



Perspective on Wuhan Viral Pneumonia

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Coronaviruses are enveloped, non-segmented, positive-sense single-stranded RNA virus. The coronavirus subfamily is genotypically and serologically divided into four genera, the α , β , γ , and δ coronaviruses. There are nearly 30 recognized CoVs that infect humans, mammals, fowl, and other animals. Human CoV infections are caused by α - and β -CoVs (1).

On December 31, 2019, Chinese health authorities reported mysterious cases of pneumonia which was presumably related to the Hunan Seafood Market in the city of Wuhan, Hubei province (2). A week later, Chinese acknowledged the causative agent was a novel coronavirus, 2019-nCoV (3). Most recently, researchers at South China Agricultural University who tested more than 1000 samples from wild animals, reported a 99% match between the genome sequences of a virus found in pangolins and those in 2019-nCoV infected patients - such observation needs to be further validated, and therefore, trans animal transmission studies necessitate more studies. To unlock the puzzle, Chinese scientists continued their investigation of such an unusual viral pneumonia outbreak and probed into its genome characteristics (4). Chinese health authorities were the first to post the full genome of the 2019-nCoV in GenBank. The genome sequences obtained from the nine infected patients (a cohort of 10 patients) were markedly similar and exhibited about 99% sequence homology within the patient cohort and was closely related (with 88% identity) to two bat-derived

severe acute respiratory syndrome (SARS)-like coronaviruses. Analysis of the clinical specimens also showed the virus belongs to a subfamily of betacoronavirus (4). Further investigation revealed 2019-nCoV share same receptor with SARS-CoV, Angiotensin-converting enzyme-II (5). Although the sample size of this study was small and did not include clinical data on disease severity and stage, it provided background information on molecular biology of the virus to possibly investigate selective experimental anti-ACE-II therapies tailored for 2019-nCoV infections. The early transmission dynamics of 2019-nCoV has been reported (6). From a pool of 425 confirmed laboratory cases at the early stage of pneumonia who were linked to the Huanan Seafood Wholesale Market, presumably the epidemic doubled in size every 7.4 days in the early stage of the disease. The median age of this study was 59 years and 56% were male, although this investigation did not specify any co-morbid condition. However, this study established human-to-human transmission among close contacts and has emphasized on the role of public health in contact tracing. The role of contact tracing in a situation like 2019-nCoV epidemic is highly critical in rapid identification of individuals who may have been exposed to the virus. Although asymptomatic transmission has been reported in Germany (7), much questions remain about the biology of asymptomatic carriers. While more robust evidence of asymptomatic transmission is needed, if validated among the global scientific communities, such finding will pose a significant challenge to prevent the transmission and to

contain the virus. However, on a positive note, it may help resolve the unknown transmission factor(s) about some of the uncertainties as to how the virus spreads.

It is now evident 2019-nCoV is the third epidemic of the coronavirus family in the past decades which has crossed species infecting vulnerable and at-risk individuals. Much of the investigational work has been attributed to the infected patients, and to date, there is no published papers on human handlers of the animals serving as the likely source of the virus. What has been documented so far is like outbreaks caused by SARS-CoV and MERS-Cov, this novel outbreak causes severe respiratory syndrome indicating a virulent capacity of the virus causing viral pneumonia especially in elderly and those with comorbid conditions with an average fatality rate of almost 3% in Hubei province (8). This fatality rate is subject to change until all infected patients are recovered. Given the current fatality rate of 3%, 2019-nCov appear to be less virulent than SARS-CoV (aprox. 10%) and significantly less virulent than MERS-CoV (aprox. 40%). Understanding the virulent factor in an error-prone RNA-dependent RNA polymerase virus such as 2019-nCoV is highly important in order to access the efficacy viral transmission as mutations and recombination of viral polymerase frequently occurs (9). It has been reported in critically ill patients who present with acute respiratory distress syndrome, there is reduction in peripheral blood lymphocytes (10). This finding in the context of adaptive immune response should be fully investigated since lymphocytes appear to be responsible in immunopathogenic events for Wuhan viral pneumonia. Particularly, the evidence of viral presence in peripheral lymph organ may provide insight for further understanding of immunopathogenesis of 2019-nCoV, let alone it provides better understanding of the pathogenic process in lung microenvironment.

To end the mystery of 2019-nCov, international research exchanges are urgently needed to coherently address so many questions about the biological, immunological and pathological characteristics of this novel virus. It appears the transmission of 2019-nCoV occurs fast by the means of miniscule contact droplets possibly via airborne transmission. The key question is correct and definitive identification of the zoonic origin the 2019-nCov reservoir as public health, economic and social consequences (national and international) are becoming more concerning. Measures to prevent or reduce transmission should be implemented in populations at risk applying the principles of public health prevention and control with emphasis on contact tracing and surveillance issues. The case characteristics should continue to be monitored and investigated to determine likely changes in epidemiology. In addition, deeper investigation of the specific

immune response to acute infection will shed more lights on pulmonary and systemic inflammatory responses associated with 2019-nCoV. The immune response to coronaviruses in general is presumed to be triggered by the innate immune system when it recognizes the corona family viruses (1). More studies are needed to delineate characteristic immune response to 2019-nCov particularly with respect person-to-person transmission of the virus. With regards to the “super-spreaders” of the virus within the healthcare facility centers reported (11), this phenomenon currently is not fully understood; however, such observations were previously made for considerable transmission of SARS and MERS inside hospitals. The super-spreaders underscore that in endemic region patients presenting with non-respiratory symptoms such as diarrhea, nausea and vomiting should be evaluated for possible Wuhan viral pneumonia. Unlocking the mysteries of 2019-nCov also necessitate stakeholders of various agencies collaborate and communicate efficiently through transparency, openness, and most importantly, unbiased data sharing – One Health concept. Within the framework of One Health, the global health community must ensure data regarding all aspects of 2019-nCov are accurate and reliable to address international public health concerns. Although is too early to fully understand the impact of 2019-nCoV especially the number of confirmed cases and fatalities are alarmingly increasing, genome investigation of this virus will provide clues to disease prevention (vaccine) and novel therapies designed to target essential structural and replicative genes.

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