

Pandemics in Perspective

Marina Morgan

Royal Devon University Healthcare NHS Foundation Trust,
Barrack Road, Exeter EX2 5DW, UK. Email: marinamorgan@nhs.net

Introduction

COVID-19 is not the first pandemic and it won't be the last.
– Norman Swan

The articles on the history of pandemics in this issue have a common theme of preventing spread of infections, some affecting mankind on a global scale. Difficulties in diagnosis, understanding modes of spread, and appropriate infection prevention and control guidance remain a problem. Lack of preparation, evolution of more pathogenic strains (whether naturally acquired or man-made) and conflicting scientific evidence confusing misguided but often well-intentioned leaders is testament to the statement that 'Those who cannot learn from history are doomed to repeat it' to paraphrase George Santayana.¹

Pandemics

Pandemics, that is epidemics 'occurring worldwide, or over a very wide area, crossing international boundaries and usually affecting a large number of people' have plagued mankind for centuries.² As fast as man exploits science to conquer infections, new infections emerge.

Lovett's account of a Marseille physician's experiences with plague in Marseille in 1720 makes riveting reading. Parallels with COVID-19 abound. Losing his family to plague, panic buying and shortages of food among the citizens after port blockades and all the fisherman died, Dr Bertrand supposedly survived three bouts of plague – unlikely,

¹ Santayana G. *The Life of Reason or The Phases of Human Progress. Reason in Common Sense*. New York: Charles Scribner's Sons; 1905, p.284. In the original: 'Those who cannot remember the past are condemned to repeat it'.

² Last JM (ed). *A Dictionary of Epidemiology, Fourth Edition*. New York: Oxford University Press; 2001.

given the protean manifestations of non-bubonic plague. Lovett describes buboes misdiagnosed as carbuncles and plague attributed to syphilis. City leaders refused to appoint physicians to the council on health. The prevailing belief that miasmas were to blame and questioning the value of quarantine allowed disease to spread – again echoes of COVID-19. Even when ‘lesions associated with plague could be reproduced in animals that he had injected with fluid from the gallbladder of people who had died of plague’ authorities remained unconvinced. Appointed to inspect the outbreak response, an eminent Montpellier physician stated that fear of plague was greater than the risk of plague. Fumigation and lime-coating disinfection was introduced – measures repeated elsewhere, including the Rotunda hospital in Dublin (puerperal sepsis) and the homes of those afflicted with scarlet fever in the late nineteenth century. In the aftermath of COVID-19, we infection specialists shared a similar sense of the relief described by Dr Bertrand when the ‘normal and common infections’ such as *Streptococcus pyogenes* reappeared.

The impact of pandemics relies on the virulence and ease of transmissibility of the pathogen and the immunological naivety of the population. The ‘Black Death’ (second or Medieval plague) and Spanish flu are most famous but there are many others: smallpox, AIDS, cholera, polio, syphilis, typhus, malaria and tuberculosis. Mankind has been fearful of extinction for centuries. Procopius, referring to the first plague of Justinian, commented: ‘There was a pestilence, by which the whole human race came near to be annihilated’. Happily, mankind survived, although so has plague. Classified as a ‘re-emerging’ infectious disease, with pockets in Madagascar and Africa, mortality remains high, approaching twelve per cent in America, where sporadic infections follow contact with sick animals or cat bites. In an outbreak of plague in diamond miners in the Congo, 67 out of 150 died of plague.

Edwards, in his paper on miasmas and the public health response to the Spanish flu pandemic, raises similar issues causing controversy during instigation of COVID-19 control measures, namely the advocacy of open windows, fresh air and whether COVID-19 was respiratory or contact spread. He mentions in 1917-18 the public health response of closing cinemas and meeting places reminiscent of recent COVID-19 restrictions. Intriguingly, mask wearing by the British public was considered impractical in 1918, yet the USA mandated mask wearing by clinicians in military hospitals and several states for civilians. Edwards mentions pipe-smoking was felt to be beneficial and protective, rebuffed by a 1969 American student study showing clinical influenza occurring 21 per cent more frequently in heavy smokers than non-smokers.³

Mask wearing, as Rhodes points out, was used in the Rome (seventeenth century) and Marseille (eighteenth century) plagues. Mask wearing at the start of the COVID-19 pandemic seemed eminently sensible to me as a microbiologist, although in the early days there was considerable argument in higher scientific echelons about their necessity and efficacy. Rhodes’ article beautifully elucidates the evolution of the surgical mask, with lovely illustrations. An orthopaedic surgeon operating in 1918 with a face mask covering his mouth well but not his nostrils is reminiscent of members of the public and some clinicians I witnessed during COVID-19. Those clinicians with facial hair failing

³ Finklea JF, Sandifer SH, Smith DD. Cigarette smoking and epidemic influenza. *American Journal of Epidemiology*. 1969; 90(5): 390-399.

'fit tests' of the close-fitting FFP3/FFP2 masks, meaning that a complete barrier to viral transit could not be guaranteed, were ordered to shave, except for those with cultural or religious objections.

I remain bewildered why it took so long in modern times to establish airborne spread of COVID-19. The 'miasmatic paradigm' was challenged by the emergence of the germ theory of Koch and Pasteur, and bolstered by the elucidation of routes of transmission of cholera (water), puerperal fever (unwashed hands and environmental contamination) and malaria (insect vector).⁴ COVID-19 stimulated urgent research into airborne spread, with the WHO eventually acknowledging in 2021 that airborne COVID-19 transmission is significant and finally acceding, categorising spread into aerosol inhalation, surface touch, and drop spray.⁵

Lessons of history could have been employed much earlier in the debate. In 1905, commissioned to study the House of Commons air after an influenza epidemic amongst MPs, Gordon gargled with a solution of *Serratia marcescens*, an easily identifiable red pigmented bacterium of low pathogenicity. Reciting Shakespeare to an empty chamber, agar plates placed on the floor 21 m away from him grew *Serratia*.⁶ Viruses are a deal smaller than bacteria!

Man's fightback against disease

Successive outbreaks and pandemics caused the decimation of populations until either natural resistance increased or strains lost their virulence. Then vaccination and antimicrobials allowed mankind a temporary respite. Shortly after Yersin's discovery of the plague bacterium (*Yersinia pestis*) Paul Louis Simond began vaccinating Indians against plague. Vaccination against smallpox, influenza and COVID-19 has been a triumph but the constant reassortment of influenza genes in different animals and humans means new strains of influenza are difficult to cover when vaccines are based on the previous year's circulating strains. Reassortment in different species, whether avian, swine or human, allows highly virulent strains to emerge, and a pan-species universal influenza vaccine seems unlikely, so avian influenza is a 'pandemic in waiting' with a likely mortality of greater than 50 per cent.

Immunotherapy

Wawrzynczak's fascinating paper on the usage of convalescent plasma (CP) in a pandemic is detailed and instructional. Immunotherapy (antibodies), immunomodulatory, and bacteriophage (viruses infecting bacteria) therapies have all been used

⁴ Jimenez JL, Marr LC, Randall K, Ewing ET, Tufekci Z, Greenhalgh T *et al.* What were the historical reasons for the resistance to recognizing airborne transmission during the COVID-19 pandemic? *Indoor Air.* 2022; 32: e13070.

⁵ Li Y. Basic routes of transmission of respiratory pathogens – A new proposal for transmission categorization based on respiratory spray, inhalation, and touch. *Indoor Air.* 2021; 31: 3-6.

⁶ Great Britain. House of Commons. Parliamentary Papers, 1850-1908 (13 February 1906-21 December 1906). London: HMSO; 1906.

for plague treatment, although nowadays, doxycycline and gentamicin are the mainstay. Intriguingly, there are very few reports of patients treated with convalescent plague serum, possibly due to the sequestration of the organism.⁷ One trial in India in the 1930s reported an impressive reduction of mortality from 47.9 to 16.7 per cent following intramuscular injections of CP.⁸

Happily, we are learning from history with CP at least. Passive immunisation with antibodies derived from blood donors is administered to susceptible immunosuppressed contacts of varicella and measles today. The Lederle immunoglobulin mentioned in Wawrzynczak's paper was also used in puerperal sepsis in the early twentieth century, *S. pyogenes* then being a major killer of women in pregnancy. During 2009-12 rates of this infection in the UK dramatically increased, along with outbreaks ('the killer flesh-eating bug'), a resurgence of scarlet fever and invasive streptococcal infections. Locally, our enviable success in treating severe toxic shock and necrotising fasciitis is mainly due to usage of immunoglobulin derived from blood donors, the last hope for neutralising bacterial exotoxins.

Conclusion

Having over-colonised and warmed up the world, trade links and international travel means infectious diseases reach remote and immunologically naive indigenous peoples. Eroding natural habitats, we are displacing fellow creatures from their homes taking with them their infections and vectors. We are culpable in inviting and encouraging new zoonoses to emerge, accelerated by inadequately controlled scientific research and biosecurity. 'The worst pandemic in modern history was the Spanish flu of 1918, which killed tens of millions of people. Today, with how interconnected the world is, it would spread faster' was the glum warning from Bill Gates.

In China, humans living closely with pigs and chicken pose a particular threat of influenza viruses mixing. The demand for cheap protein necessitated massive units for production of rapidly grown poultry, birds in close proximity all immunologically challenged. Diseases spread easily between birds in such conditions and easily transmit outside the intensive units if biosecurity measures fail. On a smaller scale, and widely reported in the press in 2021, the aptly named Mr Gosling acquired avian influenza from pet Muscovy ducks which sadly all had to be culled. Happily, the strain did not affect him badly but decimation of birds globally with strains of 'highly virulent avian influenza' sadly continues.

Finally, with warp speed advances in genomic research, scientists are augmenting the pathogenicity of microbes artificially. The 1918 Spanish flu was recreated in a laboratory, using genetic codes retrieved from ice-bound bodies. Such genetic manipulation, whether for altruistic or biowarfare purposes, can result in accidental or intentional release into the population, as has been suggested happened in Wuhan.

⁷ Jawetz E, Meyer KF. Studies on plague immunity in experimental animals. II. Some factors of the immunity mechanism in bubonic plague. *Journal of Immunology*. 1944; 49(1): 15-30.

⁸ Norman-Walker JN. Treatment of plague cases with convalescent human serum. *Indian Medical Gazette*. 1937; 72(8): 469-473.

Lifting the lid on Pandora's box with genetic manipulation – especially 'gain of function' experiments – poses a significant risk of new iatrogenic pandemics.

Unless we learn the lessons from the history, I have a deep sense of foreboding the COVID-19 pandemic will not be the last.

Keywords

COVID-19, pandemics, plague, immunotherapy

Biographical Details

Marina Morgan FRCPath is Consultant in Microbiology and Infection at the Royal Devon University Hospital and Senior Lecturer, University of Exeter Medical School.

Morgan M. Pandemics in Perspective. *Topics in the History of Medicine*. 2022; 2: 8-13.

Topics in the History of Medicine is an Open Access publication of the British Society for the History of Medicine made available under a Creative Commons Attribution-NonCommercial 4.0 International Licence which allows unrestricted redistribution in any medium or format for non-commercial purposes provided the original work is properly credited. <https://bshh.org.uk>

© *The Author(s)*, 2022.