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Emergence of infectious diseases

Risks and issues for societies

Serge Morand, Muriel Figuié, eds

éditions Quæ

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Contents

Foreword by Frédéric Keck, Anthropologist, CNRS

Emerging infectious diseases. For the past two decades, this term has been used to designate a new stage in the history of public health, and more generally in the government of living beings. The first alert regarding emerging infectious diseases (EIDs) is generally said to be the appearance of the Ebola virus in Zaire in 1976, but this event is significant because it came after the announcement by the World Health Organization of the end of the global smallpox vaccination campaign. The emergence of new infectious diseases only comes as a surprise if one takes the viewpoint of an international organization which was expected to be devoting its time henceforth to chronic diseases. The explosion of the AIDS pandemic at the end of the twentieth century sadly proved this assessment to be wrong.

In this respect, the notion of EIDs signals the end of a certain modernity. The belief that infectious diseases could be eradicated by vaccination was linked to a method of hierarchical organization based on Pasteur's idea of the war on germs. If infectious diseases continue to emerge, it is because nature manages to deflect the means that humanity uses to control them. "Nature strikes back" is one of the tenets of this new world vision, as heralded by biologist and environmentalist René Dubos in the 1950s. This idea is also expressed in the post-Cold War period as "Nature is the greatest bioterrorist threat". Those involved in the fight against EIDs now have to follow the ways in which the germs mutate, anticipate their propagation and send early warning signals. Networks – more flexible and mobile – are replacing hierarchical organization.

This switch is neither simple nor evident, and the contributions in this book explore how EID have led to reorganize the world, changing our conceptions of agency and nature.

To further complicate this switch, take the relationship between the notions of emergence and mutation, considered to be two methods of describing what appears to be new, as a measuring stick. Ever since Darwin, we have known that living organisms come about by means of discrete mutations selected by environments. The mutation/selection pairing is based on a reversible notion of what is living: one particular mutation will be selected in a certain environment, but not in another. On the contrary, the notion of emergence introduces an element of irreversibility. In physics and biology, it designates the appearance of properties through the composition of elements which did not possess these properties. When a new pathogen emerges, it provokes reactions of fear, mobilization and organization to such an extent that it has a profound effect on the environment in which it appears. Even if it were then to disappear, "nothing would be the same again".

Influenza has thus become an EID model since it combines the potential of mutation (as revealed by the sequencing of its RNA segmented into a single strand) with the catastrophic character of emergence (ceasing of economic activity being considered to

be a more serious event than the outbreak itself). A broad reflection needs to encompass this accumulation of properties on physical, biological and sociological levels.

From this perspective, it is essential to focus on one of the central notions used to describe this emergence: the animal reservoir. A pathogen acquires new properties when it passes from one species to another, via a mechanism described as a spillover. Discrete mutations become catastrophic when they find an evolutionary bottleneck in a change in population. The notion of animal reservoir is a means of mapping the discontinuities of transformation within the human population. Zoonoses are diseases which pass from animals to humans and vice versa, demonstrating a vital solidarity in exposure to environmental changes. One of the lessons of the ecology of EIDs is that the reduction in the number of species actually promotes rather than reduces the appearance of new pathogens, since it brings with it a greater proximity of humans to certain species.

Once the emergence has been mapped among living beings, the social worlds which it mobilizes then need to be described. Various stakeholders with often conflicting interests are concerned by any new pathogen, including ecologists, veterinarians, doctors, public health authorities and even the military. Sociologists and anthropologists are mobilized to describe the behaviour of the populations driving the emergence, and to draw up a list of the collectives involved, who are both creating and involved in this new image of the world. The need for surveillance becomes a new watchword in terms of reorganizing global vision, based on the "One World, One Health" principle, although consideration must be given to the plurality of this expression.

That an event as minor as the mutation of a pathogen jumping the species barrier should become the motor of such a reorganization of the social world, that a phenomenon as continuous and reversible should bring about irreversible discontinuities – this is real food for thought for those who seek to describe the contemporary. By going back and analysing each of the thresholds that the emergence has gone through, the descriptive approach is also a critical one, as it uncovers the contingences of what has become evident, but also the potentials inherent in the emergence. This work, by multiplying the perspectives on emerging infectious diseases, provides indispensable material for what is a necessary collaboration between biological, social and environmental sciences.

Introduction

The aim of this book is to demonstrate the mechanisms by which the concept of emerging diseases is establishing itself as a new means of treating infectious diseases as well as the new configurations which this re-framing is bringing about, both in the world of research and in terms of public decision-making. To do this, it will take a multidisciplinary look at emerging infectious diseases (EIDs), taking in biological, political, sociological and historical approaches across five chapters.

More than simply providing multidisciplinary insight into the subject, the authors also illustrate the way in which the concepts, scientific results and plans of action by international and governmental agencies interact and contribute to the co-construction of the EIDs. Furthermore, the book demonstrates that re-framing infectious diseases as emerging infectious diseases poses new challenges, such as collective mobilization around a good whose status as a 'common good' is up for debate. It will provide the lay person, the researcher, the practitioner, the expert and the decision-maker with some key elements for understanding this make-up of the problem and some responses to it.

The first two chapters take complementary views of the mechanisms and the factors behind the emergence – biological for Serge Morand and socio-political for Nathalie Brender and Claude Gilbert.

In the first chapter, Morand explains to us the characteristics of emerging diseases, and the factors which encourage their appearance, born out of epidemiology, ecology and biogeography. This enables him to answer numerous questions: What are the emerging pathogenic organisms? What are the ecological and biological mechanisms which create their emerging characteristic? Are they new or different from historic emergences (the plague, typhus, etc.)? Can one say that there is a biogeography of emergence?

These questions help to give distanced and critical insight into the production of knowledge of the biological mechanisms of emergence. What is truly new in emerging diseases as defined by Stephen Morse in 1995? "The trends in all global infectious disease outbreaks are similar to those that are limited to EIDs alone. Global disease outbreak trends are also increasing exponentially. There is to a certain extent an epidemic of epidemics," says Morand. By which process of spatialization of emergence does the knowledge produced enable countries and regions to be designated as sources or targets of new epidemic threats? And why is so much attention being focused on bats while parasitic diseases within emerging diseases are being "neglected"?

It is the emergence of a new representation of the world which is accompanying the work of researchers, where the human and the non-human, the domesticated and the wild, share a greater epidemiological community. It is also an opportunity to update the old geography of threat and security, with very clear dividing lines between the intertropical zones in developed countries that are the epicentres of the emergence (since they are at

the centre of the current ecological changes), zones of vulnerability which could amplify them due to the human population density and the weakness of the health systems, and those areas able to increase visibility by means of biotechnologies.

In the second chapter, Nathalie Brender and Claude Gilbert provide a different perspective on the mechanisms of emergence, namely that of social sciences. From this point of view, emergence is not only a rupture, a disorder which arises in nature, but also results from the convergence of interests of those who contribute to the emergence of emergence. For the social sciences, it is as much viruses, sufferers and scientific challenges which are being created by the emergence of new pathogens as it is a new type of public problem, of which the recognition as such "seems to depend on their nature, but also possibly even more so on their mode(s) of appropriation".

While the first chapter deals with the question of the 'competencies' of the viruses, vectors and hosts etc., the second chapter, following the emergence and re-emergence of influenza on a national (France) and international scale, reveals in parallel other necessary competencies for 'candidates for emergence', notably their capacity to become part of the strategic priorities of leading stakeholders. This also tends to reframe the problem itself: "Not only was the emergence of the pandemic influenza issue largely determined by the WHO's interest in promoting it, but its classification shifted according to the organization's successively changing positions". If the stakeholders who tackle the problem transform it, they themselves are transformed by the problem since they owe it to themselves to make the necessary adjustments to be both more effective and more widely accepted. The next question is the capacity of those involved to ensure that 'their' problem becomes part of the long-term agenda, and to update the interest it can create so that it can ward off competition from new emergences. This process is similar to that described in the first chapter regarding the co-evolution of pathogens with their hosts, their vectors and their environment.

In the third chapter, Patrick Zylberman tackles the question of emerging risks and in this case infectious emerging risks by means of the history of the international and political relations of the American 'superpower'. A paradigm shift in governmental policies was effected, with the focus shifting from prevention of risks to security. In this new context, preparing for worst-case scenarios takes centre stage.

Zylberman retraces the evolution of the role of health-related security within US national security, from a marginal one at the end of the Cold War to a central one with the emergence of new global threats including pandemics and bioterrorism. The first conference on emerging viruses, held in Washington in 1989, was one of those key moments, both in terms of the multidisciplinary dimension of the participants (virologists, ecologists, agronomists, veterinary scientists, anthropologists, etc.) and by putting the focus of causality back onto humans. "Humans are engineers of microbial circulation," said conference organizer Stephen Morse.

The second event, as Zylberman explains, came during the presidency of Bill Clinton, who implemented the National Domestic Preparedness Program just before the end of

his term in 2001. This turning point from health-related prevention to preparedness was strengthened by Clinton's successor, with George W. Bush opting for continuity via this new governance organization for germ-related threats, while the origins and content of this preparedness can be found in the early 1990s.

The most important aspect, according to Zylberman, resides in the construction of worst-case scenarios. With the implementation of the Homeland Security Council, such scenarios prompt those involved in governance to play their roles in crisis situations, and to invent stories to be able to overcome the situations. Fiction and the imaginary become the new tools for managing threats which are completely out of the realm of usual risk analysis.

In the following chapter, Muriel Figuié questions the collective response capacity to these risks, whose potential scope, complexity and uncertainty call for the mobilization of a growing number and a wider variety of stakeholders than traditional risk management. The chapter runs through the difficulties of implementing a coordinated action among these stakeholders, be they individuals, collectives that are formalized to a varying degree, states or international organizations. In the health sector, whenever it is a question of mobilizing the public, individualist and culturalist approaches tend to dominate. This chapter invites us to go beyond these approaches by highlighting the delicate balance between individual and collective rationales, and also between institutional, local, national and international rationales.

This chapter also demonstrates that while emerging diseases 'invite' ever larger and more disparate collectives to be mobilized, it is also the collectives themselves which define and delineate their points of focus. This construction is not without consequences. At the moment, international organizations intend to promote surveillance of emerging diseases to the status of global public good. By doing this, they are establishing the defence of an interest that is theoretically supposed to be shared (where everyone would benefit from working together) as a principle of coordinated collective action. However, the chapter demonstrates the diversity of interests, and the necessary debate of compromises and arbitration.

In the final chapter, François Roger justifies the essential yet ambiguous role of health surveillance at the heart of global governance concerns. It should make it possible to detect what seems to be becoming more and more unpredictable as early as possible. This surveillance is not without contradictions, and analysis of the epidemiological transitions which have accompanied the socioeconomic development of societies shows this. Health surveillance must address the challenges that reveal the complexity of the problem at hand. It is also crucial to know what should be monitored. Anticipation requires keeping an eye on the signals which herald the possible emergence of a disease and not the emergence of the diseases themselves. These signals are mixed, as are the mechanisms of emergence. What are they? The evolution of biological diversity, agricultural practices, antibiotic use? On what level do they need to be observed? Moreover, how can we prevent these signals, which are weak and uncertain, from replacing the dangers themselves in collective fears?

Health surveillance, as Roger reminds us, appeals first and foremost to empirical sciences. It is necessary to research and appreciate microbial diversity to develop prevention tools and medical responses. Health surveillance next appeals to mathematical forecasting sciences along with risk analysis. Moreover, surveillance implies organizing a permanently increasing network of ever more diverse people, due to the complexity of the systems being monitored. Surveillance also requires new organizational, legal, economic and governance tools, since it is necessary to manage the sharing of costs and benefits between the various social groups, sectors (health, agriculture, environment etc.), and countries. It raises questions of ethics, since "you cannot keep everything under surveillance". This implies economic arbitration in terms of efficiency, but also societal and moral choices. Emerging diseases are more than a health issue. With the aim of anticipating them comes a whole network of surveillance which re-organizes itself, leaving the sphere of specialized organizations and breaking into all sectors at every level of human life.

By treating emerging diseases like hybrid objects, by constantly going back and forth between the biological and social dimensions, this book seeks to develop a pluralist approach to health (Dozon and Fassin, 2001). Its ambition is first and foremost to avoid too positivist an interpretation, which would reduce emerging diseases to merely a piece of data from our natural environment and uncovered by biological sciences. Equally, it wishes to avoid too relativist an interpretation, which would turn it into a simple social construct, and only ever the provisional result of a power struggle between those who have an interest, and different rationales and cultures, all of whom are competing. This delicate balance, between the two extremes that are the authoritarianism of what is 'real' and socio-centrism (Larrère, 1997), is necessary to fully understand what is at stake in this epidemic of epidemics.

1. Biogeography and the ecology of emerging infectious diseases

Serge Morand

A major epidemic of Ebola occurred in West Africa in 2014, causing more than 11,000 deaths by the time the outbreak ended in mid-2016. This extremely deadly haemorrhagic fever of viral origin created a serious regional health crisis and led to fears that it would spread across the globe. In its early days, and for many months, the epidemic received little attention from international institutions, particularly the World Health Organization (WHO). The turning point came when a few cases appeared in Western countries, most of which were health workers who had been repatriated after being infected when treating patients. The risks of introducing and spreading the virus in Western countries became very significant when secondary infections, once again affecting health workers, occurred in Spain and the United States. The health crisis suddenly shifted from a regional concern to a global one.

Ebola is an illustrative example that can be used to examine fundamental questions about the ecology and epidemiology of emergence. This disease is caused by infection from a virus carried by bats. Human contamination occurs not only by handling infected bats, which is assumed to be the cause of the first case of the West African epidemic, but also through contact with wild animals, primates or antelopes infected with the virus that are hunted or sold as bushmeat. But large epidemics like the one observed in West Africa or previous epidemics in Central Africa are the result of contact transmission between sick people and healthy individuals (more specifically, when caring for the sick or when coming in contact someone who has died of the disease). The disease is then transmitted directly between people, with no need for transmission from the animal reservoir until transmission is under control and the virus persists only in bats.

This epidemic raises a number of questions about the ecology and geography of emergence. What are these emerging pathogens? What are their origins? Why are bats so frequently mentioned? What is the link with humans: who infects whom and how? Are there any geographic 'hotspots' of emergence? Is Africa unique, or the tropics in general? Is this Ebola health crisis in West Africa a bat problem, or is this health crisis more indicative of an environmental crisis coupled with a social crisis?

An emerging infectious disease is defined by Steven Morse (1995) as an infection that has recently appeared in a population or that has existed before, but whose incidence or geographic range is increasing rapidly. We should note that this definition also relates to the rise of bacterial resistance to antibiotics. But how is this concept of emergence, derived from the work of scientists such as Steven Morse, supported by comparative studies in global epidemiology?

Human history has been profoundly marked by emerging infectious diseases such as the Black Death in the Middle Ages or the Spanish flu at the end of the First World War. Infections also contributed to the decimation of Native American and Pacific Islander populations following European colonization (McNeill, 1976). These emerging diseases are ever present in our collective experiences. The emergence of the AIDS, SARS, avian influenza (H5N7), swine flu (H1N1), West Nile virus and the recent Ebola virus in West Africa remind us that infectious diseases, still a global risk for world health, maintain a hold on our imaginations. Are these recent emerging pathogens new or different from the emergence and epidemics such as bubonic plague, smallpox or typhus that have occurred throughout human history?

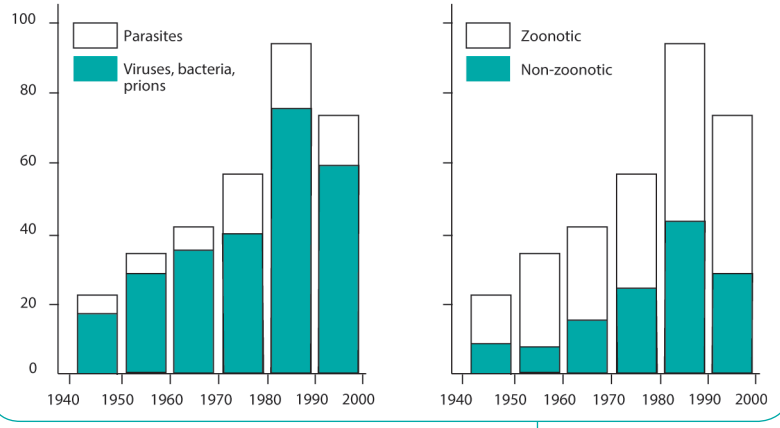
Characteristics of emerging infectious diseases

The human species is infected with a large number of pathogens, undoubtedly making us the most parasitized species on Earth. More than 1,400 species of parasites and microbes have been listed as pathogenic in humans (Cleaveland *et al.*, 2001) and, of these, more than 60 percent are of zoonotic (i.e., animal) origin. The percentage of zoonotic pathogens observed in all infectious diseases affecting humans is the same as the percentage observed for the newly emerging infectious diseases. Thus, emergence does not present an original character within the total diversity of infectious diseases that have and still continue to affect humanity.

The study by Jones *et al.* published in *Nature* in 2008 will serve as a guide for the ecological and epidemiological analysis of emergence and improve understanding of the dynamics. Since its publication, this study has been cited more than 2,000 times in scientific literature, demonstrating both the interest of the subject for the scientific community and how original it is. This study contributed to the effective implementation of several programmes by the United States Agency for International Development (USAID). These programmes aimed to detect and prevent emerging diseases in their likely places of emergence. However, we will come back to this point when discussing the geography of emergence. This study also provided the scientific basis for the One Health initiative led by the United Nations Organization for Food and Agriculture (FAO), the World Organisation for Animal Heath (OIE) and the World Health Organization (WHO).

In their study, Jones *et al.* (2008) showed a significant increase in the number of emerging infectious disease (EID) events from 1940 to 2000 (Fig. 1). They then noted that the agents

Figure 1. Evolution of the number of emerging infectious diseases (EIDs) from 1940 to 2000, according to the type of pathogens (parasites or viruses and bacteria) (left) and according to the type of zoonotic transmission (involving wild or domestic animals) or non-zoonotic (environmental, vectors without animal reservoirs, direct human-to-human contact) (right).



Adapted from Jones *et al.*, 2008.

responsible for these EIDs are mostly viruses and bacteria. Parasites, i.e., worms (such as nematodes or tapeworms) and protists (such as malarial agents) account for a minority of these newly emerging agents. Finally, more than 70% of these EIDs originated from animals (mainly wild).

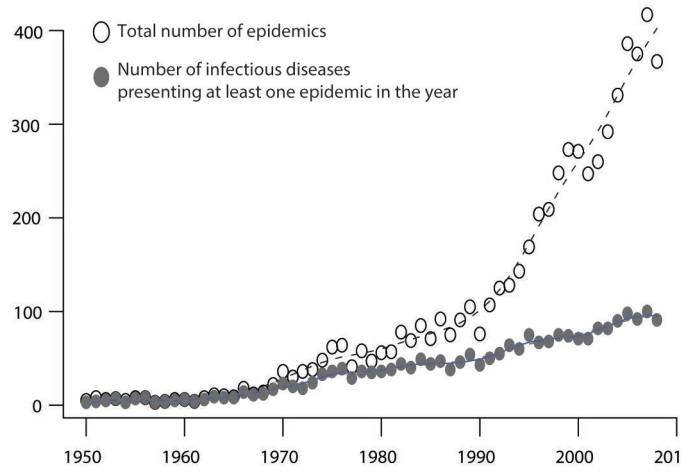
The Jones *et al.* (2008) study focuses on three characteristics of these EIDs: (1) there is an epidemic of EIDs (2) mainly due to microbes (viruses and bacteria), (3) many of which originate in wild animals.

In trying to answer the question as to whether these EIDs are different from the infectious diseases that have and still do affect human populations, we must recognize that the number of infectious diseases that are present in a country or a geographic region and the number of infectious disease outbreaks are two distinct issues.

The number of diseases, or the burden of infectious diseases, is a static measurement that corresponds to the sum of medical knowledge of a given country or region. Although it obviously takes into account past eradications or new emergences, the number of diseases is a measure of how endemic infectious diseases have become in a geographical area where infectious agents may circulate without significant epidemic outbreaks.

The number of epidemics is a dynamic and temporal measurement, which shows the number of remarkable epidemiological events at a given moment or over a given period.

Figure 2. Evolution of the number of epidemics of infectious diseases in the world from 1950 to 2010: total number of epidemics in the year (upper curve in black), number of infectious diseases presenting at least one epidemic in the year (lower curve in grey).



Adapted from Morand, 2015.

Detecting and reporting an epidemic event requires a public health service that is able to monitor, identify and carry out national and international outbreak notifications. The quality of the public health service depends on the financial resources allocated to it and, indeed, there is strong correlation between the number of epidemics affecting a country and its GDP or per capita expenditures for the public health system. The wealthier a country, the more it is able to detect, characterize and report different epidemics internationally, regardless of the number of diseases present in the country. This bias has been taken into account in all published studies (including that of Jones and his colleagues).

Analysing trends in the global epidemiology of infectious diseases has been the subject of several studies, most having used the online database GIDEON (which includes data from the WHO). The trends in all global infectious disease outbreaks are similar to those that are limited to EIDs alone (Smith *et al.*, 2014, Morand *et al.*, 2014c). Global disease outbreak trends are also increasing exponentially (Fig. 2). There is an epidemic of epidemics of all types of infectious and parasitic diseases.

Although less dramatic than the total number of outbreaks, there is also a significant increase in infectious diseases with at least one epidemic in a year. This indicates a rise in different kinds of infectious diseases, including EIDs, presenting an outbreak over the last 60 years. Finally, EID events share two characteristics: more than 60% of these outbreaks are from zoonoses, and the causative agents are mostly viruses and bacteria.

At least two studies have explored these epidemic patterns regionally in Europe and Asia Pacific (Morand and Waret-Szkuta, 2012; Morand *et al.*, 2014a). They also showed the same exponential increase in infectious disease outbreaks. These two regions, which have different socioeconomic and environmental profiles, with high intra- and inter-country variability, showed strikingly similar trends and patterns in the dynamics of their infectious diseases. This raised the question of what common factors might explain such similarity.

What are these emerging pathogens?

The increase in not only emerging but all infectious diseases in recent decades mainly concerns bacteria and viruses. For tropical medicine, this is a major change. Tropical medicine has long focused on parasitic diseases caused by helminth worms (schistosomiasis, tapeworms and intestinal strongyles) or protists such as trypanosomes responsible for sleeping sickness and Chagas disease. Although these diseases are still public health problems, they are not in the scientific mainstream of emerging infectious diseases or even in the global dynamics of epidemics (McIntyre *et al.*, 2011). A new medical field has been created for 'traditional' tropical diseases that are losing the attention of health policies, donors and scientists while new journals are cropping up for these 'neglected tropical diseases'. Some of these neglected infectious diseases are re-emerging (such as leptospirosis), suggesting that the 'emerging' label attached to an infectious disease is first and foremost an indication of emerging scientific, social and political interests.

Going back to the definition of emergence given by Steven Morse, for an infectious disease to become emerging, it must be new and/or expand its geographical range. Starting with the new aspect of an infectious disease, the development of molecular biology must be considered along with its applications in the biomedical and epidemiological field with new rapid and less expensive methods to detect and characterize pathogens (still requiring significant technical advances). While medical or veterinary parasitology still relies on macroscopic characterization of parasites, such as the use of the optical microscope, the development of molecular methods has helped refine the distinction of certain species (within species complexes) or genetic variability between different circulating strains. Microbial infectious diseases, i.e., bacterial and virologic, greatly benefited from the rapid growth of these new molecular techniques. The coronavirus responsible for SARS is the best example of the rapid detection and characterization of a new infectious agent. New species and strains have been and can be characterized by these new tools very quickly. These advances led to virtual real-time sequencing and analysis of the circulating strains of the Ebola virus in West Africa. A new profession appeared: virus or 'bug hunter' as defined by Nathan Wolfe.

Paradoxically, this scientific and technological development is part of the rise in EIDs. Emergences are easier to see and different emergences are better characterized because of the financial, technological and scientific resources available to detect them and identify the causative pathogens. Accordingly, any analysis of temporal epidemiological trends

must take into account the means that a country or the international community could use to monitor epidemics and characterize the pathogens that are circulating and emerging.

The rise of new high-throughput sequencing techniques also makes it possible to carry out an unbiased investigation of the entire community of microbes and parasites that an individual or an animal species harbours. This is what is referred to as the microbiome (all bacteria living on the skin or in the digestive tract), the virome (all viruses including pathogens and retroviruses) and the parasitome (all parasites). Brand new explorations of living beings are now possible, similar to the great expeditions conducted by museums of natural history. However, the consequences for societies are very different. Once again the example of bats and the first studies of their viromes provide a good example.

Based on characterization of part of a bat's virome, a species of flying fox that is a reservoir of many emerging viruses, Anthony *et al.* (2013) statistically extrapolated their results to the potential number of all viruses circulating in mammals. Without going into the many methodological and statistical biases of such work, the authors arrived at a number of more than 320,000 viruses waiting to be discovered in mammals.[1] All of these 'possible' viruses were presented as 'potential' sources of future EIDs. But the authors concluded that the complete characterization of these viruses (it would multiply by a factor of 60 the number of known characterized viruses) would cost $6.3 billion, a "small fraction of the cost of many pandemic zoonoses". This work and these quotations have been widely reported by the international press (the BBC, *Le Monde* and major American networks).

A year later, in 2014, an Ebola outbreak erupted in West Africa. Would the characterization of all mammalian viruses proposed by Anthony and his collaborators have helped prevent and contain this epidemic? Are bats the culprits of this epidemic, and if so, would a wildlife surveillance strategy or even monitoring of bushmeat hunters as promoted by Nathan Wolfe (2011) have prevented and contained the epidemic?

What are the animal reservoirs of these new emerging infectious diseases?

Woolhouse *et al.* (2005, 2008) have characterized the reservoirs of these emerging parasites and microbes. Their articles again show that viruses and bacteria are the main agents at the origin of emerging infectious diseases, and that emergences are overwhelmingly zoonoses. But the main interest of these studies is the characterization of animal reservoirs of zoonoses (Fig. 3).

First of all, ungulates (hooved animals such as cattle, horses, goats and sheep) appeared as major reservoirs of new emergence, but carnivores (dogs, mostly cats) also play an

1. It should be noted that over 5,000 virus species have been fully characterized and that the total estimated number of viruses on Earth is 10^{31} (a one followed by 31 zeros!), with most being bacteriophages, viruses that infect bacteria.