual reliance between human, animal, plant, microbial, and ecosystem health (Rabinowitz et al., 2013). This includes the 'One Medicine' or 'One Health' initiatives like the One Health Commission, the One Health Initiative and the Comparative Clinical Science Foundation (Zinsstag et al., 2011). The term 'One Medicine' was coined in 1976 by Calvin W. Schwabe in recognition of the mutualism of human and animal health, nutrition and livelihood (Schwabe, 1984). This mutualism is further supported by the close genomic relationship of humans and animals (Peters et al., 2007). Today, the appreciation of the interdependence of the well-being and health of humans, animals and the ecosystems, evolved the term 'One Medicine' towards 'One Health', to include public health, ecology and broader societal dimensions (Zinsstag et al., 2011).

In support of One Health, PREDICT was launched in 2009 (USAID, 2016a). The PREDICT project is part of United States Agency for International Development's (USAID's) Emerging Pandemic Threats (EPT) program, designed to identify zoonotic viral threats with pandemic potential at wildlife-human viral transmission interfaces (Kelly et al., 2016). It has successfully improved surveillance and laboratory capabilities for monitoring humans (that have had animal contact) and wildlife for new and known pathogens with outbreak potential; defined ecological and human causes of zoonosis; and reinforced and perfected models for predicting outbreaks. It became the largest zoonotic virus surveillance project worldwide, successfully identifying and predicting the emergence of pathogens from wildlife. It also established infrastructure and expertise required for the operation of pandemic threat surveillance and diagnostics to support the One Health Workforce (OHW). The huge success of EPT led to the launch of EPT 2 which aims to discover diseases of known and unknown origin; minimize the possibility of disease outbreaks by reducing human activities that promote disease spillover; boost national readiness; and ultimately to reduce the repercussions of novel zoonotic pathogen emergence (USAID, 2016b).

In Southeast Asia, there is the One Health Network South East Asia platform supported by the European Union to promote collaboration, networking and sharing between Southeast Asian One Health programs (Massey University New Zealand, 2014). It presently hosts two programs, LACANET and ComAcross. LACANET is a Cambodia and Laos effort aimed at improving detection of zoonotic diseases, developing capabilities for surveillance, promoting regional and national collaborations, and researching into land-use change and wildlife trade – the two main causes of disease emergence. On the other hand, ComAcross is a Thailand, Cambodia and Laos effort aimed

at assembling a multidisciplinary framework to address complex One Health problems and to improve integration between public health, animal health, agriculture and livestock, ecology, environmental science, social science and engineering.

Besides the One Health Network South East Asia platform, in Southeast Asia, there is also BiodivHealthSEA supported by the French ANR CP&ES. It investigates the impact of global changes and global governance on zoonotic diseases, biodiversity and health (Morand et al., 2014). Together with ComAcross, BiodivHealthSEA and a few other bodies have proposed in a Southeast Asian interdisciplinary conference that ecosystems could reveal potentially harmful developments for human health (Walther et al., 2016). They made recommendations for the implementation of the One Health approach; future research direction; education, training, and capacity building; potential science-policy interactions; and ethical and legal considerations. These recommendations should influence legislation and enforcement, thereby strengthening the health and resilience of Southeast Asian societies.

As typical with large programs, EPT, EPT 2, LACANET, ComAcross and BiodivHealthSEA will need to apportion sufficient funds and resources for conducting surveillance, laboratory diagnosis, consumables, equipment and infrastructure. It is therefore critical that they continue to collaborate with partners like the CDC, WHO, OHW, Food and Agriculture of the United Nations, Institut Pasteur du Cambodge and Lao-Oxford-Mahosot Hospital-Wellcome Trust Research Unit, to strengthen their capacity in surveillance and laboratory capabilities, and to ensure that efforts are not replicated. It is also important that One Health programs continue to receive the support and funds that they need to sustain their work. The extent of support for animal disease surveillance in communities is largely built upon its understanding of the dangers of zoonoses to human health, trade and the economy, rather than out of interest in wildlife health. Accordingly, it is crucial to boost public awareness of the importance of wildlife health to societies. Lastly, governments are occasionally unwilling to announce potential disease outbreaks for various reasons, including preventing the disruption of trade. Hence, it is important that reporting of wildlife diseases be standardized and made necessary, and for a reporting global clearinghouse to be established.

Altogether, 'One Health' is a unifying paradigm encouraging integration and leverage of existing capabilities among clinicians, veterinarians, ecosystem health professionals, researchers and governments. Ultimately, this will hopefully lead to the development and application of sustainable and effective community health interventions, thereby reducing zoonotic disease emergence, outbreaks and repercussions, and addressing some of the biggest multidisciplinary challenges of the 21st century.

Conflicts of interest

None.

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