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Editorial overview: Intraspecies transmission of viruses: Human-to-human transmission
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Infection of humans by viruses from animal hosts — so-called zoonoses — occur relatively frequently around the world. Examples over the last few decades include human infections caused by avian influenza A viruses of hemagglutinin subtypes H5, H6, H7, H9, and H10, swine influenza A viruses of subtypes H1 and H3, Hendra virus and Nipah virus, Severe Acute Respiratory Syndrome (SARS)-coronavirus and Middle East Respiratory Syndrome (MERS)-coronavirus, West-Nile virus, and Ebola virus. Fortunately, most zoonotic infections occur as isolated cases or small clusters, posing little risk to the public at large. However, some zoonotic infections may trigger local or regional outbreaks, spread to humans in various parts of the world, or even result in widespread global outbreaks known as pandemics.

The critical factor determining the ultimate fate of zoonotic infections is the ability of the pathogen to transmit efficiently from human-to-human. Luckily, pandemic spread of zoonoses is an exception rather than the norm. Influenza A virus is such a rare exception on occasion, notorious for its ability to cause pandemics; in the last century alone, four pandemics have occurred when animal-origin influenza virus subtypes entered humans and acquired sustained human-to-human transmissibility in its novel host. Even when the virulence is low — as was the case with the 2009 pandemic — the impact on public health and the economy can be very high with such outbreaks.

Nevertheless, it is important to realize that even for influenza, most zoonotic viruses (e.g. avian subtypes H5, H6, H7, H9, H10) have not started pandemics, as these viruses did not acquire the ability to spread among humans upon numerous zoonotic events. The fact that one virus or virus subtype within a virus genus or family can acquire the ability of sustained human-to-human transmissibility in its novel host. Even when the virulence is low — as was the case with the 2009 pandemic — the impact on public health and the economy can be very high with such outbreaks.

For many virus families, including numerous zoonotic viruses (e.g. lyssaviruses, bunyaviruses) but also for various microorganisms (e.g. *Borrelia burgdorferi*, *Coxiella burnetti*, *Streptococcus suis*), no historical records of pandemic spread are available and for these pathogens, human-to-human transmission currently does not occur or is negligible. In contrast, for several other virus families, there is good historical evidence of their pandemic potential (like the orthomyxoviruses mentioned above), or such potential can be inferred from phylogenetic analyses of contemporary viruses from human and animal hosts. For instance, among the paramyxovirus and pneumovirus families,
Emerging viruses: intraspecies transmission

There are eight members endemic in humans — parainfluenza viruses types 1–4, measles virus, mumps virus, respiratory syncytial virus, human metapneumovirus —, that were all once confined to animal hosts, based on phylogenetic evidence. There are also four endemic coronaviruses — 229E, OC43, HKU1, NL63 — that spread efficiently in humans around the globe. At some point in time, these pathogens must have emerged as pandemic strains. Given this historical evidence or inference, how confident can we be that newly emerging members of the paramyxovirus family such as Hendra virus and Nipah virus would not emerge as the next pandemic strain, especially considering that limited human-to-human transmission has already been observed? And would it be possible that novel animal-origin coronavirus like SARS-coronavirus and MERS-coronavirus would become similarly transmissible as endemic human coronaviruses?

Unfortunately, there are still major gaps in our knowledge of (the efficiency of) various transmission routes of both endemic and zoonotic pathogens and the host and pathogen determinants of transmission. We do know that human-to-human transmission of zoonotic and endemic pathogens may follow very distinct routes, which are not necessarily mutually exclusive; via aerosols or respiratory droplets, via direct or indirect contact, via the fecal-oral or foodborne route, or via arthropod vectors as intermediate hosts or carriers of the pathogens. Understanding the route and efficiency of transmission during outbreaks with zoonotic pathogens is of crucial importance to adopt specific early intervention strategies to stop outbreaks or reduce their impact. As an example, the prevention of direct contact between new cases of human infection and people in their surroundings was sufficient to stop the direct contact between new cases of human infection and reduce their impact. As an example, the prevention of specific early intervention strategies to stop outbreaks or with zoonotic pathogens is of crucial importance to adopt route and efficiency of transmission during outbreaks hosts or carriers of the pathogens. Understanding the foodborne route, or via arthropod vectors as intermediate droplets, via direct or indirect contact, via the fecal-oral or necessarily mutually exclusive; via aerosols or respiratory droplets, via direct and indirect contact, and via arthropod vectors. In this issue of Current Opinion in Virology, the summaries of the discussions from the ANTIGONE expert meeting are described. De Graaf et al. describe pathogen, host, and environmental factors that are important for sustained human-to-human transmission of fecal-oral and foodborne transmitted zoonotic pathogens. Herfst et al. discuss a framework of drivers that facilitate human-to-human transmission of pathogens that transmit via the air, in the form of aerosol or respiratory droplets. Martina et al. describe the complex interactions between pathogens, arthropod vectors and humans that determine exclusive enzootic (sylvatic) cycles versus urban (human) cycles for arthropod-borne pathogens. Finally, Richard et al. describe host, pathogen, and environmental factor that determine human-to-human transmissibility via skin contact, sexual contact and respiratory contact and contact via multiple routes.

In another four chapters, individual viruses that represent the same transmission routes are discussed for various newly emerging and re-merging viral diseases. Vasilakis and Weaver discuss the spread of the Zika virus through mosquitoes in various parts of the world, in comparison to related flaviviruses like West Nile virus, dengue virus, Japanese encephalitis virus, and yellow fever virus. Lawrence et al. focussed on the 2014–2015 Ebola virus outbreaks in West Africa, and lessons learned about human-to-human transmission via contact and the potential molecular basis of transmission and host adaptation. Clayton focussed on the transmission of Nipah virus as an example of an emerging zoonotic virus from the paramyxovirus family that includes members that are transmitted via the air in the form of either aerosols or respiratory droplets or by direct or indirect (respiratory) contact. Finally, De Graaf et al. discussed norovirus transmission via the fecal-oral and foodborne route, which represents an increasingly recognized problem around the globe.

Collectively, these contributions provide an excellent summary of the current state of knowledge of proximal drivers of zoonotic virus transmission as determined by the pathogens, their host(s), and the transmission interfaces (e.g. environment, surfaces, air, and arthropods) as well as more distal drivers that can influence virus transmission on regional or global scales. Commonalities between viruses and non-viral emerging infections are also described, because the virology field can learn valuable lessons from the microbiology and parasitology fields, and vice versa. Although there are many unique features for each route of pathogen transmission, common features that determine efficient human-to-human transmission
are also described. Some of these features that contribute to efficient human-to-human transmission are very obvious, such as a high pathogen load in human excreta, low infectious dose in humans, high relative stability in the interface (air, surface, and environment), specific tissue tropism, among others. At the same time, it is sobering to see how little we know even about these very basic features. Therefore, each of the papers also identified major knowledge gaps that require future research in order to better control emerging zoonotic pathogens. Should we indeed aim to improve our ability to model and predict potential pandemics of zoonotic origin and to provide input to the development of more effective and timely prevention and control measures, increased knowledge about virus transmission and host, virus, and environmental determinants thereof is urgently needed. Such additional research will possibly lead to novel pharmaceutical and non-pharmaceutical early intervention strategies to combat emerging zoonotic infections with human-to-human transmission potential.