

Apocalyptic virus: The Silent Killer of an Era

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Abstract:

Emerging and re-emerging infectious disease has caused a deleterious effect in the world. Nearly 14 million people lost their lives by fighting against these diseases. These emerging infectious diseases can cause epidemics and pandemics. History itself has shown that viruses cause a lot of pandemics and caused a lot of destruction. These infectious agents will always be after humans to cause diseases. But we can hinder them through our scientific techniques. In 2015, WHO proposed the names of 10 potential viruses that can cause the next outbreak and pandemic. All of these viruses are those that once occurred in two decades and cause a lot of destruction. Some of them are still infecting humans. Surveillance plays a crucial role in detecting and responding to these infectious agents. Molecular technology, phylogenetic and phylogeographic analysis has revealed that by predicting these outbreaks we can hinder their chain of transmission. Genomic epidemiology is being used for the development of interventions and limiting the spread of these infectious diseases. World Health Organization and Global Outbreak Alert and Response Network have proposed a response system to affected countries. In case of an emergency outbreak, the team of GOARN is needed to reach those countries within 24 hours. There is some control measure which is being used to prevent the spread of existing outbreak and occurrence of a future outbreak.

Keywords: Pandemics, coronavirus, surveillance, phylogeographic analysis, genomic epidemiology.

1. Introduction:

Infectious disease has taken tons of lives and causes disastrous effect on the entire population. About 14 million deaths occur every year in developing countries due to these infectious diseases

[1].Between 1940 to 2004, more than 350 infectious diseases have arisen [2]. These emerging infectious diseases turn out to be a threat to the world. Amid these infectious agent, some are zoonotic viruses that emerge from animals and causes diseases to humans. The severity of the disease varies with each viral infection. Depending on the transmitting ability of the virus, it can either cause limited outbreaks that can lead to large epidemics or global pandemics[3]. The events of new emerging infections have been countless and diverse over the past two decades. These events not only include novel viruses like Severe Acute Respiratory Syndrome and Middle East Respiratory Syndrome and Coronavirus but also the known rivals that have reoccurred like Ebola and Zika virus that causes outbreaks or in worst cases pandemics[4][5][6][7][8]. If we look at history, we can find many outbreaks and pandemics that have resulted due to the spread of human-to-human infection. The most important characteristic of a pandemic comprises the broad geographical area, the transmission of disease, newness, severity, high incidence rate, low population immunity, and contagiousness. The catastrophe related to pandemics not only harms health, the economy, and society but also causes political and social obstruction [9]. The reappearance of a virus depends on some factors i.e., overpopulation, domestic travel, change in the pattern of land use, conflicts, and global warming[10]. The interaction between humans and the reservoir increases due to these factors that allows the viruses to remerge and spread more easily. Association between the virus genetics, ecology and the factors of the host is so convoluted that it is impracticable to know the causative agent of the next epidemic. Though the termination of an outbreak can be either natural or by limiting it but still need to retaliate it more with scientifically instructed, productive and vigorous techniques[11][12].

The study conveys the importance of awareness and preparedness. As we are surrounded by infectious viruses and they are going to cause more outbreaks and pandemics, we need to get ahead of them and prepare ourselves to combat them.

2. Snapshots of pandemics:

Pandemics have been accompanying the human race for a very long time from plaque to covid19. We have seen that pandemics due to infectious diseases are still following the human race and will accompany us in future as well. As a medical historian cited that " one pandemic will drive another". If a disease occurs together, it will take over the other disease. [2][13][14]. We can observe from history that how plaque took over leprosy in the first millennia. Afterwards, syphilis befell, and it ruled the world for the past half millennia. Then it was replaced by tuberculosis which

became a pandemic in the 17th century. Later in the 19th century, an outbreak of smallpox befalls and was declared a pandemic. Three pandemics; Spanish flu, Hong Kong flu and Asian flu which break out in the 20th century and wiped more than 20 million lives in the world [2][9][15][16]. After that HIV arrived and took nearly 35 million lives. Then HIV was followed by crucial epidemics of the new millennium i.e., SARS, Swine flu, Ebola epidemic, MERS and Zika epidemic which are still present. It was now the turn of pandemic of 21st century Covid-19 that is horrifying the whole world even today by taking a lot of lives as shown in table1. Hence, the world's archives are full of epidemics and pandemics but still, it does not abolish humankind. A lot of people might have been wiped out but still, humanity came up with new techniques and efforts to tackle it.[17][18]

Name	Causative agent	Death rate
Plaque	smallpox / measles	5 M
Japanese smallpox	Variola major virus	1 M
Black death	Yersinia pestis	200 M
Cholera	Vibrio cholera	> 1 M
Yellow fever	Virus/mosquitos	1-15 lac
Spanish flu	H1N1 virus	40-50 M
Asian flu	H2N2 virus	1.1 M
Hong Kong flu	H3N2 virus	1 M
AIDS	Virus / chimpanzee	23-35 M
Swine flu	H1N1 virus/ pigs	200,000
SARS	Corona virus	770

Ebola	Ebola virus	94,521
MERS	Coronavirus	850
Covid-19	Coronavirus	4,042,921 [19]

Table no 1: Major pandemics occurred over time.[18][20][21]

3. Potential pandemic causing pathogen:

List of infectious pathogens have been developed by different researchers and health experts in a meeting held on 10 December 2015 in Geneva in order to make preparation to prevent an outbreak. table2. The aim of developing the list of diseases was to provide an outline for Research and Development (R&D) preparation to combat with a future outbreak. This can be achieved by making therapeutic interventions, vaccines, diagnostic measures, besides focusing on development of behavioral therapy and covering the critical gaps in scientific theory. [22]

Pathogen	Disease name	Case fatality	Overview
Nairovirus (tick-borne virus)	Crimean Congo Hemorrhagic Fever	10%-40%	Crimean Congo Hemorrhagic Fever is a viral hemorrhagic fever with an incubation period of 1-13 days. It is normally transmitted through tick or by direct contact with animals having viremic tissues. It is endemic in Asia, Balkan, Middle East, and Africa and has the potential to cause an epidemic. It is very difficult to treat and prevent. Although antiviral drug ribavirin shows effective results[23][24].
Zaire Ebola Virus	Ebola virus disease	25%-90%	EBD is a severe and fatal disease whose an incubation period is 2-21 days. It is transmitted through wild animals, human-human direct contact, and contaminated materials. The 2014-2016 outbreak in west Africa was more disastrous comprising of more cases and deaths than all

			other outbreaks. It can be prevented by maintaining a proper hygiene . Currently there is no treatment for EBD but simple interventions i.e., oral or IV fluids can be proved effective. Medication is given to reduce specific symptoms like diarrhoea, vomiting and blood pressure. A vaccine named rVSV-ZEBOV is proved effective and is being used in the current outbreak in Congo[21][25]
Marburg virus	Marburg hemorrhagic fever	24%-88%	Marburg virus is responsible for causing deadly hemorrhagic fever with an incubation period of 2-21 days. It belongs to the same family as the Ebola virus and is responsible for causing outbreaks as well. A person might get this infection primarily, by continuous exposure to the Rousettus bat that inhabits the caves and mines. It is spread through human-to-human transmission and contaminated materials. although there is no treatment present for this disease, treating specific symptoms, supportive care and a range of immune therapies and drug therapies can improve the chances of survival. It can be prevented by community engagement, social mobilization, safe burials, and surveillance[26][27]
Lasa virus	Lasa hemorrhagic fever	1%-15%	Lasa hemorrhagic fever is a zoonotic disease caused by a single-stranded RNA virus that belongs to the family Arenaviridae. The virus uses a multimammate rat as a host. These rats do not get infected but release the virus in their faeces and urine. About 80% of cases are asymptomatic. Its, incubation period is 6-21 days. It can be transmitted sexually or by contacting contaminating objects and food. Lasa virus has caused endemic in Benin, Nigeria, and other West African countries. There is no vaccine for the disease, but the antiviral drug ribavirin shows effectiveness in

			treating the disease. we can prevent disease by following good hygienic protocols[28][29]
MERS-CoV	Middle East Respiratory Syndrome	35%	MERS is a zoonotic viral disease that was spotted in Saudi Arabia first in 2012. Dromedary camels are the reservoir of this virus. Though its origin is not completely known several genomic analyses have shown that bats have transmitted the virus to camels. The symptoms can range from asymptomatic to respiratory disease to death. Close contact with the infected patient may transmit the disease. direct and indirect contact with infected camels may also spread the infection. Currently, there is no vaccine and treatment present. But, it can be stopped by following general hygienic precautions[30][31]
SARS associated coronavirus	Severe Acute Respiratory Syndrome	14-15%	The disease SARS first started in China at the end of February 2003, then it spread to 29 other countries as well. The SARS virus is airborne and transmitted through small droplets just like influenza and cold. It was the very first transferable disease of the 21 st century that has transmitted across the path of air transportation. Its incubation period is 2-7 days. There is no treatment and vaccine for the disease yet, but the outbreak can be controlled by containment and preventive measures.[32][33][34]
Nipah virus	Nipah virus infection	40-75%	Nipah virus infection is a zoonotic disease 4-14 days and as long as 45 days. Fruit bats are natural reservoirs of this virus and the host cannot get the disease in either way if infected or inoculate experimentally. They are narrow ranged viruses that can infect dogs, cats, pigs, and humans. It can be transmitted from human to human directly or through contaminated food. the clinical manifestation ranges from no symptoms at all to respiratory infection

			(acute, mild, and severe) to fatal encephalitis. Since there is no vaccine and treatment for this disease, therefore, the infection can be controlled by following preventive protocols i.e., using PPE and avoid consumption of contaminated saps.[35][36]
Rift valley fever virus	Rift Valley Fever	<1% but 50% in patients with hemorrhagic fever	RVF is a zoonotic disease with an incubation period of 2-6 days. The virus belongs to the genus Phlebovirus and was first identified in the farm of Rift Valley of Kenya during an epidemic among sheep. The infection causes death and as well as abortion of livestock that results in significant economic loss. It can be transmitted by a vector i.e., mosquito bite commonly Aedes and Culex, direct or indirect contact with organs and blood of infected animals. No human-human spread is reported yet. The symptoms can vary from mild to the severe form. There is no treatment for patients having mild symptoms, but general supportive therapy is given to patients with severe symptoms. A non-licensed inactivated vaccine has been made and is used to protect livestock and laboratory personal from RVF infection. But it is not commercially available for other applicants. Vaccinating animals is the only way to prevent the disease in them. Following protective measures to avoid mosquito bite and also using PPE while contacting the livestock can reduce the risk of deaths and human infection.[37][38][39]
Chikungunya virus	Chikungunya	9.2% in 2017	Chikungunya is a mosquito-borne RNA virus that belongs to the genus alphavirus. It causes its first outbreak in 1952 in Tanzania. The infection is being reported in 40 countries. Mosquito Aedes aegypti and Aedes albopictus are responsible for its transmission. Once the mosquito gets infected it can spread the virus for entire life. Usually, its

			incubation period is 4-8 days, but it can range from 2-12 days. There is no drug treatment and vaccine for this infection. But clinical trials for a vaccine is going on which may take several years to become available for the public. Until then preventing oneself from a mosquito bite can protect people from getting the virus.[40][41][42][43][44]
Zika virus	Zika virus disease	8.3%-10.5%	Zika virus disease is a mosquito-borne disease with an incubation period of 3-14 days. It was first recognized in 1947 in monkeys in Uganda. In 1952 the first human cases were recognized in the United Republic of Tanzania and Uganda. Up till now about 86 countries have been reported cases of zika virus disease. infection during pregnancy results in causing microcephaly or another congenital abnormality in the fetus. The virus is transmitted by the Aedes genus of mosquito which is responsible for spreading chikungunya and yellow fever as well. There is no treatment or vaccine for this disease. Preventing mosquito bite is the only way to protect oneself from this disease.[45][46]

Table 2: List of pathogens that need urgent R&D attention**4. Outbreak prognostications:**

Epidemics have disastrous consequences i.e., unhealthy condition, high death rates, economical loss and social destabilization. Surveillance plays an important role in identifying and retaliating to epidemics minimizing their disastrous consequences[47]. According to CDC (center of control of diseases and prevention), about 60% of human infectious disease are zoonotic diseases. The worst global pandemics that have occurred, all originate from animals. Just like the bubonic plague that arises in rats and covid-19 that arise in pangolins and then transmitted to bats then to humans. We can prevent the spread of viruses from animal to human by tracking these zoonotic diseases. There are some approaches used by virus trackers to pinpoint animal diseases that can spread to humans.[48] Those approaches are as follows:

4.1 Breakout identification:

The outbreak starts when a doctor observes the symptoms that deviate periodically and in severity. At this time, the most important thing is to identify the causative agent of a disease. which can be done by using traditional methods (PCR, ELISA etc.), rapid diagnostic tests (CRISPER Cas 12/13), conventional methods (microscopy) and methods based on genome sequencing. Metagenomics has made it easy to detect viruses without having any previous information about them. The identification of virus makes us capable of answering some important questions like., (1) Is the virus novel? (2) Do we have strategies to combat it? The genomic epidemiology of the virus can provide the understanding of these questions more in-depth which cannot be achieved by using a conventional method. Phylogenetic analysis is also very important as it provides information about the origin of the virus, its evolutionary attributes, a link between previous outbreaks, the chain of transmission and possible host [8][49][50][51].

4.2 Tracing the chain of transmission:

The interconnection of the world leads to a wide range of disease epidemics in recent years. Most frequently from unforeseen sources, including SARS and MERS coronavirus [6][7], Influenza virus H1N1 [52], Ebola virus [8] [53] , Zika virus [5] and now SARS-Cov2 [54][55]. The chain of transmission of who is infected can be determined by sequencing the viral genome. By tracking the chain of transmission, we can reduce the spread of the outbreak. Traditionally this task is accomplished by interviewing the patients. The limitation of this technique is that it is time-consuming, and constrained accessibility and openness of the patients. This technique cannot be achieved in large outbreaks. In contrary to traditional methods, the genomic-based techniques can provide more information in-depth, as phylogenetic analysis can link the transmission of disease from one incident to the next [56]. The genome sequencing method was used to determine the identification and transmission of foot and mouth disease in the UK [57][58][59]. Genomic data along with the phylogenetic analysis performs an important role in providing information about the sudden outburst of the Western Ebola virus which was linked to Ebola survivors. Thus, revealing that the virus can transmit sexually [60][61][62]. Phylogenetic tree and complete genome sequencing data of Covid-19 virus has provided an insight about its reservoir and interspecies and

human-human transmission[63]. Not any of these information has been possible without genetic sequencing. The advantage of using viral genome depends on several factors that can deduce the chain of transmission of infection.

1. Mutational rate of the virus.
2. The period between the viral infection.
3. The number of infected samples [64][65]

Powerful tools that can reduce the amount of transmission are provided by viral epidemiological genomic data and provide new ways of transmission of disease [60][65][66][67].

4.3 Outbreak mapping:

As mentioned above, epidemiological data is very important for the detection of an outbreak as well as for identifying the foundation of viruses and their transmission pattern. The phylogeographic technique is used to construct a map about the history of viral spread from the place of an outbreak [65][68]. This technique plays an important role in providing information about the factors that are responsible for the spread of the virus. This technique depends on both metadata and other data\ sources that can provide information about host mobility, geographical, epidemiological and demographical context [65][69]. Phylogeographic analysis was used to identify the transmission of novel coronavirus around the globe (Fig.1)[70]. The first epidemiological map study was performed by Dr John Snow in 1854 in a cholera outbreak. He used both statistical data and a map to identify the cause of the outbreak. Besides the hand depicted map, epidemiologists now use a graphic information system (GIS) that has increased the outbreak inquiry and retaliation. Moreover, can portray complex information to the decision-maker and public simply and effectively [71].

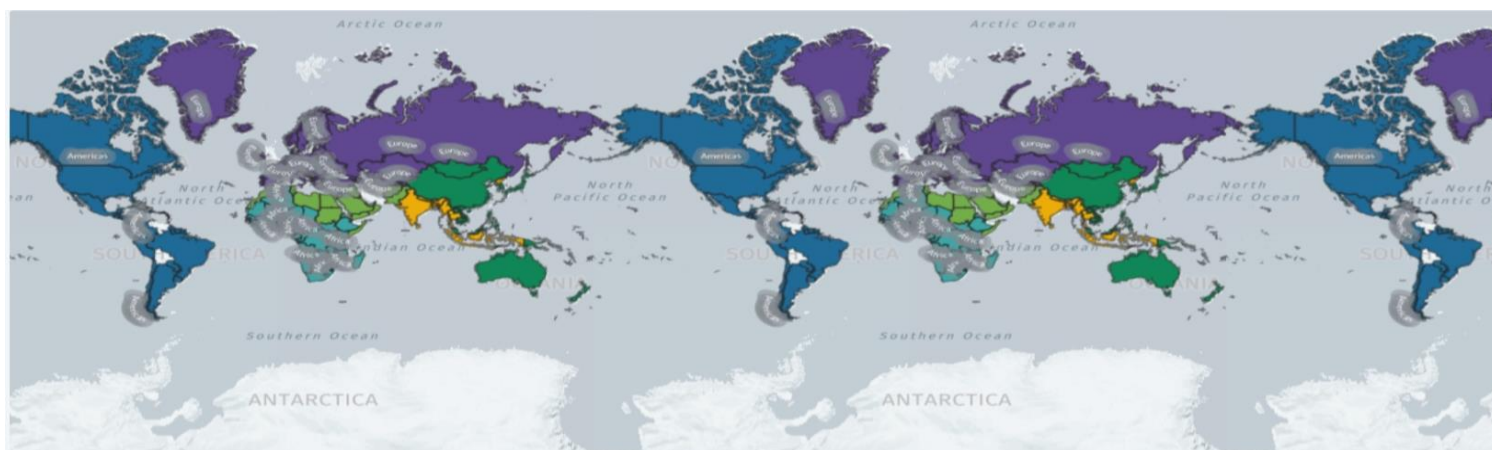


Figure 1: Spread of covid-19; determining the chain of transmission of covid-19 around the different region of the world . Data retrieved from WHO [19].

5. Response to an outbreak:

When an outbreak occurs the first response is to minimize its spread. There is a task force that works with health organizations and try their best to stop the next outbreak in the world [72]. Genomic epidemiology is used to provide intervention strategies for infectious disease. By using metadata, accurate sampling and statistical context, the genome of a pathogen shows its method of transmission in an outbreak. Therefore, allowing to development of the targeted intervention [55]. WHO provides a response system to affected countries. The resources needed for this response system is taken from WHO and Global Outbreak Alert and Response Network (GOARN). The GOARN teams are trained to reach the place of an outbreak within 24 hours. Since 2000 this international response system has been introduced in Afghanistan, Bangladesh, Burkina Faso, Cote d'Ivoire, Egypt, Ethiopia, Gabon, Kosovo, India, Pakistan, Republic of Congo, Saudi Arabia, Sierra Leone, Sudan, Tanzania, Uganda, and Yemen [73].

6. Preventing upcoming outbreak:

The threat of infectious disease is increasing every day, some of these diseases have re-emerged while some of them are novel. These diseases can cause massive destruction to areas having limited health resources and where appropriate detection is difficult [74] The disease can occur with a simple non-noticeable symptom but gradually it causes an epidemic and then pandemic. To prevent the world from the further infectious outbreak, some control measures should be followed.

6.1Non-drug treatment:

Non-drug treatment is the simplest control measure one can perform. It not only acts as the first line of defence but also is the only intervention when there is no other treatment available. It includes the basic hygienic protocols like washing hands, avoid socializing etc. This method is very effective in controlling the spread of contagious infections. Unluckily, these methods do not always work. If someone is attacked by an infectious disease, he should seek medical help. The Sooner the disease fades away, the easier it would be to control its spread.

6.2Quarantine:

When an infectious disease is detected, it is important to control its spread. The technique used to interfere with the chain of transmission is to separate the infected individual by quarantining him. During an outbreak, CDC has federal authority to call for quarantine. They have the authority

to close all the public areas to stop the spread of an outbreak. For example, in the case of novel coronavirus all the public places were called for lockdown [75][76].

7. Conclusion:

Zoonotic diseases have now become a threat to the world. Most of the 21st-century epidemics and pandemics occur due to zoonosis majorly involving viruses. These viruses are so small yet they can bring an apocalypse. Whether it is bubonic plaque or novel coronavirus, these apocalyptic microbes especially viruses have created a havoc. Due to various modern medical techniques a lot has changed which has rendered some of the disease agents weak to cause an outbreaks. Agencies like WHO and CDC all over the world are working hard to find a way to control these killer infectious diseases that have the potential of causing a pandemic. But it is not only the job of agencies to perform this task. Every human being should play their role to stop and prevent the existing and future outbreaks. Our community has a lack of knowledge, most of them do not know about the severity of the infectious disease. Government should start awareness campaigns to educate the public about the severity of infectious agents. The public should follow all the control measures they are asked to follow. The scientific community is already trying their best to protect us from these infectious agents. Day by day development in medical technology helps to improve the chances of living a healthier life. But is there any possibility that anthropogenic activities might be a reason for more outbreaks now than ever?

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References:

1. Dawson PM, Werkman M, Brooks-Pollock E, Tildesley MJ: **Epidemic predictions in an imperfect world: Modelling disease spread with partial data.** *Proceedings of the Royal Society B: Biological Sciences* 2015, **282**.
2. Gonzalez JP, Souris M, Valdivia-Granda W: **Global spread of hemorrhagic fever viruses: Predicting pandemics.** In *Methods in Molecular Biology*. . Humana Press Inc.; 2018:3–31.
3. Hall CM, Scott D, Gössling S: **Pandemics, transformations and tourism: be careful what you wish for.** <https://doi.org/10.1080/1461668820201759131> 2020, **22**:577–598.
4. Drosten C, Günther S, Preiser W, van der Werf S, Brodt H-R, Becker S, Rabenau H, Panning M, Kolesnikova L, Fouchier RAM, et al.: **Identification of a Novel Coronavirus in Patients with Severe Acute Respiratory Syndrome.** *New England Journal of Medicine* 2003, **348**:1967–1976.
5. Grubaugh ND, Faria NR, Andersen KG, Pybus OG: **Genomic Insights into Zika Virus Emergence and Spread.** *Cell* 2018, **172**:1160–1162.
6. Zaki AM, van Boheemen S, Bestebroer TM, Osterhaus ADME, Fouchier RAM: **Isolation of a Novel Coronavirus from a Man with Pneumonia in Saudi Arabia.** *New England Journal of Medicine* 2012, **367**:1814–1820.
7. Ksiazek TG, Erdman D, Goldsmith CS, Zaki SR, Peret T, Emery S, Tong S, Urbani C, Comer JA, Lim W, et al.: **A Novel Coronavirus Associated with Severe Acute Respiratory Syndrome.** *New England Journal of Medicine* 2003, **348**:1953–1966.
8. Holmes E, Dudas G, Rambaut A, Nature KA-, 2016 undefined: **The evolution of Ebola virus: Insights from the 2013–2016 epidemic.** *nature.com* [date unknown],
9. **Qiu W, Rutherford S, Mao A, Chu C. 2017. The pandemic... - Google Scholar.** [date unknown],
10. Grubaugh ND, Ladner JT, Lemey P, Pybus OG, Rambaut A, Holmes EC, Andersen KG: **Tracking virus outbreaks in the twenty-first century.** *Nature Microbiology* 2018 4:1 2018, **4**:10–19.
11. Holmes E, Rambaut A, Andersen K: **Pandemics: spend on surveillance, not prediction.** 2018,
12. Wolfe N, Dunavan C, Nature JD-, 2007 undefined: **Origins of major human infectious diseases.** *nature.com* [date unknown],
13. **Grmek MD, Fantini B. 1997. Histoire de la pensee... - Google Scholar.** [date unknown],
14. Habicht ME, Pate FD, Varotto E, Galassi FM: **Epidemics and pandemics in the history of humankind and how governments dealt with them A review from the Bronze Age to the Early Modern Age.** *rtsa.eu* [date unknown], doi:10.32049/RTSA.2020.2.03.
15. Fenner F, Henderson D, Arita I, Jezek Z, Ladnyi I: *Smallpox and its eradication.* [date unknown].
16. Organization HK-B of the WH, 2011 undefined: **The classical definition of a pandemic is not elusive.** *SciELO Public Health* [date unknown],

17. Gostin LO, Tomori O, Wibulpolprasert S, Jha AK, Frenk J, Moon S, Phumaphi J, Piot P, Stocking B, Dzau VJ, et al.: **Toward a Common Secure Future: Four Global Commissions in the Wake of Ebola.** *PLoS Medicine* 2016, **13**.
18. Grubaugh ND, Ladner JT, Lemey P, Pybus OG, Rambaut A, Holmes EC, Andersen KG: **Tracking virus outbreaks in the twenty-first century.** *Nature Microbiology* 2019, **4**:10–19.
19. **Coronavirus disease (COVID-19).** [date unknown],
20. **Infographic: The History of Pandemics, by Death Toll.** [date unknown],
21. **Ebola virus disease.** [date unknown],
22. **WHO | WHO publishes list of top emerging diseases likely to cause major epidemics.** *WHO* 2017,
23. **Crimean-Congo haemorrhagic fever.** [date unknown],
24. Raabe VN: **Diagnostic testing for Crimean-Congo hemorrhagic fever.** *Journal of Clinical Microbiology* 2020, **58**.
25. Jacob ST, Crozier I, Fischer WA, Hewlett A, Kraft CS, Vega MA de La, Soka MJ, Wahl V, Griffiths A, Bollinger L, et al.: **Ebola virus disease.** *Nature Reviews Disease Primers* 2020, **6**:1–31.
26. **Marburg virus disease.** [date unknown],
27. Ndjoyi-Mbiguino A, Zoa-Assoumou S, Mourembou G, Ennaji MM: **Ebola and marburg virus: A brief review.** In *Emerging and Reemerging Viral Pathogens: Volume 1: Fundamental and Basic Virology Aspects of Human, Animal and Plant Pathogens*. . Elsevier; 2019:201–218.
28. **Lassa fever.** [date unknown],
29. Warner BM, Safronetz D, Stein DR: **Current research for a vaccine against Lassa hemorrhagic fever virus.** *Drug Design, Development and Therapy* 2018, **12**:2519–2527.
30. **Middle East respiratory syndrome coronavirus (MERS-CoV).** [date unknown],
31. **Middle East respiratory syndrome coronavirus (MERS-CoV).** [date unknown],
32. **Severe Acute Respiratory Syndrome (SARS).** [date unknown],
33. Hui DSC, Zumla A: **Severe Acute Respiratory Syndrome: Historical, Epidemiologic, and Clinical Features.** *Infectious Disease Clinics of North America* 2019, **33**:869–889.
34. **WHO | Update 49 - SARS case fatality ratio, incubation period.** *WHO* 2015,
35. **Nipah virus.** [date unknown],
36. Ang BSP, Lim TCC, Wang L: **Nipah virus infection.** *Journal of Clinical Microbiology* 2018, **56**.
37. **Rift Valley fever.** [date unknown],
38. **Rift Valley Fever | CDC.** [date unknown],

39. Barbeau DJ, Albe JR, Nambulli S, Tilston-Lunel NL, Hartman AL, Lakdawala SS, Klein E, Duprex WP, McElroy AK: **Rift Valley Fever Virus Infection Causes Acute Encephalitis in the Ferret.** *mSphere* 2020, **5**.
40. **Chikungunya fact sheet.** [date unknown],
41. Chouin-Carneiro T, Vega-Rua A, Vazeille M, Yebakima A, Girod R, Goindin D, Dupont-Rouzeyrol M, Lourenço-de-Oliveira R, Failloux AB: **Differential Susceptibilities of *Aedes aegypti* and *Aedes albopictus* from the Americas to Zika Virus.** *PLoS Neglected Tropical Diseases* 2016, **10**.
42. Silva MMO, Tauro LB, Kikuti M, Anjos RO, Santos VC, Gonçalves TSF, Paploski IAD, Moreira PSS, Nascimento LCJ, Campos GS, et al.: **Concomitant Transmission of Dengue, Chikungunya, and Zika Viruses in Brazil: Clinical and Epidemiological Findings from Surveillance for Acute Febrile Illness.** *Clinical Infectious Diseases* 2019, **69**:1353–1359.
43. Goyal M, Chauhan A, Goyal V, Jaiswal N, Singh S, Singh M: **Recent development in the strategies projected for chikungunya vaccine in humans.** *Drug Design, Development and Therapy* 2018, **12**:4195–4206.
44. Gogia A, B S, Kakar A: **CHIKUNGUNYA: A Mortality Report.** *Open Forum Infectious Diseases* 2017, **4**:S518–S518.
45. **Zika virus.** [date unknown],
46. Da Cunha AJLA, De Magalhães-Barbosa MC, Lima-Setta F, De Andrade Medronho R, Prata-Barbosa A: **Microcephaly case fatality rate associated with Zika virus infection in Brazil.** *Pediatric Infectious Disease Journal* 2016, **36**:528–530.
47. WHO: **Mapping the risk and distribution of epidemics in the WHO African Region: a technical report.** [date unknown],
48. **Can we successfully predict the next pandemic?** [date unknown],
49. Coelho -The Alchemist P: **Towards a genomics-informed, real-time, global pathogen surveillance system.** *Nature Publishing Group* 2017, **19**.
50. Ziegler CM, Botten JW: **Defective Interfering Particles of Negative-Strand RNA Viruses.** *Trends in Microbiology* 2020, **28**:554–565.
51. Briese T, Paweska JT, McMullan LK, Hutchison SK, Street C, Palacios G, Khristova ML, Weyer J, Swanepoel R, Egholm M, et al.: **Genetic detection and characterization of Lujo virus, a new hemorrhagic fever-associated arenavirus from southern Africa.** *PLoS Pathogens* 2009, **5**:e1000455.
52. R.D. H: **NOVEL SWINE-ORIGIN INFLUENZA A (H1N1) VIRUS INVESTIGATION TEAM EMERGENCE OF A NOVEL SWINE ORIGIN-INF A(H1N1) VIRUS IN HUMANS.** 2009, **0**:2605–2615.
53. Baize S, Pannetier D, Oestereich L, Rieger T, Koivogui L, Magassouba N, Soropogui B, Sow MS, Keita S, De Clerck H, et al.: **Emergence of Zaire Ebola Virus Disease in Guinea.** *New England Journal of Medicine* 2014, **371**:1418–1425.

54. **Post-acute COVID-19 syndrome.** *nature.com* [date unknown],
55. Ladner J, Grubaugh N, Pybus O, medicine KA-N, 2019 undefined: **Precision epidemiology for infectious disease control.** *nature.com* [date unknown],
56. Hall M, ... MW-R scientifique et, 2016 undefined: **Using genomics data to reconstruct transmission trees during disease outbreaks.** *ncbi.nlm.nih.gov* [date unknown],
57. Cottam E, Haydon D, Paton D, ... JG-J of, 2006 undefined: **Molecular epidemiology of the foot-and-mouth disease virus outbreak in the United Kingdom in 2001.** *ncbi.nlm.nih.gov* [date unknown],
58. Cottam EM, Thébaud G, Wadsworth J, Gloster J, Mansley L, Paton DJ, King DP, Haydon DT: **Integrating genetic and epidemiological data to determine transmission pathways of foot-and-mouth disease virus.** *Proceedings of the Royal Society B: Biological Sciences* 2008, **275**:887–895.
59. Morelli MJ, Thébaud G, Chadœuf J, King DP, Haydon DT, Soubeyrand S: **A Bayesian Inference Framework to Reconstruct Transmission Trees Using Epidemiological and Genetic Data.** *PLoS Computational Biology* 2012, **8**.
60. Mate SE, Kugelman JR, Nyenswah TG, Ladner JT, Wiley MR, Cordier-Lassalle T, Christie A, Schroth GP, Gross SM, Davies-Wayne GJ, et al.: **Molecular Evidence of Sexual Transmission of Ebola Virus.** *New England Journal of Medicine* 2015, **373**:2448–2454.
61. Blackley DJ, Wiley MR, Ladner JT, Fallah M, Lo T, Gilbert ML, Gregory C, D'ambrozio J, Coulter S, Mate S, et al.: **E P I D E M I O L O G Y Reduced evolutionary rate in reemerged Ebola virus transmission chains.** *advances.sciencemag.org* [date unknown], doi:10.1126/sciadv.1600378.
62. Diallo B, Sissoko D, Loman N, ... HB-C infectious, 2016 undefined: **Resurgence of Ebola virus disease in Guinea linked to a survivor with virus persistence in seminal fluid for more than 500 days.** *academic.oup.com* [date unknown],
63. Shereen M, Khan S, Kazmi A, ... NB-J of advanced, 2020 undefined: **COVID-19 infection: Origin, transmission, and characteristics of human coronaviruses.** *Elsevier* [date unknown],
64. Duffy S, Shackelton L, Genetics EH-NR, 2008 undefined: **Rates of evolutionary change in viruses: patterns and determinants.** *nature.com* 2008, doi:10.1038/nrg2323.
65. Grubaugh N, Ladner J, Lemey P, ... OP-N, 2019 undefined: **Tracking virus outbreaks in the twenty-first century.** *nature.com* [date unknown],
66. Campbell F, Strang C, Ferguson N, Cori A, Jombart T: **When are pathogen genome sequences informative of transmission events?** *PLoS Pathogens* 2018, **14**.
67. Resik S, Kouri V: **Limitations to Contact Tracing And Phylogenetic Analysis in Establishing HIV Type 1 Transmission Networks in Cuba Preliminary survey of male circumcision in selected parts of Central and West Africa View project CMV Congenital infection in Cuba View project.** *liebertpub.com* 2007, **23**:347–356.
68. Faria N, Suchard M, Rambaut A, virology PL-C opinion in, 2011 undefined: **Toward a quantitative understanding of viral phylogeography.** *Elsevier* [date unknown],

69. Lemey P, Rambaut A, Bedford T, Faria N, Bielejec F, Baele G, Russell CA, Smith DJ, Pybus OG, Brockmann D, et al.: **Unifying Viral Genetics and Human Transportation Data to Predict the Global Transmission Dynamics of Human Influenza H3N2.** *PLoS Pathogens* 2014, **10**.
70. Rito T, Richards MB, Pala M, Correia-Neves M, Soares PA: **microorganisms Phylogeography of 27,000 SARS-CoV-2 Genomes: Europe as the Major Source of the COVID-19 Pandemic.** [date unknown], doi:10.3390/microorganisms8111678.
71. *Mapping for Surveillance and Outbreak Investigation.* [date unknown].
72. **Outbreak Response - The Task Force for Global Health.** [date unknown],
73. **WHO | Coordinated rapid outbreak response.** *WHO* 2020,
74. **Preventing epidemics and pandemics.** [date unknown],
75. **Recalls, Market Withdrawals, & Safety Alerts | FDA.** [date unknown],
76. **Preventing and Containing Outbreaks | National Geographic Society.** [date unknown],

