

Emerging zoonoses and pathogens of public health significance – an overview

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Summary

Emerging zoonotic diseases have assumed increasing importance in public and animal health, as the last few years have seen a steady stream of new diseases, each emerging from an unsuspected quarter and causing severe problems for animals and humans. The reasons for disease emergence are multiple, but there are two main factors – expansion of the human population and globalisation of trade. Current issues such as the increasing movement of a variety of animal species, ecological disruption, uncultivable organisms, and terrorism, all imply that emerging zoonotic diseases will in all probability, not only continue to occur, but will increase in the rate of their emergence. The recurring nature of the crises dictates that closer integration of veterinary and medical communities is warranted, along with improved education of the general public and policy makers.

Keywords

Emerging disease – Global trade – Public health – Zoonosis.

Introduction

Emerging diseases are occurring at an unprecedented rate in animal and human populations and are causing major consternation for both public health and veterinary communities. The OIE (World Organisation for Animal Health), established in 1924 as the premier multilateral body overseeing global animal health, published a major review on zoonotic diseases, 'An update on zoonoses' (25), in 2000, 76 years after the organisation was founded. Now, only four years later, comes a second publication, 'Emerging zoonoses and pathogens of public health significance'. The OIE's recent and accelerating emphasis on emerging and zoonotic diseases parallels the phenomenon occurring outside the walls of this organisation, as recognition grows that the most powerful enemy might not be the next world war, a nuclear bomb, or even acts of terrorism, but rather Mother Nature. An apocalyptic vision of emerging disease has come into focus over the last few years, as it is apparent that an emerging disease with high transmissibility and high mortality could surface from an unnoticed quarter and drastically reduce the human population before sufficient resources and expertise could be effectively marshalled. In fact, the occurrence and re-occurrence of severe acute respiratory

syndrome (SARS) has demonstrated that a devastating emerging disease may be closer to reality than to hyperbole. As Yogi Berra, a great American baseball player noted for his oxymoronic utterings, once said, 'the future ain't what it used to be'.

The term 'emerging disease' has a fairly broad definition and in general, encompasses any one of three disease situations:

- a known agent appearing in a new geographic area
- a known agent or its close relative occurring in a hitherto unsusceptible species
- a previously unknown agent detected for the first time.

However, with all three categories, the majority of diseases emerge into humans from an animal source. It is well established that 75% of all emerging diseases that have affected people over the last two decades have occurred as a result of an animal pathogen moving into the human host, and are therefore classified as 'zoonotic'.

'Zoonosis' refers to any disease agent that moves into humans from an animal source. The word was coined in

1855 by Rudolf Virchow, a German physician, who was studying *Trichinella*. Virchow's work on trichinellosis helped to convince him of the importance of linking human and veterinary medicine, something he emphasised throughout his career. Although today Virchow is best known as the 'father of pathology' and for elucidating the cellular theory of disease, it is his notion of 'one medicine' that resonates most closely with the current status of global health.

The effects of population increases and globalisation

What are the factors that contribute to emerging zoonotic diseases and why are we seeing so many now, whereas in decades and centuries past their appearances were not so noteworthy? The principal answer is simple – increasing numbers of humans. As the human population expands, and moves from continent to continent, and as various species are mixed together for trade, personal satisfaction, or technological advances, microorganisms are transferred to novel niches, with pathogenic results. A second answer lies in the phenomenon of globalisation. Globalisation has created market forces that drive the interconnectedness of industries, cultures, and, yes, of organisms as well. As informed consumers view investment opportunities on their computer screens and act accordingly, the world is no longer defined so much by geopolitical boundaries as by the terms fast or slow. In the fast world, the 'electronic herd' generates a volume of international commerce that was inconceivable just a few decades ago (12). And, as the electronic herd wags its giant tail, world trade grows at a rapid pace. International commerce has tripled in the last twenty years, with unprecedented levels of traffic in people, animals and animal products.

These two unrelenting forces of population growth and globalisation have combined in a synergy to expand possibilities for agents to move from comfortable domains into new unexplored niches, often with lethal results. Neither force is receding and together they are having pleiotropic and unprecedented impacts. As articulated in a recent National Academies of Science report, a myriad of factors in our interconnected global village are creating the microbial equivalent of 'a perfect storm' (28). However, unlike a major climatic event, where various meteorological forces converge to result in a cataclysmic tempest, this microbial perfect storm will not subside. There will be no calm after the epidemic, rather the forces combining to create the perfect storm will continue to collide and the storm itself will be a recurring event.

What do we know about all the possible microbes that we are moving around and mixing together? In a paper by Cleaveland *et al.* (8), all known pathogens of humans,

domestic livestock, and domestic carnivores, were catalogued and categorised based on their ability to move from one species to another. Surprisingly, of the 1,415 known pathogens of humans, 61.6% have an animal origin. A total of 616 pathogens were documented for domestic livestock, with 77.3% considered 'multiple species', i.e. capable of infecting more than one type of animal. For domestic carnivores, the total was 374 pathogens, with 90% being classified as 'multiple species.' It is apparent, therefore, that there is considerable promiscuity among animal pathogens. As unusual species are grouped together, swapping of microflora can easily occur. Cleaveland made no attempt to catalog the number of agents found in wildlife, and understandably so, as the list would not only be enormous, but also notably incomplete, as we lack detailed knowledge about existing diseases of so many wild species of animals. Given the numbers of species of hosts, the numbers of species of pathogens, and the ever-increasing opportunities to create new permutations, it should come as no surprise that emerging zoonotic diseases have taken centre stage in public and animal health issues.

Examples of recent emerging zoonoses

Examination of some recent examples of emerging zoonoses provides evidence of the impact and unpredictability of these diseases.

Ebola virus

Ebola virus is the prototypical emerging zoonotic disease. With respect to the number of cases and degree of contagion, Ebola is only a bit player in the global drama of emerging diseases, however, because of its continuing re-emergence and very high mortality, Ebola is one of the most well known emerging zoonoses. This disease has done more to raise public consciousness, and therefore to augment funding levels, than any other emerging zoonotic disease. When the disease breaks out, it is often linked to consumption of contaminated bush meat, a growing trend in many regions of Africa as a result of political and economic forces. However, the source of the virus remains unknown. There is no doubt that when the disease emerges in humans or primates it has passed from another species, probably one that is not affected clinically (20).

Bovine spongiform encephalopathy

Bovine spongiform encephalopathy (BSE) provides a very painful example of a serious and emerging zoonotic problem moving to new areas as a result of trade. With

globalisation, contaminated meat and bone meal was spread from one country to another, usually in a totally unsuspecting manner. One can envision these shipments as a kind of 'Trojan cow', bringing destruction to dairy and beef industries, and engendering massive public health consternation. In infectious disease training, students are schooled in mechanisms of disease transmission. Today, a new mechanism of transmission needs to be added to the existing list of 'aerosol, fomite, vectors, etc.' and that new mechanism, which we discovered painfully with BSE, would be 'in cargo vessels and eighteen-wheeler trucks'. Detection of BSE has been particularly problematic as the causative agent is neither organism nor toxin, but rather a post-translationally modified host protein, or prion. The concept of an 'infectious protein' required an initial suspension of disbelief among disease specialists, but now the theory has been fairly widely accepted. The infectious particle, a non-degradable form of a host protein, finds its way into a new host (through ingested contaminated meat and bone meal), journeys to the brain and there, slowly initiates conversion of other normal host cell proteins to the non-degradable state. These abnormal proteins build up within neurons, impede normal function, and histologically appear as cellular and parenchymal 'holes', hence the term spongiform encephalopathy.

Nipah virus

In 1999, Nipah virus destroyed the swine industry in Malaysia while simultaneously creating massive and understandable public panic. The virus, which amplified in the respiratory tracts of swine, was carried on the air generated by coughing hogs, to infect humans, where it went directly to the brain to cause haemorrhagic and necrotic tracts (7). The virus that was isolated from humans and swine was 'new' to science. Investigations indicated that it had been dormant in fruit bats for decades, if not centuries. The forces that unleashed this quiet commensal were related to habitat destruction, climatic events, and expansion of industrialised agriculture.

Rift Valley fever

Rift Valley fever is, as the name suggests, an African disease, and it affects both livestock and humans. Prior to 2000, Rift Valley fever was never seen outside of Africa. In September of 2000, the disease spread to the Arabian Peninsula and emerged there with ferocity, causing severe disease among livestock and in humans, with over 1,700 cases of clinical illness and 216 deaths (21, 23). Trade, combined with favourable climatic factors, allowed a portal of entry and subsequent amplification, creating first an emerging disease in livestock, and then a significant public health crisis for the region.

Alveolar echinococcosis

Alveolar echinococcosis, a smoldering and highly fatal parasitic infection, is making insidious moves from its historic home in the Arctic to many new and more southerly climes (18). Interestingly, it was Rudolf Virchow who, in the 1850s, recognised that alveolar echinococcosis was an infectious process. Prior to that, the medical community assumed the disease was a malignancy because of its proclivity for such rapid and expansive growth. Now, 150 years later, alveolar echinococcosis is again on the medical radar screen, as translocation of Arctic carnivores to depleted more southern reserves, is causing a re-emergence of this parasitic zoonosis.

Severe acute respiratory syndrome

The SARS pandemic mobilised public health systems worldwide and the economic costs were staggering. Despite the most intensive epidemiological investigations and emergency response ever mounted to an infectious disease, the source of the agent remains elusive, making it extremely difficult to predict when and where the next resurgence may occur (2).

Monkeypox

Monkeypox made headlines in 2003 when it surfaced in North America after jumping ship, as it were, from African rodents to North American prairie dogs, all grouped together as part of the exotic 'pocket pet' trade. In the United States of America (USA), there were a total of 37 human cases in four different states, all with exposure to sick or dying prairie dogs (6).

Factors affecting the emergence of zoonotic diseases

Emerging zoonotic diseases have created a new kaleidoscopic lens through which we view the world. These diseases will not only continue to emerge but will probably do so at an ever increasing rate. To take the visual metaphor further, how do we project the kaleidoscopic image into a crystal ball to see what the future might hold? Unfortunately, predictions are not possible, and each new disease that has emerged has come from an unsuspected source. However, what is certain is that there will be many more diseases and both veterinary and public health communities need to be prepared. It is worth considering several prominent and overlapping issues that will impact emergence. These issues include, among others, movement of animals, ecological disruption,

uncultivable microorganisms, chronic diseases, improved surveillance, and terrorism. Each is considered below.

Movement of animals

The volume of trade in animals around the world is large and continues to grow. The animals that are transported fall into one of several categories – livestock and poultry, exotic animals for pets, and wildlife. All of these types of commerce are fodder for potential emergence.

Livestock and poultry

With respect to livestock and poultry, the production of animal protein in the world continues to expand. It has to. The number of people in the world is projected to be 7.7 billion by 2020, with the largest increase coming from the developing world. If current trends continue, there will be a significant percentage of people in the developing world whose diets will be modified from plant-based to meat- and dairy-based. To supply these needs, global livestock production in 2020 will have to be double what it was in 2000 (11). Agribusiness has become global and whereas the intensive rearing of animals for consumption dictates considerable savings in terms of economies of scale and efficiency, in intensive agriculture, larger quantities of goods and materials flow within a country and between countries, so potential for disease spread is high. Also, it is intuitive that larger collections of animals provide more optimal incubating conditions for the expansion of an emerging zoonotic disease, e.g. Nipah virus and highly pathogenic avian influenza.

Exotic animals

Non-domestic species are also participating in travel associated with globalisation. International legal trade in wildlife resources is approximately US\$159 billion per year (9). In the USA alone, it is estimated that there are 16.8 million pets classified as non-dog, non-cat 'small animals' in homes (1). The trend has spread beyond North America. Prior to 2003, the USA was exporting approximately 15,000 prairie dogs per year as pets to other countries, primarily Japan (5). Many pet prairie dogs escape or are intentionally released into the wild. One can envision prairie dogs, perhaps infected with monkeypox, plague, or tularemia, populating the sewers of Tokyo or Los Angeles, only to emerge to engender some new public health plague, as a sort of horrific life imitates art event, akin to a Grade B horror film. Annually, 1.9 million reptiles are imported into the USA each year, from 80 different countries. Most of these are lizards. On the flip side, nine to ten million reptiles are exported from the USA each year, mostly red-eared sliding turtles (3). And, in 2002, 49 million amphibians entered the USA (13). It is apparent, therefore, that the traffic in non-traditional species is robust, all creating the meteorological forces of a perfect microbial storm.

Zoological collections are also locations where etiological agents could pass from one species to another, to begin a new disease. There are 1,200 professionally managed zoos and aquaria throughout the world. Among these institutions, trade is well documented. Of the 1.65 million animals kept in 586 institutions in 72 countries on six continents, 82% of new zoo mammals, 64% of birds, and the majority of reptile species are zoo-bred (17). This translates into a plethora of possibilities for potential pathogen travel. An African rodent born and raised in an Asian zoological collection could be found in a South American zoo housed next to Arctic mammals from North America. The number of permutations of new organismal biomes for commensals or pathogens to explore just increased exponentially.

Illegal trade in non-domestic species is difficult to quantify, but assumed to be extremely lucrative, and second only to drug smuggling in profitability. Of course, it is a rhetorical question to ponder the feasibilities of examining records of traffic and so it is impossible to determine what kind of microfloral swapping may be occurring in this criminal and extensive commerce.

Wildlife

In recent years, live animal trading markets and the consumption of bush meat have received increased attention, largely due to their connections with outbreaks of SARS and Ebola.

Consumption of bush meat

Although humans have hunted and eaten meat from wild animals for millennia, consumption over recent years has increased dramatically (22). In Central Africa alone, it is estimated that 1 million to 3.4 million tonnes are consumed annually. Although the focus tends to be on African practices, many other areas of the world participate in harvesting, transporting and selling wild animals for food. For instance, 25 tonnes of turtles are exported from Indonesia every week and 28,000 primates are hunted annually in Peru. The modern phenomenon of transporting meat in a supply chain that can be hundreds of kilometres long amplifies the potential spread of pathogens. Microbial flora from these animals can find their way into new hosts and/or new continents, with unpredictable results.

Live animal markets

It is also worth considering the live animal markets, often referred to as 'wet markets.' These establishments, popular in both developing and developed parts of the world, offer a variety of species, usually domestic, in an assuringly fresh state for consumers. Unfortunately, in this fresh state they are also eminently capable of coughing and defecating, effectively spewing potential pathogens to neighbouring animals and humans. Although some of these wet markets

have been recognised for decades as potential sources of disease emergence, e.g. highly pathogenic avian influenza from live bird markets, the recent evidence of civet cats with SARS coronavirus and serological positivity among wet market workers in China raises anew the considerable risks associated with these practices (14, 32).

Ecological disruption

Ecological disruption is another major issue to address and may be one of the most dangerous factors in the emergence of new zoonotic diseases. As humans encroach on new habitat, it is a certainty that they will be exposed to novel pathogens that could move from their four-footed or avian niches into humans to engender disease. In addition, there is the anthropogenic movement of pathogens into new geographical locations, a phenomenon that has been termed 'pathogen pollution' (10). Anthropogenic movement of uninfected hosts to new regions might also allow for diseases to emerge. An example here is the introduction of brushtail possums from Australia into New Zealand. In New Zealand, the possums have served as a very viable reservoir for bovine tuberculosis (30). Interestingly, biosecurity is a concept usually applied to a patient or animal, laboratory, clinic, or farm. Perhaps it is time to adjust the concept of biosecurity to a larger dimension, that of the ecosystem. By applying biosecurity to one small sector, as we have in the past, we may be inadvertently damaging the ecosystem in ways that will encourage the emergence of yet another disease. One needs only to examine the unintended impact of the application of the insecticide DDT (dichlorodiphenyltrichloroethane) decades ago to appreciate the pleiotropic effects of environmental manipulation. Veterinarians have recently been encouraged to think about biosecurity in a wider sense, that is, to develop policy and apply animal health care with the idea of encompassing the environment in its totality (19).

Uncultivable microorganisms

Another major issue concerning emerging zoonoses is the presence of previously unrecognised pathogens. As stated above, humans can be affected by over 1,400 different disease agents, the majority of which are zoonotic. All of these pathogens are known, that is, identifiable by some means, usually cultivation. What about all those microorganisms which we have not yet identified or which are not cultivatable by current methods? The last decade of microbial ecology has been described as 'inventory-expanding' as molecular genetics has allowed investigators to identify a multitude of uncultured microorganisms in a variety of settings (31). Using cultivation-independent 16S ribosomal ribonucleic acid gene-based surveys demonstrates that natural diversity of prokaryotes far exceeds the numbers of previously

recognised agents. These new organisms are proving to be the majority of bacteria in many microbial communities, both natural and engineered. It has been estimated that we can cultivate only about 0.4% of the bacteria in the natural world (26). This translates into a mind-boggling assortment of previously unknown organisms within each ounce of seawater or teaspoon of earth. How many might be able to infect and cause disease in a novel host? The crystal ball does not yet answer, but there are hazard lights flashing in a precautionary mode.

Chronic diseases

Along a similar line, it is being demonstrated that many chronic diseases are being caused by uncultivable organisms or infection with organisms decades earlier. An example is the recent association of *Toxoplasma* infection with schizophrenia. Acute infection with *Toxoplasma* and also immune compromise activation of *Toxoplasma* are clearly associated with often significantly altered mentation. Chronic mental illness was not, until recently, thought to have a potential link with *Toxoplasma* infection. However, serological studies indicate that patients with schizophrenia have a higher percentage of antibodies and, in the majority of studies, the difference was statistically significant (29). Consequently, a disease previously thought to be non-infectious (i.e. schizophrenia), may in fact have a zoonotic origin. How many other long-term debilitating diseases may also have been triggered by infection with an agent much earlier in life?

Improved surveillance

As investigations intensify, new and variant forms of existing disease are inevitably uncovered more readily. A perfect example is the discovery of bovine amyloidotic spongiform encephalopathy (BASE), by Italian researchers (4). With increased surveillance for BSE in Italy, over 1.6 million brains were tested. When testing samples from 103 positive cases, they found a distinctly different type of spongiform encephalopathy, one that is present in other parts of the brain. The new BASE prion differs in that there are fewer sugars attached to it. It is distressingly similar to some isolates from human sporadic classical Creutzfeldt Jakob disease.

Terrorism

The last, but not least, issue to address is the threat of terrorism. Although bioterror agents are all previously recognised pathogens, there is always the possibility of an amateur or professional microbiologist with antisocial tendencies and a maniacal agenda who could slightly alter an organism to create and unleash a new disease. This is all

part of the new tapestry of tomorrow that was forecast so aptly by Yogi Berra in his statement about the unpredictability of the future.

Conclusions

In watching the steady stream of new and emerging diseases, one is reminded of the carnival game, 'Whack-a-mole'. In this game, the participant is given a rubber mallet and tasked with defeating each mole that appears out of any of a series of holes. The satisfaction derived from neutralising one mole is immediately replaced with the drive to beat back the next mole that appears out of one of many holes. The operator must act quickly to eradicate each new surfacing mole. Is this our current strategy in responding to emerging disease, i.e. beating back each new disease as it puts its head out of the hole?

It is clear that the biomedical science, public health, animal health, and policy communities need to move quickly to address all of the underlying reasons for disease emergence. The interface between human and animal health is becoming increasingly blurred. Animals and people are inextricably interconnected, like the lines in an Escher drawing. With global trade, habitat change, and a myriad of lifestyle issues surfacing and evolving, the connections are increasingly fluid, with lines constantly moving and shifting. We face a huge challenge in being prepared to recognise and respond to each new emerging zoonotic disease. Without adequate connections between

human and animal health, we are lost. Virchow's initial call to consider one medicine is more relevant than ever.

The recent coordinated efforts of the major international players in human and animal health – the OIE, the Food and Agriculture Organization of the United Nations, and the World Health Organization – to address first BSE and then highly pathogenic avian influenza, are of some comfort. The lack of individuals prepared to deal with animal health on a population level, both for food animal populations as well as for public health and other regulatory endeavours, has reached crisis point (15, 16, 19, 27). As articulated recently in a USA publication for veterinary medicine, 'Despite the twin threats of agroterrorism and new and emerging diseases... [there has been a] sharp decline in the number of government veterinarians and other animal health professionals responding to animal emergencies' (24). However, animal health is not alone in lacking infrastructure to rapidly produce sufficient disease expertise. There has been a decline in public health infrastructure worldwide, some of which has been reversed in recent years, due to recurring infectious disease crises and more concerted public attention. With the new global health mosaic created by the kaleidoscopic lens of emerging diseases, animal and public health are inextricably intertwined. There is an urgent need to rebuild expertise in a synergistic way, to effectively expand competencies and scientific knowledge in new, integrated areas, and within a greater global context. The health of the world depends on it.



Aperçu des zoonoses et des pathogènes émergents importants pour la santé publique

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Résumé

Les zoonoses émergentes acquièrent une importance croissante pour la santé publique et la santé animale. Ces dernières années ont vu un flot ininterrompu de maladies nouvelles, de provenance insoupçonnée, qui ont donné lieu à de graves problèmes chez l'homme et les animaux. L'émergence de ces maladies relève de causes multiples, dont les deux principales sont l'explosion de la démographie humaine et la mondialisation des échanges commerciaux. Les problèmes actuels, comme l'intensification des mouvements de diverses espèces animales, les perturbations de l'environnement, l'apparition d'organismes non cultivables et le terrorisme, donnent à penser que, selon toute vraisemblance, les zoonoses émergentes continueront non seulement de se manifester, mais que le phénomène ira croissant. Le caractère récurrent des

crises exige une intégration plus étroite des communautés médicale et vétérinaire, qui ira de pair avec une sensibilisation accrue de la population et des responsables politiques.

Mots-clés

Commerce mondial – Maladie émergente – Santé publique – Zoonose.



Repaso de las zoonosis emergentes y los patógenos de importancia para la salud pública

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Resumen

En los últimos años las enfermedades zoonóticas emergentes han ido cobrando una importancia creciente en el terreno de la salud humana y animal, en la medida en que surgían sin parar nuevas enfermedades procedentes siempre de lugares insospechados y causantes de graves problemas para el hombre o los animales. Aunque tal proliferación se explica por múltiples razones, hay dos factores que revisten especial trascendencia: el aumento de las poblaciones humanas y la mundialización del comercio. Otros fenómenos actuales como el movimiento cada vez más intenso de diversas especies animales, los desequilibrios ecológicos, la existencia de organismos incultivables o el terrorismo llevan a la obligada conclusión de que, con toda probabilidad, no sólo seguirán apareciendo nuevas enfermedades zoonóticas sino que además ello tendrá lugar a una cadencia más rápida. El carácter recurrente de las crisis impone una integración más estrecha entre los círculos veterinarios y los médicos, combinada con una mejor labor pedagógica dirigida al gran público y a los responsables políticos.

Palabras clave

Comercio mundial – Enfermedad emergente – Salud pública – Zoonosis.



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