Editorial overview: Emerging viruses: interspecies transmission

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Emergent viruses and associated diseases comprise various and rather quite distinct entities, which can arise in a large part of the living world. Indeed, emerging viruses have been, and are still, frequently reported in a great variety of animals, from insects to humans, as well as in plants. Furthermore, some of these diseases, associated with emerging viruses, had recent major public health impact, as exemplified in humans by the AIDS [1], hepatitis C pandemics [2], or the current Ebola disease epidemic, or in crops by cassava mosaic disease, which seriously compromises food security in East Africa [3]. How can we define such emerging entities? Firstly, it can be a new disease, due to a yet unknown virus. In humans, the natural reservoir of such a virus is frequently an animal. These zoonoses include some coronaviruses present in specific bat species and the severe acute respiratory syndrome, hantaviruses present in rodents and various clinical syndromes, and some filoviruses, as Marburg and Ebola viruses, living in fruit bats and the associated hemorrhagic fevers. For plants, new viruses in crops are also thought to emerge from wild reservoirs: for instance, the Maize streak virus originates from wild African grasses. Strictly speaking, these are considered as real emergences. Secondly, it may be a known disease, in which one finds the causative viral agent. Here, we can cite for human diseases, some clinical hepatitis and the hepatitis C virus, the severe Adult T cell leukemia/lymphoma and the human retrovirus HTLV-1, as well as a the Kaposi's sarcoma and the human herpesvirus 8. Examples in plants would be the identification of virus complexes associated with many known diseases of perennial crops, for example, grapevine leaf roll disease. Here, we are rather talking about 'emergence of knowledge'. Finally, it may be an already known virus, associated with a known disease, but with an epidemiological profile different from what was known before. We can mention the spread of West Nile virus in the United States in the early 2000s, the arrival of Chikungunya in the American continent in 2013, the dramatic current Ebola outbreak in West Africa, or the world-wide emergence in different temperate crops of Tomato yellow leaf curl and other begomoviruses associated with the spread of highly efficient vector species.

The causes of the emergence or resurgence of such viruses are many and varied [4,5]. The emergence of a new viral associated disease or of a new virus is indeed the result of a sequence of successive steps, sometimes complex, and is often related to the entanglement of several factors: socioeconomic or particular cultural activities, increased mobility of human, animal and plant mobility ('the world is a global village'), human exploitation of the environment as deforestation or increase of agricultural or otherwise human managed land, resulting in loss of biodiversity or ecosystem simplification, disruption of human, animal and plant health systems in

armed conflict, urbanization with development of huge slums of great poverty and basic hygiene, decreased interest in the surveillance and control of infectious diseases, use of unsterile medical equipment as part of therapeutic and/or mass vaccination and, finally, the ability of certain viruses to adapt quickly to a changing environment. This last point may be particularly significant for RNA and small single-stranded DNA viruses. It is crucial to note that all the factors that will increase the density of the human, animal and plants population, the density of vectors and/or reservoirs, and that will promote contact between these three elements, will favor emergence process.

Interspecies transmissions at the origin of the emergence of new viruses are common [6,7]. One can mention for humans many arenaviruses and bunyaviruses having especially rodents as wild reservoirs, but also SIV and STLV retroviruses found naturally in many species of non-human primates. Finally, bats now appear as very important reservoirs of many viruses (Nipah, Hendra, Ebola, Coronaviruses, among others) that have recently emerged or are emerging in humans. Interspecies transmission is also considered as a first step in plant virus emergence. Although it is considered that host jumps are easier among taxonomically related species, reservoirs of emergent plant viruses often have not been identified, which has limited understanding emergence [5]. Interspecies transmission as related to emergence is a new vast field of research promoted, among other factors, by the power of high-throughput sequencing and related bio-informatics methods. After the initial stages of interspecies transmission per se ('spillover') following the encounters between the virus (and its natural reservoir) and the new host, viruses often need to adapt to the new host, resulting in virus loads high enough for transmission and spread in the new host population [7–9]. Dispersion in the new host population often follows new epidemiologic dynamics, and may be attained through various modes of transmission, including for humans sexual, nosocomial, direct contact, and aerosols, or through different vector species or new modes of host propagation (e.g., asexual vs. seed multiplication) in plants.

Some of these means of dissemination in the new host population have been well characterized, allowing efficient controls over inter-human and inter-crop transmission. However, understanding the initial stages of the emergence and the specific mechanisms for inter-species transmission of many viruses continues to be very limited. Microbiological studies, especially in populations at high risk of emergence, are absolutely necessary to get new information about the early events of the emergence process.

Hepatitis E virus (HEV), a small (7.2 kb), non-enveloped single-strand DNA virus that belongs to the *Hepeviridae* family, is the cause of a self-limiting acute hepatitis E endemic in large areas of the world. Nicole Pavio *et al.* report the current data on the zoonotic origin of viral hepatitis E. Such possibility was suggested following the discovery of some animal strains of hepatitis E closely related to human HEV in countries where sporadic cases of hepatitis E were autochthonous. Domestic pigs and wild boars have been now recognized as the main HEV reservoirs. Thus, besides being primarily transmitted via fecal-oral route in human, infection through consumption of undercooked or raw meat and meat products contaminated by HEV has clearly demonstrated that such virus is a foodborne zoonotic pathogen. Direct contact with infected animal reservoirs is also a common source of zoonotic HEV.

Rodents are also important reservoirs for emerging viruses in humans, especially arenaviruses and hantaviruses. All hantaviruses, which belong to the *Bunyaviridae* family, share a negative strand DNA (12 kb). Some Hantaviruses can cause, in specific areas of the world, very severe diseases in humans (as hemorrhagic fever with renal syndrome or pulmonary syndrome). The occasional spillover of hantaviruses from rodents to humans are at the origin of such severe clinical syndromes. In their review, Edward Holmes and Yong-Zhen Zhang emphasize the fact that rodents have long been considered as the primary host of hantaviruses with a classic model of hantavirus evolution thought to reflect a process of virus-rodent co-divergence over a time-scale of millions of years. The recent findings that bats, moles and shrews are also reservoirs of Hantaviruses, associated with relatively frequent cross-species transmission, have greatly challenged such a theory for hantavirus evolution.

Bats are now recognized as a reservoir of a huge variety of viruses, especially RNA viruses, belonging to different families [10]. Such major and recent discoveries raise crucial questions concerning our understanding of the virus-bat interface, which is impacted by intrinsic (especially immunological features) as well as extrinsic factors. Among these viruses, some are zoonotic and responsible of very severe infection in humans including filoviruses-related diseases due to Marburg and Ebola viruses. Sylvain Baize reviews the situation of the current epidemic of Ebola disease that began in West Africa in 2014. Indeed, after being restricted to Central Africa for 35 years, the Ebola virus has suddenly emerged in Guinea in early 2014 and spread rapidly to Liberia and Sierra Leone. Some fruit bats appear to act as the reservoir for Ebola virus. However, the exact origin of the cross-species transmission responsible for the current epidemic in West Africa remains unknown.

Avian influenza viruses have been known to cause human diseases for more than 50 years. Recent outbreaks of such viruses have raised major public health concerns both in

poultry and humans, especially in Asia. Jasper Chan and colleagues emphasize in their review the role of birds in the cross-species transmission and emergence of zoonotic avian viruses. Intrusion of human into natural habitats of wild birds, domestication of wild birds as pets and mostly the increasing poultry consumption by humans have facilitated the emergence and dissemination of avian viruses that can cause zoonosis. Indeed, avian influenza viruses are usually amplified and mixed in the poultry population before cross-species transmission from poultry to humans occurs. Epidemiological, as well as host factors, as the distribution in the human versus. avian respiratory tract, of the different types of viral receptors can greatly modify the magnitude of the emergence process.

Non-human primates are considered to be the likely sources of viruses that infect humans and thus may pose a significant threat to human population. This is well illustrated by some retroviruses. Indeed, the emergence of human immunodeficiency virus type 1 in humans has resulted from several independent interspecies transmissions from different SIVs from chimpanzees and gorillas in the western part of Central Africa, probably during the first part of the last century. Similarly, the origin of most Human T cell Lymphotropic virus type 1 subtypes appears to be linked to interspecies transmission between STLV-1-infected monkeys and humans, followed by variable periods of evolution in the human host. Réjane Rua and Antoine Gessain review here the data on the cross-species transmission and molecular evolution of the simian foamy viruses, another retrovirus that can infect humans and can be considered as a model of restriction of retroviral emergence after spillover.

Although emergence of plant viruses has received less attention than for viruses causing diseases in humans or domestic and wild animals, consequences for food security, for the economy of large sections of society and for ecosystem composition and dynamics, hence, for society at large, can be as serious as for human diseases. Classical hypotheses of plant pathology about ecosystem simplification and disease emergence, which converge with similar hypotheses in animal pathology [5,11], have just recently started to be tested experimentally or empirically. As Marilyn Roossinck and Fernando García-Arenal review here, the few recent studies available point to a role of ecosystem simplification in plant virus emergence. Interestingly, analyses of virus infections in wild plants strongly suggest that the outcome of plant–virus interactions is highly environment-dependent, varying between mutualism and disease emergence. These pioneer studies also underscore the relevance of virus emergence into wild plants from crops, with high potential impacts in wild ecosystems.

The relationship between agriculture and virus emergence has been well analyzed for Rice yellow mottle

virus (RYMV), an RNA virus endemic of Africa with a narrow host range limited to the rice genus. RYMV was first reported in Kenya in 1966 and is presently the cause of the major viral disease of rice throughout sub-Saharan Africa. Denis Fargette and colleagues analyze the role of the transition from traditional to intensive cropping systems, and of crop expansion, in the emergence of RYMV in vast regions from East to West Africa, and in its evolution and diversification under different agroecological conditions.

The processes leading to virus adaptation to a new host have been analyzed in detail in some plant–virus systems. Adrian Gibbs et al. present studies on the evolution of another RNA virus, Turnip mosaic virus (TuMV), from a lineage of monocotyledon-infecting potyviruses to become a world-wide pathogen of brassicas (e.g., cabbage and rape family) with strain specialization on different host species. Their work underlines the relevance of mutations, which are found in different genomic regions and may occur in ephemeral combinations, in host adaptation and specialization.

Geminiviruses are single-stranded DNA viruses that account for a large fraction of recently emerged plant viruses, and that severely constrain agricultural production worldwide. Recombination is inherent to the replication mechanism of these viruses, and its role in geminivirus evolution has been extensively analyzed. Pierre Lefeuvre and Enrique Moriones review recent work on the role of recombination in host switches and host range expansion, as well as in adaptation to different vectors, taking as case studies recently emerged geminiviruses such as Maize streak virus and Tomato yellow leaf curl virus(es).

Although research on plant viruses often lags behind that on human-infecting viruses, experimentation with plants allows to establish genotype–phenotype relationships of viruses on their eukaryotic hosts (as opposed as in cell culture) more easily than with animals. Thus, the distribution of the fitness effects of mutations has been characterized recently in different hosts for some viruses. As Stephanie Bedhomme et al. review, the fitness effects of mutations may differ and even change sign, according to the host, resulting in antagonistic pleiotropy that may hinder virus adaptation to a new host. Also, epistatic interactions between different mutations may result in rugged fitness landscapes that determine the accessibility of evolutionary pathways what, again, will condition host adaptation and, hence, emergence.

Most viruses causing diseases in plants are vectored, mostly by hemipteran insects, and the interactions with the insect that result in transmission have been much studied. Although vectored viruses are more likely to become emerging threats, and emergence cannot occur

without the proper vector, the role of vectors in plant virus emergence remains largely unexplored. This is clear from Alberto Fereres' perspective, in which it is discussed what is known about the role of vectors as drivers of plant virus emergence, and what still needs to be understood.

What will be the future of viral emergence in humans, animals and plants remains unknown [12]. Indeed, any prediction in the field of viral emergence remains very difficult and hazardous, as recently exemplified by Ebola in West Africa and Mers coronavirus in Saudi Arabia or by the continuous emergence of new begomoviruses in plants.

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