Perspective

SARS-CoV-2 and biomimetics: What saves the planet will save our health

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The underdeveloped opportunity to use the broad awareness of the diversity of animal life and comparative physiology (i.e. biomimetics) as nature´s own roadmap to provide novel insights and solutions from burden of life style diseases has recently been discussed (1-4). As human health, environmental changes and animal welfare are closely related (i.e. the "one health" or "planetary health" approach), such studies require close interdisciplinary collaboration, including medical doctors, veterinarians, zoologists, climate researchers, ecologists, biologists and anthropologists (5). The ongoing coronavirus 2019 (Covid-19) pandemic is an excellent example of the urgent need for global interdisciplinary collaboration and planetary health research, integrating human and animal health with environmental sustainability and ecosystem health. To begin with, it is worth noting that there is simply nothing uniquely Chinese about the Covid-19 outbreak. The explanations for why so many epidemics seem to arise in China may not only be cultural, but also a matter of its current economic geography paired with the close interface between wildlife, livestock and humans (6). This is abundantly clear if we compare China to the US, or Europe, when the latter were hubs of global production and mass industrial employment. The geography of blame, naming a germ after a country or ethnic group, has often been a symbol of helplessness during previous pandemics, detracting from the global aspect and unfairly labelling a country or ethnic group as being solely responsible. Ironically, the 'Spanish flu' pandemic of 1918, likely originated from a farm community in south-western Kansas (7). While previous pandemics were mainly linked to crises resulting from wars, modern pandemics may be linked to a crisis based on environmental pollution, exploitation of the natural world, wildlife abuse and subsequent cumulative consequences on human health.

The transformative impacts of the Covid-19 pandemic on human welfare, socioeconomic and political structures are enormous. The planet is already experiencing an extraordinary loss of biodiversity (an ongoing sixth mass extinction) linked to human activity: illegal wildlife trade, habitat destruction, pollution, global warming, and over-consumption of a sugar-rich high-protein diet, superimposed on population growth (8). As gut microbiota regulate immune defences against respiratory tract influenza A infection (9), the role of the foodome in the severity of respiratory involvement during Covid-19 infection requires attention. Furthermore, a "normal" food supply system has developed as factory farming, with massive numbers of livestock and poultry kept at high density, creating an environment ripe for the genesis of new viral diseases (10). Climate change can impact both vector-borne diseases, and even the evolution and progression of viruses, such as influenza A (11), while atmospheric pollution, due to small airborne particles, may also enhance spread of SARS-CoV2 (12). Thus, anthropogenic environmental changes are redefining the nature of 21st century pathologies (8), and pandemics, such as Covid-19, may not be an exception in years to come.

It is estimated that three out of four new infectious diseases have emerged from human-animal contact in the US alone (13) and zoonoses are responsible for >2 billion cases of human illness and over 2 million human deaths each year (14). While the origin of the Covid-19 virus is still not certain, most studies suggest it originated in bats and infected people were exposed via the sale of wild meat at a wet market in Wuhan, China (15). Indeed, bats are believed to be one of the more common wildlife species that carry diseases with zoonotic disease potential for domestic animals and humans. Their special flight physiology, with a high body-temperature may have perfectly adapted viruses (16) (17) to survive a febrile status in infected human patients. Over the last century human activity has destroyed natural habitats and wildlife to develop more anthropocentric landscapes (6), providing the basis for emerging disease 'hotspots' and the spill-over of new viral zoonoses (8). Exploitation of wildlife through hunting and trade facilitates close contact between wildlife and humans and has increased opportunities for animal–human interactions and facilitated zoonotic disease transmission (18). In bats stressed by entrapment, deforestation, infections and climate change, spillover of the virus is more likely to occur. Indeed, intestines of virus-infected bats that were also co-infected with fungus, contained on average 60-fold more corona-virus RNA than bats with virus alone (19). Since SARS-CoV-2 recently was shown to infect intestinal cells of bats and the virus replicate in human intestinal organoids (20) there is a possibility of transmission to humans by contact with bat faeces, without need for an intermediate vector.

We contend that lessons from nature (biomimetics) provide solutions for understanding, treating and preventing emergent diseases. Biomimetic solutions, generated from insights into the natural world may provide ingenious solutions not only for chronic non-communicable lifestyle-related diseases (1), but also for zoonotic diseases. It seems likely that the major therapeutic dilemma in severe Covid-19 infection (the combination of an inappropriate inflammatory response (cytokine storm) with reduced innate antiviral defence mechanisms (21)) has been solved in bats. Studies of bats actually may help provide a biomimetic solution, which builds on evolution through natural selection, for ideal solutions to conquer diseases and survival in extreme environments. Although there is a relatively large diversity of zoonotic viruses in bats, viral diseases in bats are mild (17). As their immune systems are poorly understood, detailed studies of bats may provide important clues for prevention and novel treatments (22). SARS-CoV-2 infection is characterized by a lack of robust type I/III interferon (IFN) signatures from infected cell lines (23) and patients with severe Covid-19 demonstrate a profoundly impaired IFN-I response as compared to mild or moderate cases (24). In Covid-19 infection, ORF3b - one of the viral proteins which is dominantly expressed - is a potent interferon antagonist (25). Coronaviruses are known to have multiple other mechanisms for evasion of the host immune response. Bats share many of the immunological features of other mammals but an understanding of the unique host viral interaction in bats may help understand the

pathogenesis of emerging zoonoses in humans. The long co-evolutionary history of bats and viruses has led to immunological adaptation of bats and the resident viruses allowing for apathogenic infection. Some of these unique immunological differences in bats that have been studied include constitutive expression of interferon signalling molecules, impaired formation of inflammasomes, absence of a number of NK-cell receptors, lack of somatic hypermutation in immunoglobulin heavy chain genes, and an altered interferon stimulated gene profile, which is not associated with an acute inflammatory response (26). Further understanding of evolutionary adaptation of both host and symbiont/pathogen may provide insights into both pathophysiology and potential therapeutic pathways.

The current SARS-CoV2 pandemic is the best proof of the necessity for recreation of sustainable human and ecosystem health (27), and for an increased protection of wildlife in its natural and undisturbed habitat, away from close human contact. A biomimetic approach would allow us to learn from animals that through evolution have managed to regulate viral persistence, and to develop novel anti-viral drugs based on the planet's own botanical medicine cabinet. A biomimetic initiative needs prompt action as loss of species diversity, habitat destruction, and pollution will prevent this opportunity to learn from the biochemical wonders of nature.

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