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Review Article

Pandemics Past Present and Future

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Abstract

The occurrence and extent of infectious ailments consisting potentials of pandemics have been seen a lot in the history. Global population has been effected by various major pandemics, including cholera, plague, flue, Middle East respiratory syndrome corona virus (MERS-CoV) and severe acute respiratory syndrome coronavirus (SARS-CoV). At present coronavirus disease known to be COVID-19 pandemic hit the globe badly.[1] Implementation and practice of public health measure like quarantine or isolation and controlling the movement through borders has remained helpful to contain the flow of diseases thus to maintain the optimum health conditions. Modern techniques of prompt diagnosis, contact mapping, drugs inventions and setting platforms in developing and production of vaccines are desired to respond the pandemics effectively. Outbreaks of sporadic infections have had serious and long lasting effects on people in the history. Such events badly affected social, political, and economical aspects of societies which last for centuries.[2] Few basic structures of contemporary medicine have been redefined in various epidemics which pushed the scientists to invent values and philosophies of epidemiology, antibiotic technologies and prevention through immunization.

Keywords: SARS-CoV, Plague, outbreaks, pandemics, Zika virus, Ebola Virus Covid-19

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Introduction

Capability of any infectious agent to communicably spread as rapidly, easily, and widely in various global proportions is termed as pandemic. Epidemic on the other hand vestiges limited to a country, region or city instead of spreading beyond national borders.[3] Epidemic is further considered in account of specific disease which spreads beyond the scientific estimates in a specific constituency. Since the upsurge occurrence of various health issues as compared to the estimates in different geographical settings is presented in terms of epidemic, pandemic, endemic and outbreaks.[4]

Occurrence of any condition at a predictable rate in a specific population is said to be endemic while an unpredictable escalation in counts of people suffering with a specified disease or appearance of disease in a new area with number of cases is called outbreak. In this view, occurrence an outbreak at a larger geographic areas is called epidemic which when covers many countries around the globe becomes pandemic. Scarce number spectacles have shaped the societies and cultures throughout the human histories as compared to the outbreaks, epidemics, endemics, and pandemics of infectious diseases even then this phenomenon could not get remarkable attention.

Throughout history, pandemic outbreaks have decimated societies, determined outcomes of wars, wiped out entire populations, but also, paradoxically, cleared the way for innovations and advances in sciences, economy, and political systems. Pandemic outbreaks, or plagues, as they are often referred to, have been closely examined through the lens of humanities in the realm of history, including the history of medicine.[5]

Any condition appears in new geographical settings and spreading in population is said emerging infection which may be zoonotic. Phenomenon of zoonosis explains the transmission of infections agents from animal to human through a pivotal mechanism and tormented human from centuries.[6] Transmission of pathogens is also influenced by climate changes (e.g. Zika virus, Chikungunya virus, Dengue virus, and Borrelia etc.) which involve vectors carrying infectious agents change their habitat especially mosquitos and ticks.[7] Various health concerns have been raised due to spread of different infectious diseases like cholera, tuberculosis and malaria etc in high proportion of people.[7]

Many infectios agents like Bacillus, Yersnia and Variola

virus etc. might be used as bio armaments thus constituting great threats for humanity. These weaponries may use both natural organisms and more virulent engineered microorganisms with high resistance and transmission properties.[8] These biological weapons are released to induce an intended diseases or death in humans. Infectious diseases pose a significant threat even in this era of modernization and pathogens bear properties of rapid transmission through travel or trade. Prediction and identification of such pathogens are desired to be focused by global surveillance to control the spillover and transmission. Present review is deliberated to discuss major pandemics which historically affected mankind like cholera, plague and influenza in the past and COVID 19 at present.

Few historical pandemics are presented in table below starting from 165 AC to date[1].

The Athenian plague

A historical pandemic of Athenian plague is a documented episode befalls in 430-26 BC during the War of Peloponnesian. Thucydides provided the history of Athenian plague, which was amongst the survivors and wrote History of the Peloponnesian war. Place of origin of Athenian plague was Ethiopia which then spread through Greece and Egypt. Primary signs of plague were presented to be fever, headache, conjunctivitis with a rash covering the body.[1,9] The plague patients then cough extruding blood, stomach cramping with extreme pain, vomiting and ineffectual retching attacks. Infected people would die in seven to eight days generally. Survivors on the other hand suffer from amnesia, partial paralysis or blindness for the rest of life. Healthcare professionals were caught the disease most often while attempting to heal patients. People in overcrowded regions were remained the hot target of plague and engulfed around 25% populations of such pandemic areas.

The Antonine plague

Outbreak of the Antonine plague was known to occure in 165-180 AD as documented by Galen and therefore also said to be the plague of Galen. This plague was originated from the Roman Empire during the sovereignty of Marcus Aurelius and smallpox is thought to be the main cause of this outbreak.[10] Soldiers returning from Seleucia were responsible to bring this plague in the Empire. Outbreak affected Italy, Greece, Egypt, and Asia Minor before ablation. The Antionine plague

Few Historical Pandemics are Presented in Table below Starting from 165 B.C to Date[1]

Name	Time period	Type / Pre-human host	Death toll
Antonine Plague	165-180	Believed to be either smallpox or measles	5M
Japanese smallpox epidemic	735-737	Variola major virus	1M
Plague of Justinian	541-542	Yersinia pestis bacteria / Rats, fleas	30-50M
Black Death	1347-1351	Yersinia pestis bacteria / Rats, fleas	200M
New World Smallpox Outbreal	1520 – onwards	Variola major virus	56M
Great Plague of London	1665	Yersinia pestis bacteria / Rats, fleas	100,000
Italian plague	1629-1631	Yersinia pestis bacteria / Rats, fleas	1M
Cholera Pandemics 1-6	1817-1923	V. cholerae bacteria	1M+
Third Plague	1885	Yersinia pestis bacteria / Rats, fleas	12M (China and India)
Yellow Fever	Late 1800s	Virus / Mosquitoes	100,000-150,000 (U.S.)
Russian Flu	1889-1890	Believed to be H2N2 (avian origin)	1M
Spanish Flu	1918-1919	H1N1 virus / Pigs	40-50M
Asian Flu	1957-1958	H2N2 virus	1.1M
Hong Kong Flu	1968-1970	H3N2 virus	1M
HIV/AIDS	1981-present	Virus / Chimpanzees	25-35M
Swine Flu	2009-2010	H1N1 virus / Pigs	200,000
SARS	2002-2003	Coronavirus / Bats, Civets	770
Ebola	2014-2016	Ebolavirus / Wild animals	11,000
MERS	2015-Present	Coronavirus / Bats, camels	850
COVID-19	2019-Present	Coronavirus – Unknown (possibly pangolins)	2.7M (Johns HopkinsUniversity) as of March 16, 2021)

spread across the enormous regions of whole Roman Empire, thus proven to be more lethal as compared to plague of Athens. This plague shattered as many as one third of the people in some areas, and reduced the roman arms with demise of Marcus Aurelius himself.[10]

The Three Plague Pandemics

The Justinian plague

The Justinian plague was the first real pandemic of plague caused by Yersinia pestis occurred in mid of the 6th century and supposed to be originated either in Ethiopia, evaded to Egypt or in Central Asia and journeyed with the routes of caravan trading.[11] The plague briskly spread from one of the mentioned localities and spread along Roman and beyond the world. Military movements along trading routes are also supposed to contribute in the spread of disease from Minor Asia to Italy, frica, and Western Europe. The Justinian plague epidemic is described as the earliest evidently documented instance reported by Evagrius, John of Ephesus and Procopius.[11]

The Black Death-Second Pandemic of Plague

This pandemic was originated in East Asia which spread through Central Asia and moved to Europe by various sea and land trading routes of medieval Silk Road. This pandemic was supposed to kill 200 million people and persisted till early 19th century in Europe.[12] The Black Death was also caused by lineages of Yersinia pestis and lasted during 1347-51 AD and responsible to kill as many as 30% of the European population. Further successive waves of this pandemic continued as in the names of Milan in 1630, The Great Plague of London during 1665-66 and Marseille plague during 1720-22. The Black Death and Justinian Plague emerged the human populations independently to make many encore rounds through Europe afterwards, occasionally destroying cities or whole societies but certainly not with the intensity alike The Black Death.[12]

Genetic epidemiological analysis of recent and ancient genomic analysis proposed that the plague wave was traveled from Europe towards Asia and eventually localized in China to originate the third pandemic of plague in mid of the 19th century started from Yunnan region of China, traveled through Canton to spread in Hong Kong. This pandemic then reached Singapore, Japan, India and Taiwan through sea routes, and presented endemic in plenty of countries around the globe. Thus the World Health Organization (WHO) classified plague as a re-emerging infectious disease since 1990's.

Spanish Flu Pandemic

Spanish flu occurred for the first time in the era of modern medicine, considering epidemiological studies, consisting specialties like infectious diseases with understanding of course of illness and nature of pandemics, initiated in February 1918 and lasted till April 1920 and outbreak is considered to be the first true pandemic. Spanish plague was the last pandemic presented devastated global consequences among societies across the world.[13] A strain of Influenza virus, known to be H1N1is a same strain reprise outbreak in the beginning of 21st century. The H1N1strain disseminated to everywhere in the world within months and in Europe, due to enormous military movements and overpopulation attributed to brisk spread, overwhelmed the USA, Africa, pacific islands and Asia.

Spanish flu also attributed a high mortality rate of around 10-20%, with more than a quarter of population in the world contracted the flue at some point, thus making the death toll well over 50 million ehich may be around 100 million demises. It is reported to kill more people in a year as compared to the Black Death killed in a century. Most of the young and health people were affected from Spanish flue. Main cause of death with Spanish flu is likely due to over activation and immense cytokine storm which overwhelmed to destroy the immune response. Thus the Spanish flu faded from global civilization quickly resulted in lack of scientific attention and established a precedent for the new pandemics and phrase as "forgottrn pandemic".[13]

Seven Cholera-Pandemics

Cholera is characterized to be an acute and fatal ailment of the gastrointestinal tract instigated by Vibrio cholera. Until 1817, cholera was endemic in Asia when first pandemic launched from India to many other regions in the world. Afterwards, five superfluous main cholera pandemics, also originated from India, spread many other countries during 19th and 20th centuries. Essential health prevention strategies at that time were the same as implemented during pandemic of Black Death.[14] Lazarettos were built to quarantine infected individuals. Contacts of infected persons and travelers coming from cholera endemic areas were essentially quarantined.

Outbreak of Smallpox

A highly contagious disease of smallpox became the reason of development of first vaccine in 1789. This disease was caused by Variola virus, highly contagious characterized by protruding skin eruptions with a high mortality rate of around 30%. It is responsible to cause hundreds of millions fatalities alone during twentieth century. A well-coordinated global effort was started in 1967, which was led by Donald Henderson and smallpox was eradicated from the world within a decade.[15]

Another outbreak of smallpox was observed in1972 in Yugoslavia as an epidemic presented with problems

of rapid spreading with highly contagion ailment in the modern era. Skin eruption and fever was observed among pilgrims returning from Middle East, where not a single case of smallpox was observed in last 30 years. Physicians failed to diagnose it correctly led to 9 demises of healthcare workers among 38 cases infested from index patient and first causality. Around ten thousand suspects and possible contacts were quarantined, borders were closed and undue travel was deferred.[15] more than 18 million population of Yugoslavia was revaccinated within two weeks. An immense and prompt response of the authorities subjected to eradicate the outbreak to normalize the society within two months only.

Influenza Pandemic

Influenza is caused by Orthomyxoviridae family known to have negative sense, single stranded RNA in an envelope. Influenza virus are responsible for 3-5 million sever ailment cases with around 0.5 million global fatalities during a typical seasonal epidemics. First well documented pandemic with Russian flu was originated during 1889-93 with a median clinical attacj rate of 60%.[16] Spanish flu was caused by A/H1N1 is also considered by genetic variation of prevailing influenza virus to new human host. A mild influenza pandemic was observed during 1968-70. A simultaneous outbreak with influenza virus was started in Southern United States and Mexico during 2009 which spread in the world within six weeks. This was for the first time when antiviral and vaccines were used simultaneously amongst isolated contacts and symptomatic patients.[16]

HIV Pandemic

Human immunodefficient virus (HIV) causes acquired immunodefficiency syndrome (AIDS) started in the USA during 1980s and progressing slowly to affect various populations in global pandemic. Initially HIV was supposed be sporadic among gay partners with mortality rates, leading to obvious stigma due to social isolation. Around 40 million people are affected from HIV and same numbers have been killed since 1981.[16] The epidemic of HIV is specially alarming in few Sub-Saharan African territories with a tope prevalence rate of almost 25%. Around 12000 people die with HIV in USA amongst around 1.2 million patients.[17]

SARS-CoV Epidemic

Epidemic of SARS-CoV was originated Guangdong province of china in 2003. Bats are considred possible natural carriers of SARS-CoV. Disease was identified within few weeks of occurrence and outbreak was reported to be present in 29 countries of Asia, Europe, North and South America. Total reported number of cases was 8437 with 813 demises presenting a mortality rate of 9.7%. Nosocomial and close family contacts are the victims of easy transmission by SARS-CoV.[18] Infection typically present influenza like syndrome to cause atypical pneumonia and shortness of breath. SARS-CoV outbreak was eradicated within seven months, however similar virus are observed to be present in bats indicating reemergence of disease in future.

Swine flu H1N1/09 Pandemic

Swine flu pandemic with H1N1 occurred in 2009, was reappearance of Spanish flu, but with minute shattering consequences comparatively. Infectious agent is considered to be generated by re-assortment of human, bird and swine flu viruses and colloquially said to be swine flu.[19] Outbreak started in Mexico during April 2009 and achieved pandemic in few weeks. It lasted up till May 2010 and considered to infect 10% people around the world with a varied range of deaths from 20 thousand to over 0.5 million.[19]

MERS-CoV Epidemic

One decade after the first epidemic of SARS-CoV, another outbreak with MERS-CoV was observed in city Jeddah of Saudi Arabia where camels are suggested to be dromedary host with bats as natural reservoir. This was started in 2012 and diagnosed in 2519 cases with at least 866 deaths till 2020 in about 27 countries. All the cases of MERS-CoV are connected to the people in Arabian Peninsula or individuals returning from endemic areas. Nosocomial transmission is considered as the most probable route and infection causes' lethal pneumonia along renal dysfunction and other clinical symptoms.[20]

Ebola Outbreak

Endemic with Ebola virus was originated in West and Central Africa during December 2013 from fruit bats with first outbreak in Guinea village. Disease spread amongst families and reported in about 28000 cases with over 11000 demises hence controlled till 2016.[21]

Zika Outbreak

Zika virus was scarcely known found to be present in the rhesus monkeys in Uganda. Afore 2014, the only known outbreak with this virus was reported during 2007 in Micronesia. Identification of this virus was done in Brazil during 2015 in which patient present dengue like symptoms. Although it is mosquito born disease, but reported to sexually transmitted also. Initially it remained unremarkable due to mild course but tragically proved to cause Guillain-Barre syndrome and severe microcephalia among developing infants of infected mothers.[22] Almost 2400 birth defects were observed in Brazil during 2015 with 29 suspected Zika infection deaths in infants.[22] Zika is still an important

public health threat due to unavailability of vaccine. Infection has spread in Central and south America, Caribbean and other states of USA since 2016.

SARS-CoV-2 Pandemic

Outbreak of SARS-Cov-2 was appeared in Wuhan city of China in December 2019 amongst a cluster of patients presenting with atypical pneumonia was then diagnosed as new Coronavirus[23] and therefore known as COVID-19. Infection with SARS-CoV-2 remains asymptomatic in about 40% cases while causes wide spectrum of ailment from mild to life threatening sickness.[23] A variety of symptoms including high grade fever, cough, shortness of breath, myalgia, fatigue, abdominal symptoms, headache, rhinorrhea, weakness, ageusia and anosmia appear in patients. Infection with SARS-CoV-2 may leads to variety of complications like pneumonia, liver & cardiac injuries, acute kidney failure, prothrombotic coagulopathy, neurologic manifestations and acute respiratory dysfunction syndrome. A cytokine storm develops in some critically ill patients which leads to macrophage activation syndrome.

Most of 60-90% hospitalized patients present with comorbidities like diabetes, hypertension, cardiovascular disease, chronic kidney, liver or pulmonary disease and malignancy. Around 80% laboratory confirmed cases present with no or mild symptoms while 14-19% is hospitalized and 3-5% require intensive care due to hypoxia or respiratory failure. Mortality rate amongst hospitalized patients is around 15-20%. Global estimated mortality rate remained to be 0.25-3%.[24] Various vaccines are developed against COVID-19 and around 16 vaccines were authorized by at least one national regulatory authority for public showing a highest efficacy of 95% till the end of April, 2021. Most of these are conventional inactivated vaccines while few are based on viral vector vaccination technique and rest is RNA vaccines and protein subunit vaccines. Around 1.53 billion doses of COVID-19 vaccine have been administered globally till the mid of May, 2021.

Conclusion

A serious threat has been posed by globalization of trades and travel of animals and animal products nowadays as potential carrier of diseases. Habitats of pathogens also have been modified due to urbanization and acquiring agricultural land for accommodations which ultimately modified dynamics of disease transmission and infections to mankind.[25] Water sanitation and hygiene (WASH) program has been launched by WHO in developing countries to limit the transmission of water-borne infections like Vibrio cholera. Primary tool to limit the dengue, malaria, zika and chikengunya is vactor control.

Pandemic preparedness plans must be emphasized as the time for onset of pandemic by pathogens is unpredictable. Human to human and zoonotic transmission protocols need to understand in depth and preventive interventions must be implemented. Healthcare interventions considering diagnostic facilities, rapid point of care and new setups to accelerate vaccine production are needed to uplift the global response against pandemics.

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