## Coronavirus from Wuhan (2019\_nCoV) in context: Lessons Learned?

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Corresponding author\* <u>Professor R.A. Kock Department Pathobiology and Population Science, Royal Veterinary</u> College, Hawkshead Lane, North Mymms, Hatfield, UK Rkock@rvc.ac.uk 01707666396 The emergence of a new coronavirus (CoV)(2019 nCoV) in Wuhan affects a sense of Déjà vu with the Severe Acute Respiratory Syndrome coronavirus (SARS-CoV) epidemic in 2003. Coronaviruses are enveloped, positivestranded RNA viruses of mammals and birds. The virus has high mutation and gene recombination rates making it ideal for pathogen evolution (1). In humans, CoV is usually associated with mild disease, the common cold. Previous emerging novel CoVs, such as SARS-CoV and Middle East Respiratory Syndrome coronavirus (MERS-CoV) - which emerged in the Middle East in 2012- were associated with severe and sometimes fatal disease. MERS-CoV was less pathogenic than SARS-CoV, with the most severe infections mainly in those with underlying illnesses. Clinically and epidemiologically, the contemporary 2019\_nCoV in China seems to resemble SARS-CoV. The genome of 2019 nCoV also appears most closely related to SARS-CoV and related bat CoVs (2). The infection has now spread widely?, with phylogenetic analysis of the emerging viruses suggesting an initial single locus zoonotic spill-over event in November 2019 (10) and subsequent human-to-human transmission. The SARS epidemic in 2003 was followed soon after by avian influenza H5N1 in 2006, centred on the Asian continent and Middle East. Other surprising viral zoonoses that have caused serious disease include Nipah encephalitic virus in pigs and humans in South East and South Asia 1999-2014, and large-scale Ebola Virus (EBOV) epidemics in 2014-16 and 2018-19 in West and Central Africa. Taken together, these events ring alarm bells about disease emergence in the 21st Century and the importance of human diseases originating from indiscriminate contacts with infected animals.

There is an increasing focus on the human-animal-environment disease interface, now encompassed in the One Health concept. Mortalities, Disability Adjusted Life Years (DALYS) and billions of dollars of economic losses from these infections demand action and investment in prevention to face novel challenges to human and animal health. Research has ensured the nature and drivers of cross-species viral "jumps" are better understood but also elusive in the detail. No reservoir population of bats for SARS and MERS CoV or EBOV have been definitively identified, despite considerable searching possibly due to source virus circulating in relatively small and isolated populations. Forensic examination has clarified the human infection sources and multi-species involvement in these diseases, some species confirmed as competent hosts (e.g. camel for MERS CoV (3), bridge (or amplifying) hosts (e.g. pigs for Nipah, non-human primates for EBOV (4) or dead-end hosts. The critical checkpoint is the "jump" and "bridging" of the viruses to humans. This occurs most frequently through the animalbased food system. In the case of SARS, the existence of markets with live and dead animals of wild and domestic origins, mixed up with human population, were the crucible for virus evolution and emergence. Once the viruses' functional proteins enabled cell entry in civets (Paguma larvata) and racoon dogs (Nyctereutes procyonoides), the bridge was established and it was only a matter of time before the jump to humans occurred (5). Sequence comparison of civet viruses suggested evolution was ongoing and this was further supported by high seroprevalence of antibodies against SARS-CoV amongst civet sellers, suggesting previous cross-species transmission events without necessarily human to human transmission (6,7). Similarly, early EBOV was mostly associated with bush meat and its consumption in Africa, Nipah is associated with date palm sap, fruit and domestic pig farms, MERS is associated with camel livestock industry and H5N1 arose from viral evolution in domestic and wild birds, to ultimately bring all these cases to humans. The 2019\_nCoV is another virus in the pipeline which originated from contact with animals in this case a seafood and animal market in Wuhan, China.

Inevitably, the health sectors are primarily reactive to these events, acting to save lives as well as undertake surveillance and control. The drama and panic typically fade into history with the substantial costs being absorbed by ordinary people, international financial systems and tax bases and life goes on as normal, but not quite. The frequency, severity and financial impact of these events is growing and the world can no longer afford to just wait and see. Especially as prevention of these threats is in theory relatively simple and where addressed has resulted in a cessation of risk. The best example being Nipah virus, where control over locating pig farms and separating them from fruit agriculture and by the same measure, fruit bats, has significantly reduced the potential for spill over. Bats have always and will always have viral populations and despite close association with humans for millennia, have not resulted in pandemics until recent times.

In conclusion, have we learned lessons? Yes and no. Yes, that these events are of Global Public Health and economic importance and need collective societal response and no, Governments and Civil Society are not heeding these warnings as the 2019\_nCoV attests to (8). Concerns have been repeatedly raised and voiced since the idea of One World One Health was first expressed around the Millennium (9). What we need to learn and shout from the rooftops is that the domestic and captive wildlife zoonotic or agricultural bridging of novel pathogens needs urgent attention, along with attention to the human insatiable appetite for meat. This is relatively easily achieved for CoV threats. Significantly reducing the trade of risky species of wild caught animals for food or other purposes, and a culturally sensitive ban on the sale of these animals in wet markets.

Vaccines and therapeutic alternatives might be possible and are needed but they are a response, as the emerging strain is unpredictable and a vaccine is unlikely to prevent the initial events. In some parts of Africa, prevention of EBOV and future CoV threats require shifts in food habits, a transition from bush meat being a cultural norm or primary source of protein and by discouraging agricultural development that brings bats into increased contact with humans or their livestock. In the Middle East, re-evaluating and improving infection prevention and control measures for camel farms, a recent introduction coincident with the emergence of MERS CoV would be a positive step forward.

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