

History is repeating itself: Probable zoonotic spillover as the cause of the 2019 novel Coronavirus Epidemic

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Zoonotic diseases have shaped the life of human beings during centuries. Particularly the dynamics and changes over time make the difference in the occurrence, emergence and re-emergence of such conditions. Pathogen transmission from a vertebrate animal to a human, also known as zoonotic spillover, represents a global public health burden, which while associated with multiple outbreaks, still remains a poorly understood phenomenon [1]. Zoonotic spillover requires a blend of several factors to ignite, including the ecological, epidemiological and behavioral determinants of pathogen exposure, and the within-human intrinsic factors that affect susceptibility to infection, as well as nutritional and cultural factors, associated with foodborne zoonotic diseases [1, 2].

Coronaviruses (CoV) have been previously on the spotlight of this discussion [3, 4]. They can infect the respiratory, gastrointestinal, hepatic and central nervous system tracts of man, cattle, birds, bats, rodents and various other wild animals (Figure 1) [5, 6]. Coronaviruses, like influenza viruses, circulate in nature in various animal species. Alpha-coronaviruses and beta-coronaviruses can infect mammals and gamma-coronaviruses and delta-coronaviruses tend to infect birds, but some of them can also be transmitted to mammals [5]. These zoonotic viruses, were not considered to be highly pathogenic to humans until the outbreak of severe acute respiratory syndrome (SARS-CoV) in 2002 and 2003 in Guangdong province, China, as the coronaviruses that circulated before that time in humans mostly caused mild infections in immunocompetent people. Ten years after SARS, another highly pathogenic coronavirus, Middle East respiratory syndrome coronavirus (MERS-CoV) emerged in Middle Eastern countries [7]. In both cases, wild animals, such as bats, were incriminated as natural host of these viruses, which

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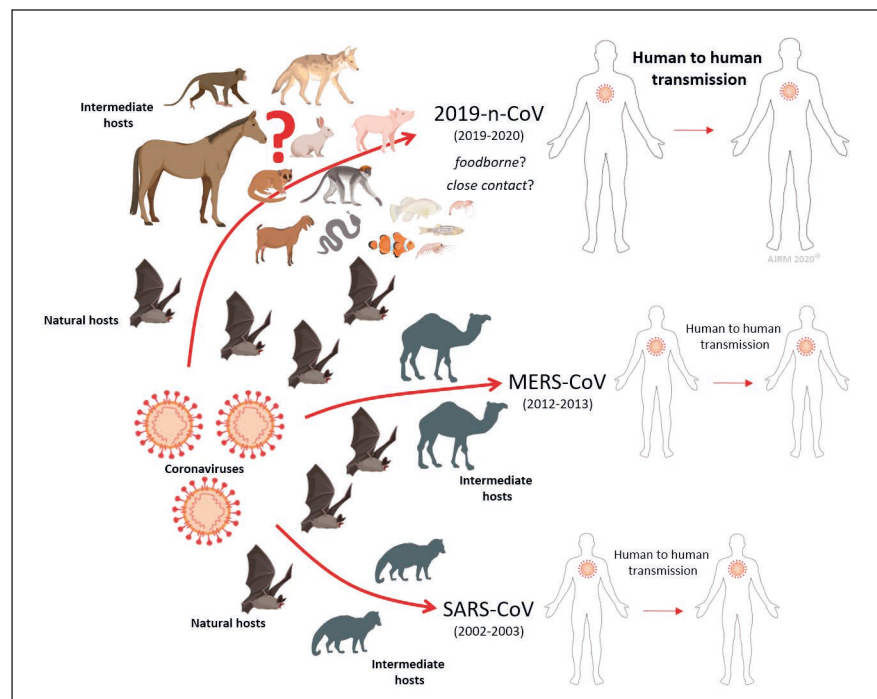
have also spilled over to humans, using as main intermediate hosts, civets and camels, respectively (Figure 1).

Although still preliminary, current data suggest that bats are the most probable initial source of the current 2019 novel CoV (2019nCoV) outbreak, that begun on December 2019 in Wuhan, China, apparently spreading from a “wet market” to multiple cities and provinces in China [5, 6, 8]. In addition, the virus has crossed borders affecting now three other continents through international travel [8-10]. In that market, local health authorities (Figure 1) initially reported exposure to wild animals as well as seafood. However, intermediate hosts are still under scrutiny, deserving more detailed field studies assessing infection and seroprevalence against this 2019nCoV (Figure 1). Transmission modes also require specific studies and dedicated attention. As it has been suggested, not only it is the likelihood of common close contacts interacting with animals - a not uncommon scenario in such type of markets - but also the possibility of foodborne transmission from animal derived matter which has recently been highlighted to influence the current epidemic (Figure 1). Given that 2019nCoV spillover events

are not resulting in self-limited cases, as occurs for example, with rabies, anthrax, histoplasmosis or hidatidosis, which usually result in no further human-to-human transmission; humans do appear to be intimately linked as key actors of the current outbreak. In support of this, is the ever-increasing trend of cases suggesting the virus is being able to be transmitted by humans, produce secondary cases, and establish limited chains of transmission. This may lead in an adaptation to human hosts and their potential role as new stable reservoirs. These are some of the initial thoughts and questions deriving from the emerging 2019nCoV, that prompt establishing comparisons with SARS-CoV and MERS-CoV (Figure 1), to other beta-coronaviruses that share similar animal natural and intermediate hosts as well the possibility to establish human-to-human transmission.

A similar scenario is also seen in Asia, with Nipah and Hendra viruses carried by bats which affect pigs, horses and humans, while exhibiting interspecies transmission and human to human transmission, albeit with lesser spreading capacity [11]. Paramyxoviruses, filoviruses (such as Ebola), reoviruses, and lyssaviruses (such as

Figure 1 - Potential animal origins of human coronaviruses.



rabies), among other virus, can also originate from other species of Chiroptera [8-12]. Even dengue and other arboviruses, have been reported to be carried by bats [13]. Zoonotic spillover from flying mammals is especially important in Asia, but has also been reported in other continents [12, 13]. In addition to human-to-human transmission, which would be of utmost relevance particularly in imported cases at the origin of the outbreak, food-borne transmission should be also be considered a latent possibility (Figure 1).

An important frontier in research on zoonotic spillover is to understand the functional and quantitative links among the determinants of spillover, which are multiple and diverse and not necessarily constantly present in the required spatio-temporal overlap between them and human exposure in susceptible hosts, to make possible these events [1]. If asymptomatic infections occurred, as has been suggested, this would add more complexity to the understanding of the transmission dynamics in this context. This epidemic of 2019nCoV, already reaching more than 8,200 cases to date (end of January 2020) (>90% in China), will not be the last one linked to zoonotic spillover events. Yet, it should be seen as a good opportunity to assess again the impact of these phenomena and the importance to understand needs for reaching a One Health approach, and the relevance of interactions between environmental, animal and human health as key element for many emerging infectious diseases.

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