Perspectives

Battling COVID-19 Using Lessons Learned from 100 Years of Fighting Against Influenza

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In 1918, a letter from a doctor at an USA Army camp read:

"These men start with what appears to be an ordinary attack of LaGrippe or Influenza, and when brought to the Hosp. they very rapidly develop the most vicious type of pneumonia that has ever been seen… and a few hours later you can begin to see the Cyanosis extending from their ears and spreading all over the face until it is hard to distinguish the colored men from the white. It is only a matter of a few hours then until death comes… It is horrible. One can stand it to see one, two or twenty men die, but to see these poor devils dropping like flies … We have been averaging about 100 deaths per day … Pneumonia means in about all cases death … We have lost an outrageous number of Nurses and Drs. It takes special trains to carry away the dead. For several days there were no coffins and the bodies piled up something fierce… It beats any sight they ever had in France after a battle. An extra long barracks has been vacated for the use of the Morgue, and it would make any man sit up and take notice to walk down the long lines of dead soldiers all dressed and laid out in double rows … Good By old Pal, God be with you till we meet again." (*1*)

This letter shed some light on the scenario of the 1918 influenza pandemic. What the physician had not foreseen was that this disease would cause 50 million people to die in the following year — many more deaths than those caused by the two World Wars. The 1918 "Spanish Flu" was the first influenza pandemic in the 20th century and also the most lethal one. Following this one, 3 more influenza pandemics have occurred as of 2020, including the 1957 H1N1, 1968 H3N2, and the 2009 H1N1, though the 1977 "Russian Flu" caused by H1N1 has also led to concentrated epidemics around the world. Compared with the 1918 pandemic, the later influenza viruses showed lower morbidity and mortality, but 100 years after the 1918 "Spanish Flu", we confronted a second severe pandemic disease caused by the coronavirus disease 2019 (COVID-19) (*2*–*3*). Up to October 28, 2020, this virus has caused 43,906,632 cases in the world with over 1 million deaths (*4*). Unlike the highly genetically related SARS-CoV virus that causes severe acute respiratory syndrome (SARS), which abated quickly because of aggressive containment procedures and relatively lower transmission capacity, COVID-19 continues spreading globally and is expected to circulate in the population in the near future. Using lessons learned from combating influenza pandemics over the past 100 years, we can use this historical perspective in our battle against COVID-19.

As stated by John Barry, the most important lesson from the 1918 influenza is to "tell the truth" (*5*). In 1918, due to the pressure to maintain wartime morale, neither national nor local government officials told the truth to the public. However, Spain was neutral in the First World War, and newspapers there could report on the disease so it was generally perceived that the pandemic had originated from Spain and led to the misnaming of the disease as the "Spanish Flu" (*6*–*7*). In countries that silenced the press, trust in authority deteriorated as the death toll increased, and this led to increased vulnerability amongst the population.

Because effective pharmaceuticals either did not exist or were not readily available, most cities suffered a tremendous death toll during the 1918 pandemic. However, cities that had imposed multiple social containment measures within a few days of detecting the first local cases had peak deaths rates of up to 50% lower than other cities that waited weeks to respond (*8*). Early implementation of some interventions, including the closure of schools, churches, and theater, was associated with lower peak death rates, but no single intervention showed an association with improved outcomes (*8*). In addition, the benefit of these multiple interventions was extremely limited if implemented too late or lifted too early, which indicated that proper timing of the response is crucial to curbing the effects of a pandemic (*9*).

San Francisco, St. Louis, Milwaukee, and Kansas City had the most effective public health interventions as they were able to reduce transmission rates by up to

30%–50% (*9*). The first official preventive measures were implemented in August 1918 and included obligatory notification of suspected cases and community surveillance. As the disease spread, closure of public places, banning gathering in crowds, cleaning streets, disinfecting the environment, and limiting the numbers of passengers on public transport, were applied in these three cities (*7*).

Besides the implementation of preventive measures, a worldwide network was established during the 1957 "Asian Flu" pandemic to study the strain soon after it emerged and involved investigators from London, Melbourne, and Washington DC. It was also the first time that vaccinations were implemented to protect high-risk individuals (*10*). Due to the low disease severity and low mortality rates, costly control measures such as school closures or quarantines were thought to be unnecessary in both the 1957 and 1968 pandemic. However, the 1968 "Hong Kong Flu" emphasized the importance of a combination of vaccinations, hospitalizations for complicated cases, and antibiotics to treat secondary infections. Hand hygiene and voluntary isolation of symptomatic individuals were further recommended in the 2009 H1N1 pandemic (*11*). These measures that were applied in response to past influenza pandemics were again widely implemented to help contain the COVID-19 pandemic.

Like the influenza virus, COVID-19 mainly spread via respiratory droplets that are transmitted during close contact (*12*) and the direct contact of the infectious surface through hands and other body parts, which means that social distancing strategies designed to block influenza transmission are also effective against COVID-19. Many countries have observed influenza incidence plunging as positive consequence of the public health response to COVID-19 during the 2019–2020 influenza season (*13*–*14*). The R_0 (reproductive number) for the SARS outbreak in 2003 was estimated to be between 2.0 and 3.0 in the early stage and quickly declined to 1.1 after stringent control measures (*15*). Studies have estimated the R_0 of COVID-19 to be 2.2 (95% CI*: 1.4–3.9) and 2.7 (2.5–2.9) (*16*–*17*), though another study has calculated a median R_0 value of up to 5.7 (95% CI: 3.8–8.9) (*18*). By comparison, the initial R_0 estimate for the H1N1 influenza pandemic in 2009 was 1.7 and later estimated between 0.17 and 1.3 after control measures were started (*15*). Because of the higher R_0 and fatality rate of COVID-19 compared to the influenza virus, more rigorous policies including active surveillance, contact tracing, mass samples testing, quarantining, and strong social distancing efforts have been needed to stop further transmission of the virus.

China and other Asian countries have been successful in controlling the spread of COVID-19 through their rigorous and early action. Following the SARS epidemic in 2003, China has prioritized developing its early response systems to public health emergencies, and in the 2009 response to H1N1, Richard Stone stated: "No country has taken stricter measures than China to protect residents from pandemic swine flu" (*19*). As the COVID-19 emerged and spread, China has applied rapid and rigorous containment efforts to block disease transmission, including locking down major cities and reducing transport between affected regions. This strategy also included rigorous social distancing, universal temperature monitoring, ubiquitous face masks wearing, and hand washing (*20*). Similarly, other Asian countries such as Republic of Korea and Vietnam also took aggressive action such as mass testing, movement restriction, and mandatory mask wearing (*21*) and have also succeeded in disrupting transmission.

When faced with a novel influenza virus that is rapidly spreading in the human population, an investigation must be conducted to uncover the origin of the virus, the intermediate host, the transmission route, and the clinical features it causes (*22*). This knowledge could help alert people to take proactive measures to prevent uptake of the virus and its spread. As a consequence, global cooperation for information sharing and virology research is needed to face the challenges continuously posed by influenza, and the Global Influenza Surveillance and Response System (GISRS) exemplified such cooperative efforts to combat infectious disease (*23*). The GISRS currently comprises 142 national influenza centers, 6 World Health Organization (WHO) Collaborating Centres, 4 essential regulatory laboratories, and 13 WHO H5 Reference Laboratories. GISRS aims at surveillance and monitoring of seasonal and emerging influenza viruses; recommendations for laboratory diagnostics, vaccines, and antiviral susceptibility; risk assessment for seasonal and pandemic influenza; and detection and response to influenza outbreaks (*24*). During the 2009 H1N1 pandemic and 2013 avian H7N9 endemic, China cooperated with other countries by sharing virus

* CI = Confidence Interval.

strains, sequences, and clinical trial information, which greatly contributed to the containment of the disease. Thus, a global platform and network similar to GISRS should be established for COVID-19 research and surveillance to integrate the global efforts against COVID-19 worldwide. In the struggle against COVID-19, we need stronger global cooperation and solidarity than any time before.

Humanity has been repeatedly endangered by infectious diseases and, each time so far, has won the fight. More infectious diseases are certain to come, though when and where they will emerge cannot be predicted. The knowledge accumulated in these battles will prepare us to overcome the crises caused by infectious diseases in the future.

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REFERENCES

1. Grist NR. Pandemic influenza 1918. Br Med J 1979;2(6205):1632 – 3. http://dx.doi.org/10.1136/bmj.2.6205.1632.
2. Huang CL, Wang YM, Li XW, Ren LL, Zhao JP, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020;395(10223):497 – 506. http://dx.doi.org/10.1016/S0140-6736(20)30183-5.
3. Zhu N, Zhang DY, Wang WL, Li XW, Yang B, Song JD, et al. A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med 2020;382(8):727 – 33. http://dx.doi.org/10.1056/NEJMoa2001017.
4. Johns Hopkins University & Medicine. COVID-19 Dashboard by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU). 2020. https://coronavirus.jhu.edu/map.html. [2020-10-5].
5. Barry JM. The single most important lesson from the 1918 influenza. https://www.dushu.com/news/12857. [2020-10-21].
6. Radusin M. The Spanish flu--Part I: the first wave. Vojnosanit Pregl 2012;69(9):812 – 7.
7. Martini M, Gazzaniga V, Bragazzi NL, Barberis I. The Spanish Influenza Pandemic: a lesson from the history 100 years after 1918. J Prev Med Hyg 2019;60(1):E64 – 7. http://dx.doi.org/10.15167/2421-4248/jpmh2019.60.1.1205.
8. Hatchett RJ, Mecher CE, Lipsitch M. Public health interventions and epidemic intensity during the 1918 influenza pandemic. Proc Natl Acad Sci USA 2007;104(18):7582 – 7. http://dx.doi.org/10.1073/pnas.0610941104.
9. Bootsma MCJ, Ferguson NM. The effect of public health measures on the 1918 influenza pandemic in U.S. cities. Proc Natl Acad Sci USA 2017;104(18):7588 – 93. http://dx.doi.org/10.1073/pnas.0611071104.
10. Henderson DA, Courtney B, Inglesby TV, Toner E, Nuzzo JB. Public health and medical responses to the 1957-58 influenza pandemic. Biosecur Bioterror 2009;7(3):265 – 73. http://dx.doi.org/10.1089/bsp.2009.0729.
11. Saunders-Hastings PR, Krewski D. Reviewing the history of pandemic influenza: understanding patterns of emergence and transmission. Pathogens 2016;5(4):66. http://dx.doi.org/10.3390/pathogens5040066.
12. WHO. Transmission of SARS-CoV-2: implications for infection prevention precautions. 2020. https://www.who.int/news-room/commentaries/detail/transmission-of-sars-cov-2-implications-for-infection-prevention-precautions. [2020-10-5].
13. Chow A, Hein AA, Kyaw WM. Unintended consequence: influenza plunges with public health response to COVID-19 in Singapore. J Infect 2020;81(2):e68 – 9. http://dx.doi.org/10.1016/j.jinf.2020.04.035.
14. Wu D, Lu JY, Liu YH, Zhang ZB, Luo L. Positive effects of COVID-19 control measures on influenza prevention. Int J Infect Dis 2020;95:345 – 6. http://dx.doi.org/10.1016/j.ijid.2020.04.009.
15. Petersen E, Koopmans M, Go U, Hamer DH, Petrosillo N, Castelli F, et al. Comparing SARS-CoV-2 with SARS-CoV and influenza pandemics. Lancet Infect Dis 2020;20(9):e238 – 44. http://dx.doi.org/10.1016/S1473-3099(20)30484-9.
16. Li Q, Guan XH, Wu P, Wang XY, Zhou L, Tong YQ, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. N Engl J Med 2020;382(13):1199 – 207. http://dx.doi.org/10.1056/NEJMoa2001316.
17. Wu JT, Leung K, Leung GM. Nowcasting and forecasting the potential domestic and international spread of the 2019-nCoV outbreak originating in Wuhan, China: a modelling study. Lancet 2020;395(10225):689 – 97. http://dx.doi.org/10.1016/S0140-6736(20)30260-9.
18. Sanche S, Lin YT, Xu CG, Romero-Severson E, Hengartner N, Ke RA. High contagiousness and rapid spread of severe acute respiratory syndrome coronavirus 2. Emerg Infect Dis 2020;26(7):1470 – 7. http://dx.doi.org/10.3201/eid2607.200282.
19. Stone R. Swine flu outbreak. China first to vaccinate against novel H1N1 virus. Science 2009;325(5947):1482 – 3. http://dx.doi.org/10.1126/science.325_1482.
20. Burki T. China's successful control of COVID-19. Lancet Infect Dis 2020;20(11):1240 – 1. http://dx.doi.org/10.1016/S1473-3099(20)30800-8.
21. Triggle CR, Bansal D, Farag EABA, Ding H, Sultan AA. COVID-19: learning from lessons to guide treatment and prevention interventions. mSphere 2020;5(3):e00317 – 20. http://dx.doi.org/10.1128/mSphere.00317-20.
22. Liu WJ, Wu Y, Bi YH, Shi WF, Wang DY, Shi Y, et al. Emerging HxNy Influenza A Viruses. Cold Spring Harb Perspect Med 2020. http://dx.doi.org/10.1101/cshperspect.a038406.
23. Hay AJ, McCauley JW. The WHO global influenza surveillance and response system (GISRS)-A future perspective. Influenza Other Respir Viruses 2018;12(5):551 – 7. http://dx.doi.org/10.1111/irv.12565.
24. Liu WJ, Bi YH, Wang DY, Gao GF. On the centenary of the Spanish flu: being prepared for the next pandemic. Virol Sin 2018;33(6):463 – 6. http://dx.doi.org/10.1007/s12250-018-0079-1.