Human and animal sentinels for shared health risks

Peter Rabinowitz[(1)], MD, MPH, Matthew Scotch[(2)], PhD, MPH
& Lisa Conti[(3)], DVM, MPH

Summary

The tracking of sentinel health events in humans in order to detect and manage disease risks facing a larger population is a well accepted technique applied to influenza, occupational conditions and emerging infectious diseases. Similarly, animal health professionals routinely track disease events in sentinel animal colonies and sentinel herds. The use of animals as sentinels for human health threats, or of humans as sentinels for animal disease risk, dates back at least to the era when coal miners brought caged canaries into mines to provide early warning of toxic gases. Yet the full potential of linking animal and human health information to provide warning of such 'shared risks' from environmental hazards has not been realised. Reasons appear to include the professional segregation of human and animal health communities, the separation of human and animal surveillance data and evidence gaps in the linkages between human and animal responses to environmental health hazards. The 'One Health initiative' and growing international collaboration in response to pandemic threats, coupled with development in the fields of informatics and genomics, hold promise for improved sentinel event coordination in order to detect and reduce environmental health threats shared between species.

Keywords

Animal, Biodiversity, Comparative medicine, Environment, Genomics, Health, Medical informatics, Medicine, One Health, Sentinel, Surveillance, Zoonosis.

Uomini e animali sentinella per la rilevazione di rischi per la salute comuni a entrambi

Riassunto

Il monitoraggio con organismi sentinelle di eventi riguardanti la salute umana per la rilevazione e la gestione del rischio di malattie in una popolazione più estesa è una tecnica diffusa che si applica all'influenza, alle condizioni occupazionali e alle malattie infettive emergenti. Anche i professionisti della salute animale effettuano di routine un monitoraggio degli eventi patologici nelle colonie e nei gruppi di animali sentinella. L'impiego di animali per la rilevazione dei rischi per la salute umana o, viceversa, di uomini per la rilevazione dei rischi per la salute animale, risale almeno all'epoca in cui uccelli (canarini) venivano utilizzati nelle miniere come primo sistema di allarme della presenza di gas tossici. Attualmente, ancora non sono state espresse le potenzialità delle informazioni sulla salute umana e animale che, se combinate, sono in grado di fornire indicazioni su "rischi comuni" derivanti dai pericoli ambientali. Tra le possibili motivazioni: la segregazione professionale che contraddistingue le comunità di lavoro sulla salute umana e animale, la separazione dei dati di sorveglianza relativi ai due ambiti e le lacune a livello di collegamento tra le risposte umana e animale ai pericoli ambientali. L'iniziativa "Una sola salute" e la crescente collaborazione inter-nazionale in risposta alle minacce pandemiche,

(1) Yale Occupational and Environmental Medicine Program, Yale University School of Medicine, 135 College Street, 3rd Floor, New Haven, CT 06510, United States of America
pmr9@email.med.yale.edu
(2) United States Department of Veterans Affairs, VA Connecticut Healthcare System, 950 Campbell Avenue, Bldg 35A – 2nd Floor, West Haven, CT 06516, United States of America
(3) Division of Environmental Health, Florida Department of Health, 4052 Bald Cypress Way, Tallahassee, FL 32399, United States of America

supportata dagli sviluppi della ricerca informatica e genomica, promettono una maggiore condivisione di informazione sugli eventi sentinella per la rilevazione e la riduzione delle minacce.

Parole chiave
Ambiente, Animale, Biodiversità, Genomica, Informatica medica, Medicina, Medicina comparativa, Salute, Sentinella, Sorveglianza, Una sola salute, Zoonosi.

Sentinel health events in human health

A sentinel health event in human health has been defined as a 'preventable disease, disability, or untimely death whose occurrence serves as a warning signal that the quality of preventive and/or therapeutic care may need to be improved' (21). This concept, that an 'index case' presenting to the attention of the medical system represents the 'tip of the iceberg' indicating that others are also at risk, has been widely applied. The United States Centers for Disease Control and Prevention (CDC) coordinates the United States Influenza Sentinel Providers Surveillance Network that tracks seasonal changes in the number of people seeking care for influenza-like illness, as well as confirmed cases of influenza (5). Similar efforts are in place in other countries and provide one source of viral isolates that allow detection of vaccine-strain mismatches and improved decision-making about choice of viral strain for future vaccine development (23). The GeoSentinel network of travel medicine providers identifies sentinel cases of significant travel-related illness that could indicate widespread risks to other travellers and residents in particular regions (8, 12). In addition, in occupational and environmental medicine, the recognition of sentinel cases of disease in workers or exposed populations can lead to identification and remediation of health hazards in the environment that are placing others at risk.

Sentinel events in animal health

As is the case for human health, the concept of sentinel surveillance and sentinel health events is an important one in veterinary medicine. In laboratory settings, veterinarians monitor the health of 'sentinel colonies' of rodents to determine whether pathogens or toxicants could be affecting the rest of the animal population. 'Sentinel herds' of domestic livestock are tested for brucellosis and other communicable diseases.

Given the acceptance of the sentinel health event concept in both human and animal medicine, it seems natural to consider and explore the possibility that animals could be useful sentinels for human health risks, and perhaps vice versa.

Animals as sentinels for human health

In the early years of the 20th century, miners in Great Britain and the United States took caged canaries into coalmines in order to provide warning of the presence of toxic gases including carbon monoxide and methane. The concept of the 'canary in the coal mine' giving warning of a human health hazard is based on several principles. First, canaries were found to be more sensitive than both humans and other animals, such as mice, to the toxic effects of carbon monoxide (2). Second, the birds were allowed to share the same air exposures as the humans. Third, the occurrence of carbon monoxide poisoning in a bird was quite recognisable to the miners, since sick birds would tend to fall off of their perches and appear visibly ill.

In 1960, Rachel Carson's publication, the *Silent Spring*, help launch the modern environmental movement (3). The implication of the book was that bird die-offs related to the use of pesticides were a warning that these pesticides, including dichloro-diphenyl-trichloroethane (DDT) and other organo-chlorine compounds, were causing wide-spread toxicity in the environment that could also be a threat to human health.

Just as with toxicants, zoonotic infectious disease agents may be detected more easily and prevented more effectively through employing the concept of animal sentinels.

Since many zoonotic agents cause clinical disease in a number of host animal species, or are detectable by serology, polymerase chain reaction (PCR), or other diagnostic methods, it seems logical that the detection of a zoonotic disease infection in an animal could provide sentinel warning to humans.

In a review of animals as sentinels for bioterrorism agents (17) (most of which are zoonotic in origin), three possible reasons for animals serving as effective sentinels were identified, as follows:

- the animals could be more sensitive than humans to infection with a particular zoonotic disease agent
- the animals could have a shorter incubation period than humans once infected
- the animals could be at greater exposure risk than humans by virtue of their feeding habits and more intense environmental exposure.

Humans as sentinels for animal health

Even when animals may be more likely than humans to develop disease from a specific environmental health hazard, it may be the human that first comes to medical attention. Human disease surveillance and clinical care services in a particular area may exceed that available for animals in the same region. Wildlife deaths in rural areas may go unnoticed by health professionals. In these situations, a sentinel health event occurring in a human may function as a sentinel for animal health. For example, a slaughterhouse worker who is diagnosed with brucellosis could be serving as a sentinel for an outbreak of brucellosis in cattle that has escaped the detection of animal health authorities and farmers (21). Therefore, stronger links between human and animal disease surveillance could benefit both animal and human health, and help to identify gaps in animal disease control and reporting systems.

Examples of shared health risk between animals and humans

The scientific literature contains many examples in which animals and humans share risk of exposure to toxicants or infectious agents. These events highlight the value of animals as sentinels for human health and the need to systematically compare animal and human health surveillance data. The following case examples illustrate these points.

Mercury poisoning

In 1956, Minamata disease was described by two physicians in Japan who observed an unusual number of patients with central nervous system disorders with unknown causes. An extensive three-year study identified the causative agent to be organic mercury. Epidemiological follow-up suggested that the cause of the outbreak was the release of mercury into the Bay from a chloralkali production facility. This industrial pollution of the surrounding waters resulted in an accumulation of mercury in fish and the consumption of these mercury-contaminated fish by local families, many of whom developed mercury poisoning that was most severe in infants and young children. Only after these tragic cases were discovered was the connection made by the authorities between the onset of disease in humans and the development several years earlier of neurological disease (called 'dancing cat disease') in local cats that consumed large amounts of fish from the harbour. Cats displayed ptyalism (excessive salivation), convulsions and ataxia (difficulty walking). Some jumped into the sea and drowned. Unfortunately, health professionals did not heed the sentinel disease signs provided by the cats in time to prevent the human poisonings. However, cats were used to discover the cause of Minamata disease. In 1957, cats were brought to Minamata from surrounding areas. Within several months they became sick with dancing cat disease, helping prove the environmental connection. (11).

A case report of mercury poisoning in a cat in Ontario is reminiscent of the Minamata episode. The cat consumed fish containing methyl mercury from a river flowing through a Native American reservation. The cat developed acute neurological signs that were consistent with mercury poisoning and further tests confirmed the exposure. The cause of this exposure was toxic waste discharged into the watershed of the reservation from an industrial plant. At the same time, studies of Native Americans living nearby who frequently ate fish from the same river revealed high levels of mercury exposure (24).

Lead poisoning

Despite nationwide efforts at prevention, lead poisoning continues to occur in the United States. According to the CDC, the greatest risk of lead poisoning to children is from lead-based paint and dust from deteriorating buildings (6).

Since primary prevention cannot prevent all cases, clinicians must rely on secondary preventive measures, including the screening of children who are close contacts with a child diagnosed with lead poisoning. Since more than 50% of United States households have pets, a 'One Health' approach to prevention of lead poisoning involves awareness that lead poisoning in an animal could be a sentinel sign indicating risk of lead poisoning in an asymptomatic child sharing the household. It is also possible that a human case of lead poisoning could alert animal health professionals to a lead poisoning risk for pets in the vicinity.

The report of the experience of a lead treatment programme with lead poisoning in animals and children supports these concepts (9). A dog was admitted to a veterinary hospital with persistent vomiting and weight loss. The owner informed that the pet lived in a house, the exterior of which had been renovated a month earlier. During admission, the dog was diagnosed with lead poisoning and recovered fully after chelation therapy. Nine months later, the dog was readmitted with a similar syndrome of vomiting, at which time the blood lead level was markedly elevated (120 μg/dl). At this point, the family's one-year-old and three-year-old children were referred for testing even though they were asymptomatic. Both were found to have lead intoxication, with blood levels of 48 μg/dl and 37 μg/dl, respectively (the CDC recommended level is <10 μg/dl). They required treatment and close follow-up. The children and the dog spent considerable time playing in the yard and that paint chips from the facade of the building had contaminated the yard, exposing both the children and the dog.

In another case, a family cat was found to present vomiting, somnolence and ataxia a month after the exterior renovation of the house next door. After the cat was diagnosed with lead poisoning, the family's asymptomatic two-year-old child was found to have lead poisoning, with a blood lead level of 24 μg/dl.

While these cases involved pets exposed at higher levels than nearby children, sometimes, as in the following case, it could be a human who had the highest exposure and provided the alert regarding the risk to nearby animals. A self-employed painter was evaluated in an occupational medicine clinic for abdominal pain, weakness and vomiting. He had recently been sanding the exterior of a Victorian era house for its new owners. Blood testing for lead revealed a significantly elevated level (112 μg/dl) and he began chelation treatment. The treating physician contacted the local health department authorities who then telephoned the owner of the house to inquire whether there were any children in the house who might need referral and testing for lead poisoning. The owner and his wife did not have any children, but did own two dogs that had been vomiting and appearing drowsier than usual. The dogs were referred to a veterinarian, diagnosed with lead poisoning, and admitted to a veterinary hospital for chelation treatment.

Anthrax

In the spring of 1979, an unusual epidemic of anthrax occurred in the city of Sverdlovsk, 1 400 miles east of Moscow. Soviet medical authorities reported that the epidemic was linked to an outbreak of anthrax among livestock in the area and that the human cases were due to people eating contaminated meat and having skin contact with contaminated animal carcasses. The size of the human epidemic, however, led to international speculation whether it was natural or accidental and, if accidental, whether it was due to activities in violation of the Biological Weapons Convention of 1972. After repeated attempts to bring independent scientific teams to Sverdlovsk, permission was granted and the investigation took place in 1992 and 1993. The investigative team, led by the renowned American geneticist, molecular biologist and Harvard biochemist, Matthew S. Meselson, PhD, included Jeanne Guillemin, PhD, noted author/sociologist/medical anthropologist, Alexis Shelokov, PhD, a vaccine expert from the Salk Institute with a long career in public health, David Walker, MD, a well known pathologist from the University of Texas Medical Branch and renowned veterinary medical epidemiologist Martin Hugh-Jones, DVM, MPH, PhD. The legendary human medical epidemiologist, Alexander D. Langmuir, MD, was involved in deciphering data for publication.

From the beginning, the team took a 'One Health' approach with human medicine and veterinary medicine professionals working side by side to investigate both human and animal cases of anthrax that had occurred (14).

Since the KGB had apparently destroyed hospital and public health records of the outbreak, the team had to locate survivors (using government compensation lists) and personally interview each person as well as family and friends of those who had died from anthrax, search local cemeteries, and comb through hospital autopsy reports and individual case histories. They also searched reports from veterinary laboratories and interviewed owners of sheep and other livestock that had died. Through this painstaking process, they were able to analyse 77 human cases and establish that most of them lived and worked in the southern part of the city.

The clinical histories of anthrax victims suggested that many of them had become sick through inhalation of anthrax spores and not from eating contaminated meat as the government had claimed. The apparently 4-km long area where cases were clustered was downwind from a military microbiology laboratory that had officially been developing an improved anthrax vaccine at the time of the outbreak. This seemed to provide evidence that the accidental release of anthrax from the military facility had caused the outbreak in humans. As human epidemiological work was proceeding, the team was investigating animal cases of anthrax in the Sverdlovsk area during the same period.

They found that in six villages located to the south (downwind) of Sverdlovsk, including one village 50 km south of the area of where the human cases had occurred, mortality in sheep and cows began to occur at about the same time that human cases were appearing in Sverdlovsk. In those southern villages, there were no cases reported in humans. Together with the human data, these animal case findings further supported the hypothesis that there had been a single release of anthrax spores from the military facility that had drifted south, causing the largest documented outbreak of human inhalation anthrax. The fact that animals died in an area almost 50 km from the nearest human case provided key information about the movement of the airborne anthrax spores and showed that there was exposure risk over a much greater area than would have been expected without the animal data. It also indicated that sheep might be more susceptible than humans since they apparently became sick and died at exposure levels an order of magnitude lower than where human cases occurred. In this way, the animal deaths served as 'sentinel events' providing warning information to humans about an environmental health hazard, in this case a pathogen that is a prime bioterrorism agent.

The success of the 'One Health' approach used in this investigation underscores the potential benefit of human and veterinary medical health professionals working cooperatively to identify 'shared risks' to humans and animals from bioterrorism agents, most of which are zoonotic in origin.

West Nile virus

In 1999, physicians in New York City were surprised to see an upsurge in cases of encephalitis without a clear aetiology. In her paper exploring the importance of linking animal and human medicine, Kahn asserts that, 'physicians treating the initial West Nile virus patients in New York City in 1999 might have benefited if they knew that for the previous month and concurrently, veterinarians in the surrounding area had been seeing dozens of dying crows with neurological signs similar to those affected by humans' (13). The crows were serving as sentinels for West Nile virus since they are hosts within the virus transmission cycle and often display neurological signs that suggest infection of this vector-borne disease. Shortly after these initial outbreaks, health departments commenced surveillance initiatives focusing on sightings of dead crows and pathology testing to confirm the diagnosis (10). Date, location, species, and condition of the bird were some of the variables that were collected for surveillance purposes. Since 1999, a number of studies (15, 16) have demonstrated the value of bird surveillance of West Nile virus for the identification of potential risk in humans. At present, a cooperative effort between CDC, veterinary health authorities, and the United States Geological Survey compiles and combines data on human, bird, sentinel animals (chickens and other animals) and veterinary cases (mostly in horses) of West Nile infection in the Arbonet system (28).

These cases demonstrate several important points about animal sentinels. First, while animals may function as sentinels for environmental health risks shared with nearby humans, their warning signals have often been recognised only belatedly or not at all. Second, sometimes it is only through investigation of a human disease outbreak that the true extent of disease in animals due to similar exposures is fully appreciated. The following section explores some of the reasons for these inconsistencies between human and animal disease surveillance.

Barriers to implementation of the animal sentinel concept

Factors preventing better integration of human and animal disease information and the vigorous use of human and animal sentinel surveillance to identify shared health risks can be divided into three interrelated categories, namely: professional segregation, data separation and evidence gaps.

Professional segregation

Professional segregation refers to the separation, from the onset of graduate school throughout professional training, of human health and veterinary professionals in many parts of the world. Despite the inter-relatedness of many health issues, these groups develop professional identities in isolation from each other. Following training, there remain no significant channels of communication between human health and animal health care providers. One manifestation of this is the tendency, among human health professionals, to adopt an 'us vs them' approach to animal health issues. Such an approach to zoonotic diseases considers the animal as a vector of potentially deadly disease to humans and therefore principal management strategies to reduce the risk of zoonotic disease include avoidance of animal contact, control of insect vectors and elimination of reservoir populations, such as rodents near human dwellings. In the case of a zoonotic infection occurring in a companion animal, such as a dog or a cat, human health concern may often focus on how to avoid contracting disease from the pet. While there can be considerable human health value in such strategies, they neglect the fact that both animals and humans may in fact be facing similar 'shared risks' of disease emergence from changing environmental conditions (18). The 'us vs them' paradigm also leads to an under-appreciation of the fact that a better understanding and the more effective control of disease in the animal population (often through environmental management) may be required in order to truly reduce human risk.

Data separation

In the United States, links between human and animal disease surveillance data remain limited. The reasons for this are multi-factorial, including the separation of animal and human surveillance efforts (13, 25, 31). For animal surveillance, the primary sources of data are local veterinarians, farmers and laboratories, including the 32 accredited full-service regional veterinary diagnostic laboratories. These individuals and institutions send notifications on reportable animal diseases to the regional Department of Agriculture, typically through a telephone and paper-based process (31). The State Veterinarian, who is usually based in a state agriculture department, collects the information. On the human side, notifiable human diseases, many of which are zoonotic, are reported by clinicians or laboratories to local or regional health departments, again often using telephone and paper-based methods, although a growing trend is to submit reports using electronic transmission (4). At the state level, the state public health veterinarian and/or state epidemiologist review the data. Usually the state veterinarian (animal surveillance) and the state public health veterinarian (human surveillance) are not the same individual and the extent and quality of communication between state departments of public health and departments of agriculture may vary according to the disease, local statutes and the individuals serving in their respective animal health and human health roles. With the exception of disease-specific directives for rabies and potential bioterrorism agents, there are few mandates for direct communication between animal health and human health authorities. A survey of United States State Veterinarians (43 of 50 states) based in agriculture departments found that only 19% indicated that they are mandated to notify public health departments about zoonotic diseases (13). As a result, many disease events in animals that are reported to departments of agriculture, some of which may have sentinel implications for human health professionals, may never come to their attention, while the reverse is true of sentinel reports in humans not being available to animal health agencies.

It is important to note that zoonotic disease surveillance within states often involves other organisations beyond the Departments of Agriculture and Health. For example, the State Department of Environmental Protection may be responsible for monitoring forest and wildlife resources and may be aware of wildlife die-offs or other disease events in wildlife. Contact between such agencies and veterinary or public health authorities may be limited and there are few mandates for disease reporting in wildlife populations.

At the national level, there are also limitations to surveillance data sharing between animal and human health authorities. The United States Department of Agriculture (USDA) Animal and Plant Health Inspection Service (APHIS) and Center for Epidemiology and Animal Health (CEAH) perform national surveillance activities (7, 31). For human health, the CDC collects national surveillance data on notifiable disease. Once again, there are few formal mechanisms for sharing surveillance data on both animal and human health on a national level, such as between the USDA and CDC. Of course notable exceptions exist, such as the Arbonet system described above, that tracks West Nile virus activity in humans, horses, birds and mosquitoes.

On the international level, there has historically been limited formal sharing of surveillance data between human health agencies, such as the World Health Organization and animal health organisations including the World Organization for Animal Health (OIE: *Office International des Épizooties*) and the United Nations Food and Agriculture Organization (FAO), although this situation may be changing, as described below.

Evidence gaps

In addition to the barriers to the use of sentinel data listed above, there remain important gaps in current scientific understanding about links between human and animal disease outcomes in response to environmental health threats (19). As a result, the human health relevance of particular disease events in an animal population may not be clear. The differential susceptibility and latency of many species to certain environmental exposures, both toxic and infectious, remains under-researched and under-reported. Evidence is generally insufficient to determine which species of non-laboratory animals provide optimal models for particular human diseases. In a similar way, the relative degree of exposure to environmental hazards for animals versus humans is poorly studied for most hazards. Our limited understanding of the complex ecology of certain vector-borne diseases, such as West Nile virus infection, makes it difficult to assess the sentinel value of monitoring particular animal populations, such as birds for disease prediction. Finally, as a result of limited comparison of human and animal surveillance data, there is a paucity of evidence on animal sentinels actually being used to effectively predict and mitigate human health risk for many infectious and toxic hazards in the environment. Therefore, while human health professions have embraced the concept of 'evidence-based medicine', there has been little effort to systematically assemble the evidence to support the routine or expanded use of animals as sentinels for human health.

Successful strategies to overcome barriers

Improved communication between human and animal health

The 'One Health' resolutions recently passed by the American Veterinary Medical Association and the American Medical Association and the joint representation on the One Health Task Force by human and animal health professionals represent unprecedented attempts to overcome professional segregation and allow for better flow of information between human and animal health professionals. However, it will take a concerted effort to extend this model to practitioners at the community level. One possible solution is to raise awareness about the 'shared risk' paradigm by identifying key health risks in the community affecting both humans and animals and proposing ways to jointly address such risks.

Another promising development is the response of international human and animal health agencies to the unprecedented global epizootic of highly pathogenic avian influenza virus infection in poultry, and the spectre of the virus becoming more transmissible in human populations leading to a pandemic. The Global Early Warning System (GLEWS) is a cooperative effort of the WHO, the FAO and the OIE to rapidly share disease information on animal and human cases of avian influenza and other zoonotic pathogens and allow for timely interventions (30). Other examples of data sharing include the recently launched Global Initiative on Sharing Avian Influenza Data (GISAID) platform for the international sharing of influenza virus sequences from both human and animal isolates (1). The Global Avian Influenza Notification System (GAINS) is a new worldwide effort to sample for influenza viruses in wild birds and make these results available to both animal health and human health scientific agencies (29). These sweeping initiatives hold great promise for better links between human and animal disease information in the future and further development of the sentinel disease event concept.

Informatics solutions to link human and animal surveillance data

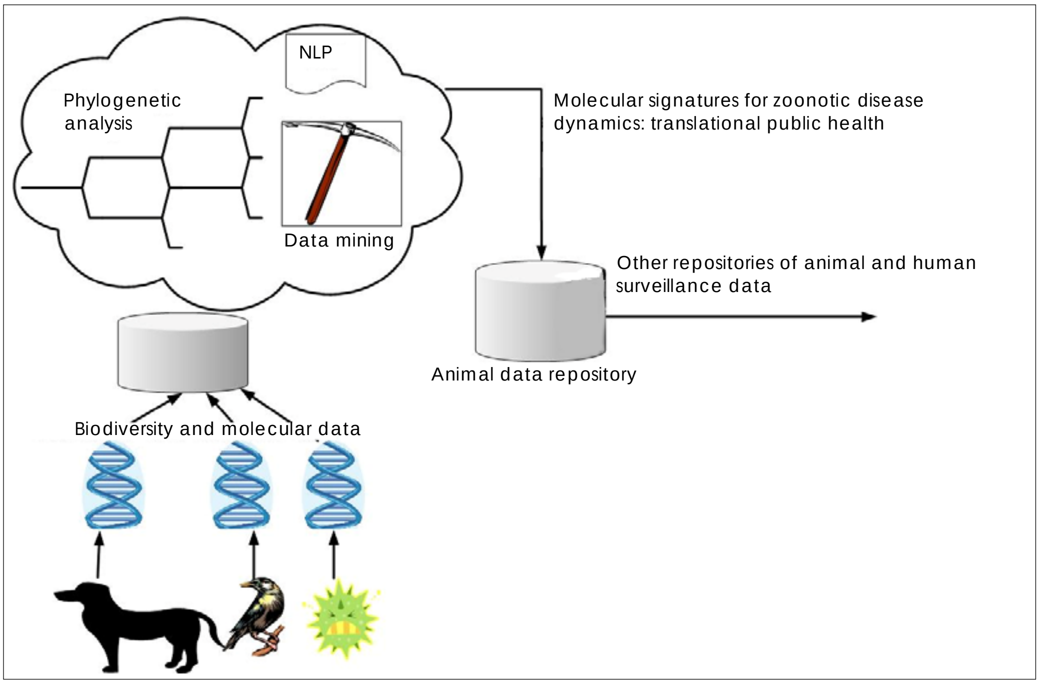
From a technological standpoint, biomedical informatics solutions are being discussed as a means to enhance zoonotic surveillance and better link human and animal data, partly as a response to veterinarians and other animal health experts taking a more active role in informatics working groups. For example, the Health Level 7 (HL7) messaging standard has been modified to meet the needs of veterinary surveillance. In addition, certain controlled vocabularies such as the Logical Observation Identifiers Names and Codes (LOINC) for laboratory data and the Systematized Nomenclature of Systematized Nomenclature of Medicine – Clinical Terms (SNOMED) for clinical data have been expanded for animal reporting (31). Examples of system architecture for biosurveillance include the Real-Time Outbreak and Disease Surveillance (RODS) system at the Automated Epidemiologic Geotemporal Integrated Surveillance (20, 27). These systems have some overlapping themes, such as the requirement of external data sources to be fed into the system, a modelling and detection component that performs statistical and mathematical analysis and a presentation component for authentication and visual display of the information to users.

Such systems could be modified to support the linkage of animal and human data for monitoring of zoonotic diseases. For example, data feeds would need to be from many different institutions that contain animal and human data, including those listed below:

- human hospitals and veterinary clinics
- agencies, such as public health, wildlife, agriculture and environmental protection
- veterinary and public health pathology laboratories.

A potential novel data source for zoonotic disease surveillance system might be the use of molecular and biodiversity data on animals. Figure 1 focuses on this concept. Large amounts of biodiversity and molecular data from organisms across the full spectrum of life is being collected and the field of 'biodiversity informatics', a new and evolving discipline, utilises informatics techniques to manage and understand this information (22).

For example, data mining and natural language processing (NLP) techniques, as well as phylogenetic analysis, support the discovery of meaningful relationships and patterns from disparate structured and unstructured biological data. This has the potential to lead to the discovery of molecular signatures of animals that are susceptible to various types of zoonotic infection. Introducing this information into a zoonotic surveillance system supports *translational public health*. With molecular and biodiversity information introduced into public health practice, epidemiologists will be able to target their population-level surveillance of a particular zoonotic disease to the most susceptible at-risk animals.



NLP natural language processing

Figure 1
Translational public health to support population-level surveillance

Addressing gaps in evidence

Research is needed to analyse links between the types of data streams being used by the GLEWS initiative and other joint human and animal surveillance. It will also be important to use such surveillance data to identify key environmental factors that drive disease emergence in animal and human populations.

Another field that requires research is the expanded use of molecular techniques, such as strain fingerprinting and genetic sequence analysis to better understand the evolution of pathogens crossing between animal and human populations and the factors that drive pathogen adaptation.

Progress on genomic sequencing of non-human animals will create opportunities for comparative genomic approaches to understanding differential susceptibility between species. Epigenetics research is also needed to understand the impact of environmental factors on expression of genes.

The Canary Database represents a Web-based effort to characterise the current state of scientific evidence regarding animals as sentinels for human health hazards, including knowledge regarding comparative susceptibility and exposure between humans and non-human animals (26). One feature of the Canary Database project is the creation of a series of systematic reviews, highlighting key issues for research as well as successful sentinel models. This work provides a model for evidence-based approaches to linking human and animal health.

In summary, it appears that there are growing opportunities to build on the changing attitudes between human and animal health communities, the increasing sophistication of informatics tools, and the greater linkage of epidemiological and molecular surveillance data on animal and human health that appears to be imminent. If the promise of the anecdotal examples listed here is borne out by such developments, the result could be significant progress in our ability to monitor and improve the environmental conditions that are critical to both human and animal health.

Acknowledgments

Portions of this paper appeared in the Kahn-Kaplan-Monath One Health News email distribution, *One Health in Action* Series Numbers 4 and 6. The authors would like to thank Bruce Kaplan, Thomas Monath, Laura Kahn, Joshua Dein, Zimra Gordon, Lynda Odofin, Matthew Wilcox and Daniel Chudnov for assistance with the development of this article.

Grant support

This material is based upon work supported in part by the Office of Research and Development, Department of Veterans Affairs, as well as the National Library of Medicine Information Systems Grant 1 G08 LM07881-01. The views expressed in this article are those of the authors and do not necessarily reflect the position or policy of the Department of Veterans Affairs or the National Library of Medicine.

Conflict of interest

The authors have no conflict of interest to disclose.

References

1. Bogner P., Capua I., Lipman D.J., Cox N.J., *et al.* 2006. A global initiative on sharing avian flu data. *Nature*, **442**, 981.
2. Burrell G. & Seibert F. 1914. Experiments with small animals and carbon monoxide. *J Indust Eng Chem*, **6**, 241-244.
3. Carson R. 1962. Silent Spring. Houghton Mifflin, Boston, 368 pp.
4. Centers for Disease Control and Prevention (CDC) 2005. Progress in improving state and local disease surveillance – United States, 2000-2005. *MMWR*, **54** (33), 822-825.

5. Centers for Disease Control and Prevention (CDC) 2008. Flu activity & surveillance. Reports & surveillance methods in the United States. CDC, Atlanta (www.cdc.gov/flu/weekly/fluactivity.htm accessed on 25 January 2009).
6. Centers for Disease Control and Prevention (CDC) 2008. About the Childhood Lead Poisoning Prevention Program (CLPPP). CDC, Atlanta (www.cdc.gov/nceh/lead/about/program.htm accessed on 22 February 2009).
7. Crom R.L. 2002. Veterinary surveillance for zoonotic diseases in the United States. *In* The emergence of zoonotic diseases: understanding the impact on animal and human health (T. Burroughs, S. Knobler & J. Lederberg, eds). The National Academies Press, Washington, DC, 90-98.
8. Davis X.M., MacDonald S., Borwein S., Freedman D.O., Kozarsky P.E., von Sonnenburg F., Keystone J.S., Lim P.L., Marano N. & GeoSentinel Surveillance Network 2008. Health risks in travelers to China: the GeoSentinel experience and implications for the 2008 Beijing Olympics. *Am J Trop Med Hyg*, **79**, 4-8.
9. Dowsett R. & Shannon M. 1994. Childhood plumbism identified after lead poisoning in household pets. *N Engl J Med*, **331** (24), 1661-1662.
10. Eidson M., Komar N., Sorhage F., Nelson R., Talbot T., Mostashari F., McLean R. & West Nile Virus Avian Mortality Surveillance Group 2001. Crow deaths as a sentinel surveillance system for West Nile virus in the northeastern United States, 1999. *Emerg Infect Dis*, **7** (4), 615-620.
11. Harada M. 1995. Minamata disease: methylmercury poisoning in Japan caused by environmental pollution. *Crit Rev Toxicol*, **25**, 1-24.
12. International Society of Travel Medicine (ISTM) 2008. GeoSentinel 2008. The global surveillance network of the ISTM and CDC, a worldwide communications network of travel/tropical medicine clinics. ISTM, Snellville, Georgia (www.istm.org/geosentinel/main.html accessed 21 February 2009).
13. Kahn L.H. 2006. Confronting zoonoses, linking human and veterinary medicine. *Emerg Infect Dis*, **12**, 556-561.
14. Meselson M., Guillemin J., Hugh-Jones M., Langmuir A., Popova I., Shelokov A., Yampolskaya O. 1994. The Sverdlovsk anthrax outbreak of 1979. *Science*, **266** (5188), 1202-1208.
15. Mostashari F., Kulldorff M., Hartman J.J., Miller J.R. & Kulasekera V. 2003. Dead bird clusters as an early warning system for West Nile virus activity. *Emerg Infect Dis*, **9** (6), 641-646.
16. O'Leary D.R., Marfin A.A., Montgomery S.P., Kipp A.M., Lehan J.A., Biggerstaff B.J., Elko V.L., Collins P.D., Jones J.E. & Campbell G.L. 2004.The epidemic of West Nile virus in the United States, 2002. *Vector Borne Zoonotic Dis*, **4** (1), 61-70.
17. Rabinowitz P., Gordon Z., Chudnov D., Wilcox M., Odofin L., Liu A. & Dein J. 2006. Animals as sentinels of bioterrorism agents. *Emerg Infect Dis*, **12** (4), 647-652.
18. Rabinowitz P.M., Odofin L. & Dein F.J. 2008. From 'us vs them' to shared risk: can animals help link environmental factors to human health? *Ecohealth*, **5** (2), 224-229.
19. Rabinowitz P., Wiley J., Odofin L., Wilcox M. & Dein F.J. 2008. Animals as sentinels of chemical terrorism agents: an evidence-based review. *Clin Toxicol (Phila)*, **46**, 93-100.
20. Reis B.Y., Kirby C., Hadden L.E., Olson K., McMurry A.J., Daniel J.B. & Mandl K.D. 2007. AEGIS: a robust and scalable real-time public health surveillance system. *J Am Med Inform Assoc*, **14** (5), 581-588.
21. Rutstein D.D., Mullan R.J., Frazier T.M., Halperin W.E., Melius J.M. & Sestito J.P. 1983. Sentinel health events (occupational): a basis for physician recognition and public health surveillance. *Am J Public Health*, **73** (9), 1054-1062.
22. Sarkar I.N. 2007. Biodiversity informatics: organizing and linking information across the spectrum of life. *Brief Bioinform*, **8** (5), 347-357.
23. Skowronski D.M., Masaro C., Kwindt T.L., Mak A., Petric M., Li Y., Sebastian R., Chong M., Tam T. & De Serres G. 2007. Estimating vaccine effectiveness against laboratory-confirmed influenza using a sentinel physician network: results from the 2005-2006 season of dual A and B vaccine mismatch in Canada. *Vaccine*, **25** (15), 2842-2851.
24. Takeuchi T., D'Itri F.M., Fischer P.V., Annett C.S. & Okabe M. 1977. The outbreak of Minamata disease (methyl mercury poisoning) in cats on Northwestern Ontario reserves. *Environ Res*, **13** (2), 215-228.
25. Teutsch S.M. & Churchill R.E. 2000. Principles and practice of public health surveillance, 2nd Ed. Oxford University Press, Oxford & New York, 406 pp.
26. The Canary Database at Yale 2008. Canary Database 2008. Animals as sentinels of human environmental health hazards. The Canary Database at Yale, New Haven, Connecticut (canarydatabase.org/ accessed on 23 February 2009).

27. Tsui F.C., Espino J.U., Dato V.M., Gesteland P.H., Hutman J. & Wagner M.M. 2003. Technical description of RODS: a real-time public health surveillance system. *J Am Med Inform Assoc*, **10** (5), 399-408.
28. United States Department of the Interior/United States Geological Survey (USGS) 2008. West Nile virus. Human, 2008. Disease maps, 2008. USGS, Washington (diseasemaps.usgs.gov/wnv_us_human.html accessed on 22 February 2009).
29. Wildlife Conservation Society (WCS) 2008. Global Avian Influenza Network for Surveillance (GAINS). A program of the global animal information network for surveillance. WCS, New York (www.gains.org/ accessed 21 February 2009).
30. World Health Organization (WHO) 2007. Global early warning system for major animal diseases, including zoonoses (GLEWS). WHO, Geneva (www.who.int/zoonoses/outbreaks/glews/en/index.html accessed on 22 February 2009).
31. Wurtz R.M. & Popovich M.L. 2002. Animal disease surveillance: a framework for supporting disease detection in public health. Scientific Technologies Corporation, Tucson, Arizona, 7 pp (www.stchome.com/media/white_papers/WHP027A.pdf accessed on 22 February 2009).

