

# Viral Pandemics in the Past Two Decades: An Overview

Pooja Bhadoria<sup>1</sup>, Gaurisha Gupta<sup>2</sup>, Anubha Agarwal<sup>3</sup>

<sup>1</sup>Department of Anatomy, AIIMS Rishikesh, <sup>2</sup>First Year MBBS Student, AIIMS Rishikesh, <sup>3</sup>Department of Hospital Administration AIIMS Rishikesh, Rishikesh, Uttarakhand, India

## ABSTRACT

An epidemic that occurs worldwide, involving many countries and affecting a large population is called as a pandemic. The ongoing corona virus disease (COVID-19) pandemic has not only adversely affected the global healthcare infrastructure, but has significantly impacted world economy, socio-political and cultural environment. There are 219 different types of viruses, known at present to be able to infect human beings. This number is just a tip of the iceberg, with the possibility of a substantial pool of undiscovered human viruses and millions of other virus species (which affect plants and non-human animals) that can be potentially infectious to humans as well. Throughout human history there have been numerous pandemics and disease outbreaks that have not only led to huge loss of life, but also hindered economic growth and development. Therefore, in this review article we wanted to highlight major viral pandemics that have occurred in the last two decades, to understand factors contributing to their emergence, transmission and suggest ways to curb future outbreaks.

**Keywords:** MERS, SARS, Swine flu, viral pandemics, Western African Ebola virus, Zika virus

## Introduction

An epidemic that occurs worldwide, involving many countries and affecting a large population is called as a pandemic.<sup>[1]</sup> There are various factors which can lead to epidemics of infectious diseases. These include a change in ecology of host population and mutation in reservoir of pathogen. Disease outbreaks may also occur when a new, emerging pathogen is introduced to a host population. When these epidemics become widespread, involving many people mostly due to effective transmission of disease amongst humans, they are classified as pandemics. The wide geographical occurrence of these pandemics is usually by pathogens that are novel to human beings, having a high attack rate, are highly infectious and are able to mutate fast, so as to evade host immunity. Of all pathogens, viruses are particularly common in causation of pandemics due to their vast species

occurrence, involvement of non-human hosts, rapid routes of transmission and higher rates of infectivity.

Aim of the present study is to collate data on previous similar pandemics, so that it can be utilized for better knowledge sharing, and learning from past experiences, to combat the present pandemic and to prepare for such pandemics in future.

Major viral pandemics in the last 2 decades mostly involved respiratory viruses like corona, causing 3 major pandemics earlier: severe acute respiratory syndrome (SARS CoV-1), Middle eastern respiratory syndrome (MERS) and ongoing SARS CoV-2 (COVID -19), followed by influenza viruses causing Influenza A H1N1 pdm 2009 (swine flu), Ebola and Zika virus infections.

## Pandemic 1: Severe Acute Respiratory Syndrome Corona Virus Infection (SARS- CoV-1)

**SARS** is a respiratory illness caused by virus SARS CoV-1 belonging to *Coronaviridae* family, and is first strain to be discovered from

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**Address for correspondence:** Dr. Pooja Bhadoria,  
Department of Anatomy, Block-A, Level-2, AIIMS, Rishikesh,  
Uttarakhand, India.  
E-mail: pooja.ana@aiimsrishikesh.edu.in

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severe acute respiratory syndrome–related coronavirus (SARS CoV) species.<sup>[2]</sup> The virus caused the 2002-2004 SARS pandemic in which 30 countries were affected. A total number of 8,422 cases were reported, with 11% case fatality ratio (CFR).<sup>[3]</sup> CFR varied from case to case depending on age-group of patients. CFR was <1% in people below age of 24, while it was >55% in those above age of 65 years.<sup>[4]</sup> The first case was reported in November 2002 from Guangdong, China. The virus was said to have originated from cave-dwelling horseshoe bats found in Yunnan province of south-western China, pointing to zoonotic origin.<sup>[4,5]</sup> The transmission was through respiratory route from droplets or fomites. Management was majorly focused on reduction and control of symptoms. There is currently no proven antiviral therapy to treat SARS. Preventive measures such as immediate isolation of confirmed cases, wearing protective gears, barriers by medical practitioners during handling of patients helped to control further spread of disease.<sup>[6]</sup> Since 2004, no more cases of SARS CoV-1 have been reported. However, till date there is no success in making effective vaccine against virus. This could be due to successful control over disease, led to lack of interest and delayed all ongoing efforts.<sup>[7]</sup>

## Pandemic 2: Influenza A H1N1 2009 (Swine Flu) Pandemic

**Influenza A** group of viruses had caused 2 major pandemics, first was the 1918 Spanish flu and other was the swine flu in the year 2009. In 2009, the virus originated as a result of triple re-assortment between avian, swine, and human viruses leading to term “swine flu” which is a misnomer as it was actually a human virus.<sup>[8]</sup> The infection was a typical lung infection known as acute respiratory distress syndrome (ARDS). All symptoms were that of conventional flu or pneumonia.

It was speculated that H1N1 virus that was responsible for the 2009 outbreak also initially circulated for several months before being recognized and identified as a novel strain of influenza virus.<sup>[9]</sup> It first originated from Mexico. The pandemic lasted for about 19 months and finally was declared over in August 2010. Worldwide, more than 214 countries were affected. Total cases that were reported were close to 700 million to 1.4 billion. The number of deaths reported to WHO were approximately more than 18,000.<sup>[10]</sup> This flu virus demonstrated a high morbidity but low mortality rate of approximately 1-4%. The pandemic was successfully controlled due to availability of an effective vaccine that incorporated this strain. Moreover, an effective antiviral treatment was also available. The immunity provided by these vaccines lasts for 1 year therefore, the vaccine has to be taken annually and yearly; circulating strains of virus are included in vaccine. Human beings have got adapted to the 2009 strain of the virus and now H1N1 2009 pdm strain is the local circulating strain.

## Pandemic 3: Middle East Respiratory Syndrome (MERS) CoV Infection

Middle East respiratory syndrome (MERS), is a type of viral infection involving the respiratory tract which is caused by a

corona virus. The virus originated from camels, therefore it is also known as the camel flu.<sup>[11]</sup> The virus belonged to genus *Betacoronavirus* and subgenus *Merbecovirus* and its receptors were identified as dipeptidyl peptidase-4 (DPP4).<sup>[12]</sup> It was first seen in a patient from Saudi Arabia in 2012. It was not very clear how the transmission of the virus took place from camels to humans. The WHO advised to avoid eating un-cooked or under cooked camel meat, drinking of unpasteurized milk and urine from camels and avoid close proximity with camels. There was minimal human to human transmission. The transmission mostly occurred due to close contact with severely ill patients and transmission from asymptomatic cases was never established.<sup>[13]</sup>

A total number of 2519 laboratory confirmed cases, with 866 deaths having a case fatality of 34.3% was reported till this year. Most of cases were reported from Saudi Arabia and around 26 countries were affected with pandemic. No specific antivirals or vaccine could be developed for this disease. The studies done on various treatment modalities like use of antivirals like Ribavirin and Interferons did not show much success in management of cases infected with MERS-CoV.<sup>[14]</sup> The virus got contained by isolation of cases and local containment measures eventually controlling the pandemic.

## Pandemic 4: The Ebola Virus Pandemic

The Ebola virus pandemic that lasted from 2013 till 2016 is by far most widespread Ebola virus disease (EVD) epidemic reported so far. The disease was first reported from Guinea in late 2013 and then it spread to Liberia and Sierra Leone.<sup>[15]</sup>

EVD or Ebola hemorrhagic fever (EHF), is a viral hemorrhagic fever. It is caused by *Ebolaviruses* belonging to family *Filoviridae* in the order *Mononegavirales*.<sup>[16]</sup> Zaire Ebola virus was the cause of EVD in the year 2013–2016 in western Africa. It caused significant mortality. The main route of transmission was direct contact with blood or infected body fluids.<sup>[17]</sup> The source of initial infection from animals to humans was in fact contact with the infected bat body fluids.<sup>[18]</sup>

The initial case was an 18-month-old boy, in Guinea, who got infected from bats in December 2013. Following this by March 2014, there were 49 confirmed cases and 29 deaths, reported to the WHO. In 2015 it spread across countries in Africa and outside Africa to Spain, USA, UK, Italy, etc., In Africa itself there were approximately 30,000 cases with 12,000 deaths.<sup>[19]</sup> The pandemic finally got contained by strict containment measures that were taken; very efficient contact tracing and community surveillance. All the cases were registered and immediately all contacts were traced and contained. An efficient community awareness of risk factors and encouraging people to use protective measures like avoiding contact with infected people and adopting hand hygiene, reduced large scale spread of infection. There was no specific antiviral treatment.<sup>[20]</sup> However, in July 2015, a vaccine, rVSV-ZEBOV, was launched that showed high efficacy in individuals. The pandemic was called over in 2016 and finally, rVSV-ZEBOV received regulatory approval in 2019.<sup>[21]</sup>

## Pandemic 5: Zika Virus Epidemic

Zika virus (ZIKV) is a virus that spreads through the bite of the *Aedes* mosquitoes: *A. aegypti* and *A. albopictus*. These mosquitoes have a typical day-biting tendency. The virus was named after the Zika forest of Uganda, from where it was first reported in the year 1947.

The disease caused by this virus is called Zika virus disease or simply Zika fever, a minor illness with fever and rash. The virus also demonstrates vertical transmission from infected pregnant female to her fetus, and can cause microcephaly and other major brain abnormalities.<sup>[22]</sup> The virus belonged to family *Flaviviridae* and genus *Flavivirus*.<sup>[23]</sup> The virus normally infects monkeys and is maintained in circulation in the enzootic cycle of mosquito-monkey-mosquito. Like other flaviviruses, human beings are accidental hosts to the virus. The most important transmission in the Zika virus disease is vertical transmission, at the time of delivery or during antenatal period causing neuronal abnormalities ranging from microcephaly to development of neurocognitive disorders in adulthood.<sup>[24]</sup>

The pandemic started in 2015 and a total number of 87 countries were affected.<sup>[25]</sup> The control of the pandemic was done by case identification, controlling mosquito spread and other preventive measures. There is no specific antiviral treatment however trials are going on for development of a successful ZIKV vaccine. Three vaccine designs have reached the stage of human trials but still an effective vaccine is yet to come.<sup>[26]</sup>

## Pandemic 6: SARS-CoV2 Pandemic

The SARS CoV-2 pandemic, is an ongoing global pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS CoV2) virus and the disease is caused by it is corona virus infective diseases (COVID-19). The virus belongs to the *Coronaviridae* family and the virus is an enveloped, positive-sense, single-stranded RNA virus. Corona viruses are known to cause infections in amphibians, birds, and mammals. Coronaviruses have initially originated from bats and rodents. The primary route of transmission is respiratory and is transmitted from droplets through coughs and sneezes up to a range of approximately 6 feet. Some studies have pointed towards a possibility of the virus being airborne as well.<sup>[27]</sup> Another mode of transmission is by indirect contact with contaminated surfaces.<sup>[28]</sup> The major and common clinical features include fever, cough, weakness, loss of sense of smell and taste. Further complications of the disease include acute respiratory disease with pneumonia.<sup>[29]</sup> Preventive measures aimed at decreasing the chances of infection include hand hygiene, surface disinfection, wearing face masks, and avoiding close contact with those showing flu-like symptoms.<sup>[30]</sup> Many countries have adopted social distancing strategies such as cancelling large public gatherings, shutting down schools, colleges, offices, and putting restrictions on travel.

It was first reported from Wuhan, Hubei province of Central China in month of December in 2019.<sup>[27]</sup> The outbreak was further declared a public health emergency of international concern on 30<sup>th</sup> January and declared as a pandemic on 11<sup>th</sup> March 2020.<sup>[31]</sup> As of 27<sup>th</sup> Dec 2020, COVID19 pandemic has affected more than 188 countries across the world, with 79,232,555 confirmed cases and 1,754,493 deaths. The pandemic has led to massive disruption of both social and economic infrastructure, affecting millions of people.<sup>[32]</sup> At present there is no established treatment for the management of COVID-19 and patients are managed symptomatically.<sup>[33]</sup> Apart from antiviral drugs a new modality of treatment has been tried with success against COVID-19 which is known as convalescent plasma therapy. Blood of previously COVID-19 infected patients contains neutralizing antibodies against SARS CoV-2 virus. Thus, the plasma from these patients containing antibodies is given to neutralize the virus.

Success with the effective vaccine has come. There are 3 major candidates of vaccine that are being tried, inactivated virus vaccine, vaccine using messenger RNA of virus (mRNA based) and vaccines utilizing recombinant protein of SARS CoV-2 on other viral vector.<sup>[34,35]</sup> Hopefully with these efforts very soon control over this pandemic is also done.

## Discussion

The ongoing Covid-19 pandemic has not only impacted global healthcare infrastructure, but has also affected world economy and socio-political framework, effectively bringing the entire world to a standstill. Hence, there was a need to conduct a review of the various viral pandemics that have occurred in the past to understand their origin, transmission and measures that were taken to prevent and control them.

The first observation made during the course of this study was that the frequency of occurrence of pandemics is increasing with time. Earlier, large-scale epidemics spanning various continents were a twice or thrice a century phenomenon, but we have experienced 6 major pandemics in the last 20 years itself. This is due to enhanced globalization, air travel, increasing population and entering into animal habitats; thereby increased close association with them.<sup>[36]</sup> There has also been a change in socializing behavior of people, with mass gatherings becoming more and more common, contributing to rapid spread of diseases.<sup>[37]</sup>

Another observation made in this study was that viruses responsible for major pandemics in last 2 decades were air-borne and of animal origin.<sup>[38,39]</sup> Growing urbanization has led to the encroachment of forest areas by humans, thus increasing animal to human contact and in turn, the chances of acquiring viruses. Hence, lack of regulation of handling of animals and animal products, rising animal-human contact (especially in case of wild areas), lack of basic hygiene practices, cough etiquettes and a general lack of awareness about spread of viruses and air-borne diseases has contributed significantly to widespread rise in occurrence of these pandemics.

Owing to experiences in handling of previous pandemics, it has been observed that the global healthcare community is much better prepared and equipped for handling and management of pandemics now, than it was before. Table 1 describes the various steps taken to curb outbreaks in the past two decades. This is evident from the fact that the time taken from identification of the first case of the virus, to its complete genome sequencing, making several diagnostic tests and now the development and licensing of vaccines are much faster than the previous pandemics. Within a few weeks of its identification, clinical trials for the vaccine and other therapeutic interventions were initiated within a month.<sup>[40]</sup>

Despite this knowledge, the ongoing COVID-19 pandemic has emerged as one of the most fatal disease outbreaks known to mankind. This can be attributed to extremely high transmissibility of the virus, human to human transmission at a very early stage

of the pandemic, more prominent community spread, and transmission from asymptomatic cases, which has led to an extremely huge surge of infection.

Therefore, the following steps must be followed to slow down the spread of viruses and prevent such outbreaks in future years:

First, all countries must make laws to regulate handling of animals and animal products, (especially exotic/wild species) and wet markets with stringent adherence and enforcement. Second, basic hygiene practices like hand washing, and use of sanitizers and disinfectants must be promoted. Social distancing, following air-borne infection control practices and cough etiquettes like, using a handkerchief while coughing/sneezing, wearing a mask when experiencing even mild flu-like symptoms etc., should be made a norm, especially during mass gatherings and air travel.

**Table 1: Steps Taken to Tackle Pandemics of Last Two Decades**

Pandemic	Duration	Steps Taken to Curb Outbreaks
Severe acute respiratory syndrome corona virus infection (SARS CoV1)	2002-2004	Syndromic surveillance Rapid isolation of cases Strict isolation of all contacts Community-level quarantine in some areas Closure of schools, universities and public places. Control of human to human transmission of disease during early phase of the pandemic. <sup>[41]</sup>
Influenza A H1N1 2009 (Swine Flu) Pandemic	2009-2010	Activation of Emergency Operations Centre within one week. Development of real-time PCR test within two weeks. There were no travel restrictions or closing of international and domestic borders. Quick home isolation of all with flu symptoms for either seven days or until symptoms subsided. Early quarantine of all foreign visitors suspected of having being in contact with infected people. <sup>[42]</sup>
Middle East respiratory syndrome (MERS) CoV infection	2012-present	Enforcement of a rapid response team, with infectious disease doctors and infection control professionals. Rapid tracking and alert system for index cases Prompt implementation and development of airborne infection control guidelines Training of healthcare workers for important infectious diseases was encouraged Measures were made for controlling overcrowding in hospitals <sup>[43,44]</sup>
Western African Ebola virus epidemic	2013-2016	All potential transmissions after reporting of the first case were tracked Vaccination of not just patients, but also of front-line healthcare workers, people in contact with confirmed cases, and their contacts was carried out. New quarantine and treatment facilities were constructed. Mobile laboratories were set up and technicians trained to test Ebola samples. Public health measures such as promoting hand hygiene, wearing masks, gloves etc., were put in practice. Safe burial practices also helped to control infection Screening of passengers at domestic and international ports and airports was done to check transmission. <sup>[45]</sup>
Zika Virus Epidemic	2015-2016	Genetically modified <i>Aedes aegypti</i> mosquitoes were released throughout Brazil on approval of country's National Biosafety Committee, to control transmission of Zika virus. Brazilian President released a decree that lead to an increase in access to private property by local and federal pest control agents. This was required for controlling and eliminating <i>Aedes</i> mosquito outbreaks in Brazil. Mass awareness and education activities to control mosquito breeding and vector control measures. <sup>[46]</sup>
SARS CoV2 infective disease (COVID19) pandemic	2019-present	A strategy of screening, containment and mitigation has been adopted to control outbreaks In Screening, devices such as Infrared thermometers/Temperature scanners are being used to detect fever associated with the coronavirus disease. <sup>[47]</sup> In Containment, those who have tested positive, as well as their contacts are traced and isolated. Mitigation stage involves steps that are taken to control the spread of infection and reduce its effects on the healthcare infrastructure. Preventive measures to control transmission include proper hand hygiene, wearing face masks, maintaining 6ft social distance. Schools, universities and workplaces across the globe have been closed. There has been cancellation or postponement of almost all major sporting, cultural, religious events. International borders were closed, and flights suspended. Domestic travel was restricted in some countries. Several countries have also imposed curfews and bans on mass mobility. <sup>[48]</sup>



Finally, there is a need to increase information and education (IEC) about the origin of viral infections, their mode of transmission and preventive strategies to promote awareness among the general population and curb rising incidences of disease outbreaks.

## Conclusion

Viral pandemics are increasing in frequency and infectivity. Great caution should be taken against airborne viral infections especially due to inter species transmission. Such pandemics have affected large populations and have caused considerable havoc on healthcare systems, especially those in developing countries. The recent SARS CoV-2 pandemic has brought the whole world to a virtual standstill severely affecting the world economy. Lessons must be learnt from such pandemics so that adequate strengthening of the healthcare infrastructure and systems can be done in order to prevent or mitigate the long-term effects of such pandemics especially in low and middle-income countries, which are as such struggling with poor health infrastructure. Primary healthcare physicians are important vehicles to bring these practices to more and more people, hence educating them is important.

## Summary points

The current review article focuses on the various viral pandemics that have occurred in the past and how they were controlled. Lessons must be learnt from such pandemics so that adequate strengthening of the healthcare infrastructure and systems can be done in order to prevent or mitigate the long-term effects of such pandemics. Primary healthcare physicians are the first contact with health services hence their knowledge is of utmost importance if we want to strengthen our public health care infrastructure.

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## Conflicts of interest

There are no conflicts of interest.

## References

1. Last JM. Epidemic: The encyclopaedia of ecology and environmental management. In: Spasoff RA, Harris SS, Thuriaux MC, editors. *A Dictionary of Epidemiology*. 4<sup>th</sup> ed. Oxford Newyork: Blackwell; 1998.
2. Tong JW, Zheng YS. Citizen lawsuits against the government in China: Twenty court cases, 2013–2019. *Chin Law Gov* 2019;51:49-53.
3. Monaghan KJ. SARS: DOWN BUT STILL A THREAT. In: Institute of Medicine (US) Forum on Microbial Threats; Knobler S, Mahmoud A, Lemon S, *et al.*, editors. *Learning from SARS: Preparing for the Next Disease Outbreak: Workshop Summary*. Washington (DC): National Academies Press (US); 2004. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK92458/>.
4. Chan-Yeung M, Xu RH. SARS: Epidemiology. *Respirology* 2003;8(Suppl 1):S9-14.
5. Hu B, Zeng L-P, Yang X-L, Ge XY, Zhang W, Li B, *et al.* Discovery of a rich gene pool of bat SARS-related coronaviruses provides new insights into the origin of SARS coronavirus. *PLoS Pathog* 2017;13:e1006698.
6. Stockman LJ, Bellamy R, Garner P. SARS: Systematic review of treatment effects. *PLoS Med* 2006;3:e343.
7. Jiang S, Lu L, Du L. Development of SARS vaccines and therapeutics is still needed. *Future Virol* 2012;8:1-2.
8. Trifonov V, Khiabani H, Rabadan R. Geographic dependence, surveillance, and origins of the 2009 influenza A (H1N1) virus. *N Engl J Med* 2009;361:115-9.
9. Butler D. How severe will the flu outbreak be? Epidemiologists race to pin numbers on the global H1N1 spread. *Nature* 2009;459:14-5.
10. Dawood FS, Iuliano D, Reed C, Meltzer MI, Shay DK, Cheng PY, *et al.* Estimated global mortality associated with the first 12 months of 2009 pandemic influenza A H1N1 virus circulation: A modelling study. *Lancet* 2012;12:687-95.
11. Rha B, Rudd J, Feikin D, Watson J, Curns AT, Swerdlow DL, *et al.* Middle East respiratory syndrome coronavirus (MERS-CoV). *MMWR Morb Mortal Wkly Rep* 2015;64:61-2.
12. Fehr AR, Perlman S. Coronaviruses: An overview of their replication and pathogenesis. In: Maier HJ, Bickerton E, Britton P, editors. *Methods in Molecular Biology*. Vol. 1282. Springer; 2015. p. 1-23.
13. World Health Organization. Rapid advice note on home care for patients with Middle East respiratory syndrome coronavirus (MERS-CoV) infection presenting with mild symptoms and management of contacts. 2013. Available from: <http://www.who.int>. [Last accessed on 2020 Sep 14].
14. European Centre for Disease Prevention and Control. Rapid Risk Assessment: Middle East respiratory syndrome coronavirus (MERS-CoV). 17<sup>th</sup> update. Stockholm: ECDC; 2015.
15. World Health Organization. Ebola virus disease in West Africa - the first 9 months of the epidemic and forward projections. *N Engl J Med* 2014;371:1481-95.
16. Kuhn JH, Becker S, Ebihara H, Geisbert TW, Johnson KM, Kawaoka Y, *et al.* Proposal for a revised taxonomy of the family Filoviridae: Classification, names of taxa and viruses, and virus abbreviations. *Arch Virol* 2010;155:2083-103.
17. Centers for Disease Control and Prevention (CDC). Ebola (Ebola Virus Disease) Transmission [Internet]. 2019. Available from: <http://www.cdc.gov/vhf/ebola/index.html>. [Last accessed on 2020 Sep 14].
18. Gonzalez JP, Pourrut X, Leroy E. Ebolavirus and other filoviruses. *Curr Top Microbiol Immunol*. 2007;315: 363-87.
19. Centers for Disease Control and Prevention (CDC). 2014-2016 Ebola outbreak in West Africa [Internet]. 2019. Available from: <https://www.cdc.gov/vhf/ebola/history/2014-2016-outbreak/index.html>. [Last accessed on 2020 Sep 14].
20. Centers for Disease Control and Prevention (CDC). Treatment [Internet]. 2019. Available from: <https://www.cdc.gov/vhf/ebola/treatment/index.html>. [Last accessed on 2020 Sep 14].
21. Busta ER, Mancher M, Cuff PA, McAdam K, Keusch G. Integrating Clinical Research into Epidemic Response: The

- Ebola Experience. Washington (DC): National Academies; 2017.
22. World Health Organization. Zika Virus Microcephaly and Guillain-Barré Syndrome Situation Report [Internet]. 2016. Available from: <https://apps.who.int>. [Last accessed on 2020 Sep 14].
  23. Knipe DM, Howley PM. *Fields Virology*. 5<sup>th</sup> ed. Lippincott Williams and Wilkins; 2007. p. 1156, 1199.
  24. Ayres CFJ. Identification of Zika virus vectors and implications for control. *Lancet Infect Dis* 2016;16:278-9.
  25. World Health Organization. Zika epidemiology update [Internet]. 2019. Available from: <https://www.who.int/emergencies/diseases/zika/zika-epidemiology-update-july-2019.pdf?ua=1>. [Last accessed on 2020 Sep 14].
  26. Hamzelou J. Zika vaccine trials begin - but fears remain over virus's impact [Internet] Wikipedia. 2016. Available from: [https://en.wikipedia.org/wiki/2015%E2%80%932016\\_Zika\\_virus\\_epidemic](https://en.wikipedia.org/wiki/2015%E2%80%932016_Zika_virus_epidemic).
  27. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, *et al.* Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2019;395:497-506.
  28. Chan JF, Yuan S, Kok KH, To KK, Chu H, Yang J, *et al.* A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: A study of a family cluster. *Lancet* 2020;395:514-23.
  29. U.S. Centers for Disease Control and Prevention (CDC). Symptoms of Coronavirus [Internet]. 2020. Available from: <https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html>.
  30. U.S. Centers for Disease Control and Prevention (CDC). How to protect yourself and others [Internet] CDC. 2019. Available from: <https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/prevention.html>.
  31. World Health Organization. Statement on the second meeting of the International Health Regulations (2005) Emergency Committee regarding the outbreak of novel coronavirus (2019-nCoV) [Internet]. 2020. Available from: <https://www.who.int>. [Last accessed on 2020 Sep 14].
  32. UNESCO. Education: From disruption to recovery [Internet] UNESCO. 2019. Available from: <https://en.unesco.org/covid19/educationresponse>.
  33. Kupferschmidt K, Cohen J. WHO launches global mega trial of the four most promising coronavirus treatments. *Science*. New York: AAAS; 2020.
  34. London School of Hygiene and Tropical Medicine. COVID-19 vaccine development pipeline [Internet]. Vaccine centre. 2020. Available from: <https://www.lshtm.ac.uk/research/centres/vaccine-centre/covid-19>. [Last accessed on 2020 Sep 14].
  35. World Health Organization. Draft landscape of COVID 19 candidate vaccines [Internet]. WHO. 2020. Available from: <https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines>. [Last accessed on 2020 Sep 14].
  36. Madhav N, Oppenheim B, Gallivan M, Mulembakani P, Rubin E, Wolfe N. Pandemics: Risks, Impacts, and Mitigation. In: Jamison DT, Gelband H, Horton S, Jha P, Laxminarayan R, Mock CN, Nugent R, editors. *Disease Control Priorities: Improving Health and Reducing Poverty*. 3<sup>rd</sup> ed. Washington (DC): The International Bank for Reconstruction and Development/The World Bank; 2017 Nov 27. Chapter 17. PMID: 30212163.
  37. Figueroa A, Gulati RK, Rainey JJ. Estimating the frequency and characteristics of respiratory disease outbreaks at mass gatherings in the United States: Findings from a state and local health department assessment. *PLoS One* 2017;12:e0186730.
  38. Pike BL, Saylor KE, Fair JN, Lebreton M, Tamoufe U, Djoko CF, *et al.* The origin and prevention of pandemics. *Clin Infect Dis* 2010;50:1636-40.
  39. Jones KE, Patel NG, Levy MA, Storeygard A, Balk D, Gittleman JL, *et al.* Global trends in emerging infectious diseases. *Nature* 2008;451:990-3.
  40. McCloskey B, Heymann D. SARS to novel coronavirus-old lessons and new lessons. *Epidemiol Infect* 2020;148:e22.
  41. Smith AW, Chiew CJ, Lee VJ. Can we contain the COVID-19 outbreak with the same measures as for SARS? *Lancet* 2020;20:102-7.
  42. World Health Organization (WHO). Influenza A (H1N1)-Travel [Internet]. WHO. 2009. Available from: [https://www.who.int/csr/don/2009\\_05\\_07/en](https://www.who.int/csr/don/2009_05_07/en). [Last accessed on 2020 Sep 14].
  43. Oh M-D, Park WB, Park S-W, Choe PG, Bang JH, Song KH, *et al.* Middle East respiratory syndrome: What we learned from the 2015 outbreak in the Republic of Korea. *Korean J Intern Med* 2018;33:233-46.
  44. Lee J, Kim WJ; Rapid Response Team. Collaborative intervention of Middle East Respiratory syndrome: Rapid Response Team. *Infect Chemother* 2016;48:71-4.
  45. Golding J. Ebola: How a killer disease was stopped in its track [Internet]. BBC News. 2018. Available from: <https://www.bbc.com/news/health-44872418>. [Last accessed on 2020 Sep 14].
  46. Carvalho DO, McKemey AR, Garziera L, Lacroix R, Donnelly CA, Alphey L, *et al.* Suppression of a field population of *Aedes aegypti* in Brazil by sustained release of transgenic male mosquitoes. *PLoS Negl Trop Dis* 2015;9:e0003864.
  47. Ferguson NM, Leydon D, Gilani GN, Nedjati-Gilani G, Imai N, Ainslie K, Baguelin M, *et al.* Impact of non-pharmaceutical interventions (NPIs) to reduce COVID-19 mortality and healthcare demand [Internet]. Imperial College COVID-19 Response Team. 2020. Available from: <https://www.imperial.ac.uk/media/imperial-college/medicine/sph/ide/gida-fellowships/Imperial-College-COVID19-NPI-modelling-16-03-2020.pdf>. [Last accessed on 2020 Sep 14].
  48. Srivastava N, Saxena SK. Prevention and Control Strategies for SARS-CoV-2 Infection. In: Saxena S. (eds) *Coronavirus Disease 2019 (COVID-19)*. Medical Virology: From Pathogenesis to Disease Control. Springer, Singapore. 2020. [https://doi.org/10.1007/978-981-15-4814-7\\_11](https://doi.org/10.1007/978-981-15-4814-7_11).