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LETTER TO THE EDITOR

PEDIATRIC PULMONOLOGY WILEY

Applying lessons from influenza pandemics to the COVID-19 pandemic

To the Editor,

Worldwide, there has been a proliferation of literature on the coronavirus disease 2019 (COVID-19) pandemic. The April 2021 issue of a local Medical Journal published seven editorials, three original articles, and one review article around the subject matter of the COVID-19 pandemic. Meanwhile, as we enter the second summer of the pandemic, clinicians, politicians, and citizens alike continue to debate the vaccines roll-out strategy for our city.[1]

The first editorial "*Can COVID-19 vaccines stop the pandemic?*" opined it is currently apparent that the pandemic has not been stopped despite the availability of vaccines, and many nations still remain in continual lockdowns.[2] In another editorial on the same subject, it is believed vaccine hesitancy should be addressed by an organized and concerted effort championed by various stakeholders in the community.[3] This campaign should include more intensive education, provision of more evidence-based facts, and public health interventions to enhance vaccine uptake. Exemption from travel bans, issuance of vaccination certificates, visitation rights at healthcare facilities, and incentives offered by the commercial sector to the employees are some of the potential strategies that could incentivize the general population to take up the vaccine, and this requires collaborative initiatives driven by policymakers.[4] A third editorial opined that the lessons learned from the severe acute respiratory syndrome (SARS) outbreak in 2003 have successfully helped to limit the spread of COVID-19 within Hong Kong, particularly the implementation of robust surveillance measures, social distancing, and universal mask-wearing.[5]

Idealistically, from a public health perspective, a small city like Hong Kong should well have steered clear of COVID-19 if full lockdown could be maintained. However, the COVID-19 pandemic is still rampant across nations and cities including Japan, India, France, and Taiwan. The global effort against the COVID-19 pandemic will require cooperation among governments, international organizations, research institutes, scientists, clinicians, and most important of all, individual citizens. The management framework should encompass several essential domains, including overall coordination, community engagement and risk communication, measurements of public health, health services and case management, prevention and control of pandemic, as well as surveillance mechanisms which are all important considerations for developing tailored non-pharmaceutical interventions for individual countries.[6]

These editorials prompt us to compare and contrast experiences between the current COVID-19 pandemic and past influenza pandemics (Table 1).[7,8] By studying and learning from the past, we could glean valuable insights to tackle the current pandemic. Both diseases are caused by respiratory viruses, but the transmissibility and severity profiles are very different. In comparison with influenza, COVID-19 tends to be less symptomatic or even asymptomatic in a considerable proportion of patients; and carriers are more difficult to detect clinically. Preventive strategies, social distancing, and personal hygiene practices are therefore important measures to limit the spread of many respiratory viruses including influenza, respiratory syncytial virus, as well as COVID-19. Prolonged cycles of continual lockdowns are likely of limited efficacy to eliminate the pandemic, and it comes with tremendous economic and psychosocial consequences. With emerging new strains and variants, both viruses are likely to be ineradicable. Vaccines have variable efficacies, and the need for regular revaccination might come with additional challenges.[9] The only difference may be that there are specific antiviral drugs for influenza but only a limited arsenal of pharmaceutical treatments with proven efficacy for severe COVID-19. One of the profound lessons from past influenza pandemics is an urgent need to develop readily available and affordable antiviral drugs and pharmaceutical treatments that can reduce mortality and morbidity in COVID-19 patients.

Meanwhile, the latest in vaccine development is an oral COVID-19 vaccine being prepared to enter phase 1 clinical trials. Borrowing the concept of the annual flu shot, ease of administration of the oral COVID-19 vaccine is considered critical to accelerate inoculation rates. The time and cost of production is also potentially much cheaper than the COVID-19 vaccines currently available in the market. Until then, many will continue to debate which vaccine(s) may be superior while the society will need to continue to live with nonpharmaceutical interventions including continual lockdowns, social distancing, and universal masked wearing.

TABLE 1 Influenza versus COVID-19 pandemics[9–11]

	Influenza	COVID-19	Similarities & differences
Epidemiology	• 5 in the last 140 years, with the 1918 flu pandemic being the most severe	• Repeated zoonoses (e.g., SARS and MERS and now COVID-19) as well as annual circulation of seasonal coronaviruses	• Both are "flu" or respiratory viruses
	• Estimated over 50–100 million deaths	• COVID-19 as of April 2021: 145+ million cases confirmed, with 3.08+ million deaths	• Similar mortality
	• Under a million deaths in 2009 swine flu pandemic	• Global death-to-case ratio is 2.1%	• Silent and asymptomatic cases in COVID-19
	• Pandemics occur irregularly	• Aerosol + airborne transmission	• Prolonged global lockdown in COVID-19
	• Aerosol transmission	• R_0 = 2–3	
	• R_0 = 1–2		
Biology of organisms	• Enveloped single-stranded RNA virus	• Enveloped single-stranded RNA virus	• Both are enveloped single-stranded RNA virus
	• Orthomyxoviridae family	• Coronaviridae family	• Circulate in non-human reservoir
	• Majority by influenza A e.g., H1N1, H2N2, H3N2, H5N1	• SARS-CoV-2	
	• Associated with antigenic shift	• Possible association with antigenic drift	
New strains/variants	• New strains transmitted to humans from another animal species (e.g., pigs, chickens, and ducks)	• New variants: B.1.1.7, P.1, B.1.351, B.1.427, B.1.429	• No life-long immunity • Need revaccination
Pathophysiology of their clinical presentation	• Haemagglutinin protein of the influenza virus binds to the sialosaccharides of the respiratory epithelial cells	• Spike protein of the SARS-CoV-2 virus binds to the angiotensin-converting enzyme 2 of the olfactory and respiratory epithelial cells	• Different viral surface protein processing
	• Viral replication within the nucleus	• Extrapulmonary cells can also be affected e.g., intestinal epithelial cells, endothelial cells and renal parenchymal cells	• Different site of viral replication
		• Viral replication in the cytoplasm	
Diagnosis	• RT-PCR test to detect influenza RNA from upper respiratory tract samples e.g., nasopharyngeal swab, nasopharyngeal aspirate	• RT-PCR test to detect SARS-CoV-2 RNA from upper respiratory tract samples e.g., nasopharyngeal swab, nasopharyngeal aspirate, deep throat saliva	• Serologic tests are not used to diagnose influenza
		• Serologic test to detect antibodies to SARS-CoV-2 to identify previous or late infections	
Wave nature	• 3–4 waves of increasing lethality	• In waves with containment and mitigation stages	• Similar
	• Mortality was greater at the beginning of the wave		
Variable mortality	• ~5%	• Overall 2%–3%	• Probably similar
	• Low mortality in children	• Low mortality, asymptomatic and silent carriers in children	• Higher in SARS and MERS
Prevention strategies	• Culling and vaccinating livestock	• Staying at home, universal mask-wearing, avoiding crowded places, social distancing, ventilating indoor spaces, washing hands with soap and	• Similar strategies

TABLE 1 (Continued)

	Influenza	COVID-19	Similarities & differences
		water often and for at least 20 s, practising good respiratory hygiene, and avoiding touching the eyes, nose, or mouth with unwashed hands	
	• Vaccinating poultry workers against common flu	• Vigilant contact tracing	• Prolonged lockdown in COVID-19 with some success but at extremely high economic and psychosocial costs
	• Limiting travel in pandemic areas	• Travel restrictions and quarantine measures	
	• Strategies to slow down a pandemic include public response measures, social distancing, respiratory hygiene, handwashing hygiene, masks, and risk communication	• Regular COVID-19 testing	
Antiviral drugs	• Oseltamivir (Tamiflu) and zanamivir (Relenza)	• No specific, effective antiviral treatment or cure (lopinavir/ritonavir or remdesivir has no good evidence)	• Antiviral for influenza
	• Adamantanes (amantadine and rimantadine)	• Glucocorticoid (dexamethasone) effective for severe cases	• Corticosteroid for severe COVID-19 cases
		• Noninvasive & invasive ventilation as respiratory support	
Pandemic vaccines	• Several	• Over 13 vaccines	• Vaccines but variable efficacies and vaccine hesitancy
	• Variable efficacies and side effects	• Variable efficacies and side effects	
	• Vaccine hesitancy	• Vaccine hesitancy	

Abbreviations: COVID-19, coronavirus disease 2019; MERS, Middle East respiratory syndrome; RT-PCR, reverse transcription-polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

AUTHOR CONTRIBUTIONS

All authors contributed to the following items (1) concept or design, (2) acquisition of data, (3) analysis or interpretation of data, (4) drafting of the manuscript, and (5) critical revision for important intellectual content.

DATA AVAILABILITY STATEMENT

All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Kam Lun Hon MBBS, MD, FAAP, FCCM[1]
Karen Ka Yan Leung MBBS, MRCPCH[1]
Wun Fung Hui MBChB, MRCPCH[1]
Daniel Kwok Keung Ng MBBS, MRCP (UK) FRCP (Edin), FRCPCH. M Med Sc (HK), MD[2]

[1]*Department of Paediatrics and Adolescent Medicine, The Hong Kong Children's Hospital, Hong Kong SAR, China*

[2]*Department of Paediatric Ward, Hong Kong Sanitorium & Hospital, Hong Kong, China*

Correspondence
Kam Lun Ellis Hon, MBBS, MD, FAAP, FCCM, Department of Paediatrics and Adolescent Medicine, The Hong Kong Children's Hospital, 1 Shing Cheong Road, Kowloon Bay, Hong Kong SAR, China.
Email: ehon@hotmail.com

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