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# Editorial overview: Emerging viruses: interspecies transmission Expect the unexpected Adolfo García-Sastre and Juergen A Richt



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Adolfo García-Sastre is professor at the Departments of Microbiology and of Medicine, and Director of the Global Health and Emerging Pathogens Institute at the Icahn School of Medicine at Mount Sinai in New York. He is also principal investigator of the Center for Research in Influenza Pathogenesis, which is an NIH-funded CEIRS (Centers of Excellence in Influenza Research and Surveillance). His research focuses on the molecular pathogenesis of RNA viruses, with special emphasis on viral innate immunity. His laboratory has made numerous contributions in the areas of pathogen sensing, type I interferon antiviral responses, viral immunity, and influenza virus molecular biology, virus-host interactions, vaccines and pathogenesis.

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Juergen Richt is a veterinary microbiologist who has worked with multiple agents of zoonotic potential, including bovine spongiform encephalopathy, animal influenza viruses, Rift Valley Fever virus, Borna virus and other emerging pathogens. He came to the College of Veterinary Medicine at Kansas State University in 2008 as the Regents Distinguished Professor. In 2010, he became Director of the Department of Homeland Security Center of Excellence for Emerging and Zoonotic Animal Diseases (CEEZAD). His An emerging infectious disease is a disease that has newly appeared or whose incidence has increased in the past 20 years and is expected to increase further in the near future [1]. Many emerging diseases are also zoonotic, that is, they spread between animals and people and have an animal reservoir [2]. Emerging and reemerging infectious diseases are a constant threat to worldwide human and animal health [1,2]. Viruses are notorious for encroaching on previously untouched habitats and hosts mainly due to changes to local ecosystems, are transported inconspicuously by travel, and can be accidentally imported via infected carrier hosts before the onset of clinical symptoms. The main drivers of emergence of viral diseases are increasing urbanization, changes in human behavior, and climate change [3]. Humans continue to influence global ecology with our ever-growing demands on land use and intensified farming to feed an increasing population, and our well-developed means of transportation allowing rapid global spread of infectious diseases. However, the successful replication of a viral pathogen in a host is a complex process involving many virus-host interaction processes [4]. Most virus-host interactions developed during the coevolution of the pathogen and the host, therefore, often leading to a host specificity of the virus that impedes interspecies transmissions. Nevertheless, viruses do sporadically cross species barriers into other host populations, including humans. A pathogen must overcome many hurdles to replicate successfully in a new host, which involves multiple stages of replication where each of them may require adaptive molecular changes of the virus [5]. Many of these interspecies transfer events are dead-end, but sometimes viruses adapt to enable continuous spread from animal to animal or human to human. Many emerging viruses with inter-species transmission capacity have RNA genomes and as such have a high rate of mutation which facilitates adaptation to new target animals and humans. For example, influenza A viruses are notorious for their ability to jump to new host species, resulting in the regular appearance of new pandemic influenza viruses in humans, the latest one being the pandemic H1N1 virus in 2009 [6].

This issue of *Current Opinion in Virology* features twelve outstanding reviews focusing on not only the recent emergence of viruses in plants, animals, and humans, but also the factors contributing to their geographic expansion.

The processes that drive cross-species transmission and emergence of viruses in natural systems are diverse and involve a range of ecological, evolutionary, and genetic factors. If rapidly evolving virus populations

work in veterinary microbiology has focused mainly on the animal-human interface, called 'One Health,' that links human medicine, veterinary medicine and the environment. He is committed to the One Health agenda in which the prevention of disease and the protection of the environment requires an innovative interdisciplinary approach. repeatedly experience comparable environmental changes and similar selective pressures, then viruses may exhibit what is known as parallel evolution. The concept of parallel molecular evolution is the independent evolution of the same genotype or phenotype from distinct ancestors. Parallel adaptation occurs in the context of several viral behaviors, including cross-species transmission, drug resistance, and host immune escape, and its existence suggests that at least some aspects of virus evolution and emergence are repeatable and predictable. Gutierrez et al. introduce examples of parallel evolution of viruses and summarize key concepts.

The importance of host range changes to virus emergence are illustrated for plant viruses by McLeish et al. Host range, together with its evolution, is determined by virus intrinsic factors, such as genetic traits determining its fitness in different hosts. Host range is also determined by ecological factors extrinsic to the virus such as the distribution, abundance, and interaction of species. Intrinsic and extrinsic factors, and the complexity of biotic and abiotic interactions, must be considered in order to provide generalizations on patterns of transmission, host range evolution, and disease emergence of plant viruses.

Similarly, there is a continuous emergence of viral diseases in aquaculture, driven by virus factors, animal host factors, environmental factors and/or anthropogenic factors. Aquaculture remains the world's fastest-growing sector producing food of animal origin. The burgeoning international aquaculture expansion and expanding global trade in live aquatic animals and their products have been accompanied by long distance geographical redistribution of aquatic animal species and their viruses. The outcome is a continuous emergence of viral diseases in aquaculture. Frederick Kibenge discusses multiple examples of emerging viruses in aquaculture. The best options for keeping abreast of the continuous emergence of viral diseases in aquaculture are at the farm level where improved disease prevention and control translate into a sustainable industry.

Effective vaccines are the cornerstone of our defenses against many virus infections including influenza virus infections, the latter resulting in approximately 500 000 annual deaths worldwide. A concerted effort is underway to develop a universal influenza vaccine to combat the imminent threat of emerging and re-emerging influenza viruses. Elbahesh et al. address the need for rapid efficacious influenza vaccines that could mitigate the impact of seasonal endemics and future pandemics, and describe the multiple platforms that are under development and/or investigation for broadly effective influenza vaccines.

The measles, mumps, and rubella (MMR) vaccine was licensed in the United States in 1971. MMR contains three live attenuated viral vaccine strains and high coverage with MMR has led to the elimination of endemic measles and rubella in the U.S. and to a substantial reduction in the number of mumps cases. The MMR vaccine, which is used in 121 countries, has an outstanding safety record. Bankamp et al. provide an update on the status of prevention of MMR infections and discuss the unique challenges associated with controlling these viral infections by vaccination.

Human adenoviruses (HAdVs) are prevalent causes of acute respiratory disease (ARD) in military and civilian communities. Over the last 20 years collaborative efforts between U.S. public health, military and academic laboratories have gathered comprehensive data documenting the emergence and re-emergence of specific HAdV types. Kajon et al. describe these new or

reemerging HAdVs. They discuss how detailed molecular characterizations of adenovirus strains are essential to assess the national and global evolution of respiratory HAdVs and to inform decisions regarding antiviral drug and vaccine development and their implementation.

Bats are an important source of emerging viruses and in the last two decades, several high impact zoonotic disease outbreaks have been linked to bat-borne viruses. Many of the emergent bat viruses are highly lethal in livestock and humans such as SARS coronavirus, Hendra virus and Nipah virus; ebolaviruses and MERS coronavirus are also linked to bats. Little is known about the major factors contributing to the risk of bat virus spillover events. Wang and Anderson discuss the concept that bats are potential reservoirs of a large number of known and unknown viruses, many of which could spill over into animal and human populations.

Porcine epidemic diarrhea virus (PEDV), porcine deltacoronavirus (PDCoV), and swine acute diarrhea syndrome-coronavirus (SADS-CoV) are emerging/reemerging coronaviruses of pigs. Sequence analyses suggest that PEDV and SADS-CoV may have originated from bat CoVs and PDCoV from a sparrow CoV, reaffirming the interspecies transmission of CoVs. Wang et al. discuss their origin and potential for intra/interspecies transmission, host receptors for virus replication, antigenic relationships, comparative pathogenesis, and disease control and prevention. Besides strict biosecurity measures, efficacious vaccines are needed for each virus for disease prevention and control.

Hepatitis E virus (HEV) infects both humans and animals, and a steady increase in HEV outbreaks among displaced populations with poor sanitation conditions has recently been seen. Sooryanarain and Meng describe the potential host, environmental, and viral factors that may be associated with the emergence of hepatitis E in humans. The existence of numerous HEV reservoir animals such as pig, deer, and rabbit results in human exposure via direct contact or through consumption of animal products. Contamination of drinking, irrigation, and coastal water by animal and human wastes leads to emergence of cases in industrialized countries and outbreaks in displaced communities with poor sanitation conditions.

Emergence and re-emergence of mosquito-borne arboviruses are of great public and veterinary health importance. Arthropod-borne viruses (arboviruses) are ecologically distinct from many other pathogens because of the involvement of arthropod vectors and animal reservoirs. Huang et al. describe several mosquito-borne arboviruses that have emerged in various geographic regions during the past few decades. Millions of infections have not only changed the epidemiology of previously obscure viruses, but also put the world's public health capability to the test. Newly recognized pathogenic mechanisms and modes of transmission demand the development of new strategies for disease control and treatment.

Crimean-Congo hemorrhagic fever (CCHF) is a virusmediated hemorrhagic disease that occurs over a wide geographic region. The virus is maintained in nature in an endemic tick-vertebrate host-tick cycle. In recent years, a variety of active and passive surveillance studies have improved our knowledge of areas with existing circulation of Crimean-Congo hemorrhagic fever virus (CCHFV). Spengler et al. describe the expansion of CCHFV into new areas through a variety of means, including introduction of infected humans, vectors, and animals. The possible implications of CCHFV emergence are discussed considering the known characteristics of the virus and its natural maintenance and transmission cycles.

It has long been speculated that climate change will lead to expansion of the global range of specific arboviruses and their associated diseases, but recent changes in the global distribution and impacts of both Bluetongue virus (BTV) and epizootic hemorrhagic disease virus (EHDV) infections of ruminants, transmitted by hematophagous midges, have been especially dramatic. MacLachlan et al. discuss how the global range of these viruses and/or their associated diseases has changed remarkably in recent years, most notably with the invasion of Europe by multiple serotypes of BTV since 1998. The unanticipated emergence of BTV and EHDV in several different areas of the world provides a uniquely sobering and unambiguous reminder of the potential consequences of climate change on the distribution and severity of vector-borne diseases.

Collectively, this *Current Opinion in Virology* describes the remarkably diverse mechanisms how viruses from plants, animals and humans emerge/re-emerge and transmit to new host species. Continuous investment in research to develop better diagnostics, antivirals, and vaccines that will mitigate the impact of these diseases is needed. Innovative ways to predict and rapidly diagnose and control novel emerging diseases will be crucial to limit the danger of such pathogens.

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