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## Chapter 4

# Ebola Virus Disease Epidemic in Light of Other Epidemics

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All epidemics are based on an outbreak of disease caused by virus or bacteria, which might or might not be new to humans, and spread through various methods, ranging from contaminated food to person-to-person transmission.

## COMMON FEATURES OF EPIDEMICS

According to previous research,<sup>1,2</sup> several factors can start an epidemic including the following:

1. Disasters (e.g., wars, famine, floods, and earthquakes)
2. Temporary population settlements
3. Preexisting diseases in the population
4. Ecological changes like floods and cyclones
5. Resistance potential of the host (i.e., nutritional and immunization status of the host)
6. Damage to public utility and interruption of public health services

There are three patterns of disease continuity in epidemics. The “sawtooth” pattern is where there are intermittent outbreaks of a disease that recede in intensity, but the disease is not eradicated from the population. The smallpox epidemics in Africa during the 1920s–1950s would be an example of such a pattern. The “tooth necklace” pattern is where the disease is eradicated from the population, but pathogen species is kept alive under controlled circumstances for preparation of vaccines and biological studies. While the escape of pathogen from confinements of laboratories has been the subject of numerous conspiracy theories, vaccination with live attenuated viruses is more likely to be the string to maintain the continuity.

The third pattern is the “tooth eruption” pattern where, like the tooth hidden within the gums and emerging independent of other teeth, the pathogen emerges and is exterminated without any relation to previous occurrences. The Ebola virus is one of the pathogens following the “tooth eruption” pattern where the disease emerged in Sudan and the Democratic Republic of Congo (DRC) in 1976, disappeared, and then reemerged in Uganda between September 2000 and February 2001, only to mysteriously disappear. It emerged again in December 2013 in Guinea.<sup>3</sup>

What is far more perplexing is why epidemics die their deaths, a phenomenon noticed since the beginning of humanity. While it is convenient to believe that measures such as vaccination of at-risk individuals, quarantine of diseased persons, and acute and timely treatment are the cause of epidemic eradication, the facts do not support such a conclusion. In fact, the largest epidemics, such as the Peloponnesian War Pestilence, Antonine Plague, Plague of Justinian, Black Death of the fourteenth century, and Spanish flu, came to an end without widespread use of any of those strategies.

There are three main theories for the spontaneous remission of epidemics:

1. There are two types of people within the exposed population: some more vulnerable and some more resistant. The people who may be resistant to the disease may be so because of previous exposure to viruses with similar structures resulting in the development of immune responses that are adequate for multiple pathogens. They might also be resistant due to superior health, including age and nutritional, and occupational advantages. The virus might eventually be faced with a population that is completely resistant to the infection.

2. Changing environment within habitats that are not conducive to the survival or propagation of viruses or other pathogens. Weather changes, including temperature and humidity fluctuations, may significantly influence the survival or propagation of a virus outside the body. Elimination of reservoirs that carry pathogens including animals, insects, food, or water, by chance or design, may disrupt the cycle of propagation. Such elimination of infection is less likely to occur within an epidemic because of diverse factors and geographical areas involved.
3. The most likely explanation is the “Sand Filter Theory,” a term coined by Adnan I. Qureshi, MD. This theory reflects the similarity between retention of particulate matter during filtration based on density of sand particles, which can be compared to pathogens within a population based on population density. Most epidemics are composed of diseases that require close contact between diseased and healthy individuals for continued propagation of pathogens. Unlike natural disasters, such as hurricanes, floods, volcanoes, and changes in climate that exist independent of population density, epidemics depend upon population density, a feature shared with reproduction rates, migrations, and predation. After population density reduces below a critical limit, such contact may not be available enough for continued propagation of pathogens.

## **SPANISH FLU EPIDEMIC (1918–1920)**

One of the most monumental of twentieth-century epidemics, the “Spanish flu” influenza pandemic in 1918, infected 25–30% of world’s population and resulted in death of almost 40million people.<sup>4</sup> The world had seen flu epidemics before. The influenza epidemic occurred in Europe in 1580s, started in Russia and spread to Continental Europe and Africa followed by another epidemic in 1743.<sup>5</sup> A more devastating flu epidemic happened in 1830–1833. The term “Spanish flu” was a misnomer because the disease did not originate in Spain. The disease was rampant in Germany, Britain, France, and the United States; wartime censors minimized early reports of illness and mortality in these countries.<sup>6</sup> During the 1918 flu pandemic, Spain’s king, Alfonso XIII (1886–1931), became very ill. His illness and recovery from the disease was reported to the world because Spain was neutral and was not under wartime censorship restrictions, while outbreaks of flu in other belligerent countries were concealed. This created the wrong impression that Spain was most affected and caused the pandemic dubbed as the “Spanish flu.”<sup>7</sup> Even President Woodrow Wilson (1856–1924) reportedly contracted the flu in early 1919 while negotiating the Treaty of Versailles, which ended World War I.<sup>8</sup>

The epidemic appeared in two phases. The first one appeared in late spring of 1918, known as the “3-day fever,” without any warning and resulted in few deaths and victims recovered after a few days. The typical symptoms of the flu were chills, fever, and fatigue resulting in a low number of deaths. During that same year in the fall, however, a highly contagious and deadly wave of influenza emerged. Victims

died within hours or days of symptom onset. Their skin turned blue, and patients' lungs filled with fluids. The flu did not discriminate between rural and urban areas ranging from densely populated East Coast to sparsely populated parts of Alaska. Young adults were among the hardest hit group, a group that usually remains unaffected by this type of epidemic. About 25% of the United States was affected within 1 year and resulted in a drop of 12 years in United States life expectancy.<sup>9</sup>

## SPANISH FLU AND EBOLA VIRUS DISEASE PANDEMICS

There were similarities between the flu epidemic of 1918 and current Ebola virus disease epidemic. The 1918 pandemic mostly killed healthy, young individuals compared to most influenza outbreaks that killed juvenile, elderly, or already weak patients. In this regard, the Spanish flu epidemic shares the same age range of most affected population subset with Ebola virus disease epidemic. Older adults may have had partial protection in 1918 from their earlier exposure in 1889–1890 flu epidemic, but it is unclear whether older adults during the Ebola virus disease outbreak had partial exposure to Ebola virus infection. Both epidemics share the unique vulnerability of pregnant women to infection. The fatality of Spanish flu virus was attributed to cytokine storm, a consequence of excessive stimulation and activity of the immune system.<sup>10</sup> An overactive immune system has been implicated in tissue injury seen in Ebola virus-infected patients as well. Younger patients have a more robust immunological response, which might explain the higher vulnerability and fatality seen in this age group during both the flu epidemic and Ebola virus disease epidemic. Another oddity was that the Spanish flu outbreak was widespread in the summer and autumn, which is a similar pattern seen with Ebola virus infection epidemic. Open quarters and outdoor dwelling permitted by warm weather did not reduce the incidence of either disease.

There were notable differences between the flu epidemic of 1918 and current Ebola virus disease epidemic. The Spanish flu epidemic had the necessary prerequisites for an epidemic. Massive troop movements and close quarters during World War I accelerated the epidemic, probably increasing transmission and the mutation. The virus' lethality might have been increased by war. These soldiers' susceptibility might have been increased by their immune systems weakening through malnourishment, stresses of combat, and chemical attacks.<sup>11</sup> The patterns of influenza pandemics have many atypical features. Pandemic emergence can follow one of these two patterns: *de novo* emergence of completely unique avian-descended virus or modification of a circulating human-adapted virus by importation of a novel neuraminidase (NA) (e.g., the 1957 H2N2 pandemic) via genetic assortment, of a novel HA hemagglutinin (HA), either with concomitant importation (e.g., the 1968 H3N2 pandemic).<sup>12</sup>

France was at the center of 1918 flu pandemic with a major troop staging and a hospital camp in Étampes identified by a British team's investigative work. This team was headed by a virologist John Oxford from St Bartholomew's Hospital and the Royal London Hospital. The virus was harbored in the birds there that mutated and passed on to pigs, kept near the front line.<sup>13</sup> During World

War I, 96,000 Chinese laborers were mobilized to work behind the British and French lines on the Western Front. This high population density could be the cause of the pandemic. In a recent report, Humphries found archival evidence that a respiratory illness struck Northern China in November 1917, identified by Chinese officials as identical to Spanish flu a year later.<sup>14,15</sup> But the Ebola virus disease epidemic did not have any identifiable predisposing causes.

## FINDING THE CULPRIT BEHIND THE PANDEMIC

Unlike the discovery and characterization of the Ebola virus in the 1970s aided by modern marvels such as electron microscopes, the influenza virus evaded researchers for decades. During the 1892 influenza pandemic, German physician Richard Pfeiffer isolated bacteria from lungs and sputum of influenza patients and labeled bacteria as the cause of influenza. Bacteria came to be known as Pfeiffer influenza bacillae and later *Bacillus influenzae* (*Haemophilus influenzae*). However, the controversy continued because strains of streptococcal, pneumococcal, and other bacteria could be found in sputum of patients suffering from the flu, and *B. influenzae* could not be found in samples from many patients with influenza. *Bacillus influenzae* could be found in healthy individuals and in those patients suffering from measles, scarlet fever, diphtheria, and varicella (chicken pox). In one article, the authors wrote “There seems to be no justification for the belief that the epidemic was due to the influenza bacillus, which is probably a secondary invader and bears about the same relation to the influenza cases as to respiratory infections of a different sort.”<sup>16</sup>

In 1918, veterinarian J.S. Koen noted similarities of influenza symptoms in pigs while he was treating the symptoms of Spanish flu epidemic in humans. In 1928, researchers N. McBryde and Robert Shope carried out experiments to identify the transmission mechanism of influenza in pigs. They took mucus from infected pigs using bacterial filters to remove any bacteria and then inserted virus-loaded mucus into healthy pigs’ nostrils to infect them. McBryde failed, but Robert Shope succeeded in transmitting the infection. His experiments finally proved that the influenza infection was indeed due to a virus.<sup>5</sup>

Finally, in 1933, researchers Wilson Smith, Christopher Andrews, and Patrick Laidrow identified the influenza virus in humans.<sup>5</sup> In the decades to come, the complete genome of the influenza virus would be characterized from a virus derived from the lung tissue of 1918 influenza epidemic victims. The tests showed that the pandemic virus contained genes derived from avian-like influenza virus strain.<sup>4</sup> Almost 90 years later, in December, a University of Wisconsin researcher, Yoshihiro Kawaoka reported that three genes (termed PA, PB1, and PB2) had been identified within the genome of the influenza virus from 1918 (isolated from lung and brain tissue samples of British politician and diplomat, Sir Mark Sykes).<sup>17</sup> These genes enabled the virus to produce three different types of proteins within infected cells, weakening the protective lining of the victim’s bronchial tubes and lungs and clearing the way for bacterial pneumonia.

An enzyme, neuraminidase, enhances bacterial growth and bacterial dissemination.<sup>18</sup> A second proapoptotic protein enhances the inflammatory response by unclear mechanisms.<sup>18</sup> And a third protein increased the production of interleukin-10 (IL-10), reducing the function of white blood cells in the lungs.<sup>18</sup>

## DEVELOPMENT OF VACCINES AND THE QUAGMIRE OF PSEUDOVACCINES

We have the same challenges in developing a vaccine against Ebola virus that we had against influenza virus. While initial challenges faced by researchers were predominantly due to lack of identification of the appropriate causative organism, this issue will not trouble modern-day researchers. William H. Park, MD, from New York City Health Department, was convinced that *B. influenzae* was the cause of the outbreak and he set about devising a vaccine and antiserum against it. This antiserum was completed on October 17, 1918. In Philadelphia, Paul Lewis worked on refining the pneumococcal vaccines. As a result, Philadelphia municipal laboratory released thousands of vaccines (a mix of streptococcal, pneumococcal, and *B. influenzae*) on October 19, 1918. Physicians at the Naval Hospital on League Island, Pennsylvania (the Philadelphia Naval Shipyard) made the vaccine from *Micrococcus catarrhalis* (now *Moraxella catarrhalis*) and *B. influenzae* and strains of *Pneumococcus*, *Streptococcus*, *Staphylococcus*. Each vaccine, administered in four dose regimens, contained 100,000,000 and 200,000,000 bacteria per cubic centimeter. These scientists noted that nonvaccinated individuals and health-care workers became sick even though strict preventive measures like use of masks and gloves were taken. From the group of ill patients vaccinated therapeutically, no one developed pneumonia-like symptoms like those seen in the unvaccinated group. Investigators noted,

*The course of the disease [in those treated therapeutically]...was definitely shortened, and prostration seemed less severe. The patients apparently not benefitted were those admitted from four to seven days after the onset of their illness. These were out of all proportion to the number of pneumonias that developed and the severity of the infection of the control cases. The effects were always more striking the earlier the vaccine was administered.*<sup>16</sup>

Finally, they concluded, “The number of patients treated with vaccines and the number immunized with it is entirely too small to allow of any certain deductions; but so far as no untoward results accompany their use, it would seem unquestionably safe and even advisable to recommend their employment.”<sup>16</sup>

In San Francisco, another group of researchers studied vaccines use. They mentioned that Spanish influenza did not reach San Francisco until October 1, 1918, therefore, staff at the training station had enough time to prepare a prophylactic vaccine even there was a great debate as to the pandemic’s cause.<sup>16</sup> The vaccine was made of *Streptococcus hemolyticus* (*Streptococcus pyogenes*), 100million, *B. influenzae*, 5billion bacteria; *Pneumococcus* types I and II, 3billion

each and Pneumococcus type III, 1 billion bacteria. It was first tested in guinea pigs and then five laboratory volunteers. After vaccination, the serum from the Guinea pigs and volunteers agglutinated when mixed with *B. influenzae* in vitro (meaning that their blood had antibodies that reacted with the bacteria). The vaccine was administered to 11,179 military personnel and civilians, including some at Mare Island (Vallejo, CA), San Pedro, and San Francisco associated with Naval Training station. In vaccinated personnel, the rate of influenza was lower compared to rates seen in unvaccinated persons. The rate of influenza in the control group was 1.5–33.8% and in the vaccinated group was 1.4% and 3.5%.

Another vaccine was used in Washington, USA, at the Puget Sound Navy Yard,<sup>17</sup> where 4212 people were vaccinated with streptococcal bacteria-derived vaccine. The rate of influenza in vaccinated persons ranged from 2% to 57% and 1.8% to 19.6% in those who received the vaccine. Investigators stated, “We believe that the use of killed cultures as described prevented the development of the disease in many of our personnel and modified its course favorable in others.”<sup>16</sup> They noted that *B. influenzae* did not play any role in the outbreak.

The use of mixed bacterial vaccine was reported by E. C. Rosenow (Mayo Clinic) in Rochester, Minnesota. In the initial study, three doses of vaccine were given to 21,000 people. He concluded that,

*The total incidence of recognizable influenza, pneumonia, and encephalitis in the inoculated is approximately one-third as great as in the control uninoculated. The total death rate from influenza or pneumonia is only one-fourth as great in the inoculated as in the uninoculated.*<sup>16</sup>

He decided to test his vaccine in nearly 100,000 people.<sup>16</sup> The results of such studies, however, were viewed with caution and skepticism. The medicine editors of the *Journal of the American Association* cautioned “the data presented are simply too inadequate to permit a competent judgment” about vaccine effectiveness in an editorial entitled “Prophylactic Inoculation Against Influenza,”<sup>16</sup> in particular, they addressed Rosenow’s paper as follows:

*To specify only one case: The experience at a Rochester hospital—where fourteen nurses (out of how many?) developed influenza within two days (how many earlier?) prior to the first inoculation (at what period in the epidemic?), and only one case (out of how many possibilities?) developed subsequently during a period of six weeks—might be duplicated, so far as the facts given are concerned, in the experience of other observers using no vaccines whatever. In other words, unless all the cards are on the table, unless we know so far as possible all the factors that may conceivably influence the results, we cannot have a satisfactory basis for determining whether or not the results of prophylactic inoculation against influenza justify the interpretation they have received in some quarters.*<sup>16</sup>

In the 1930s, researchers finally concluded that influenza was, in fact, caused by a virus and not a bacterium. At the University of Michigan, Thomas Francis Jr. and his team of researchers along with U.S. army made a vaccine by



using killed cells through stimulating body's specific immunity against influenza virus, two decades later in 1944. The virus loses its virulence when cultured in fertilized hen's eggs showed by Thomas Francis Jr. Earlier work of Frank Macfarlane Burnet became the basis for Thomas Francis Jr.'s effort.<sup>5</sup>

The story of vaccine development may have lessons for investigators involved in vaccine development for the prevention of Ebola virus disease. A 2010 article described the performance of 13 bacterial vaccine studies conducted from 1918 to 1919. The authors concluded that, despite the limited number of bacterial strains in the vaccines, the pneumonia attack rate could have been reduced by some vaccines after viral infection through cross-protection from multiple related strains.<sup>11</sup> Vaccinologist Stanley A. Plotkin, MD, was more skeptical and posits, "the bacterial vaccines developed for Spanish influenza were probably ineffective because at the time it was not known that pneumococcal bacteria come in many, many serotypes and that of the bacterial group they called *B. influenzae*, only one type is a major pathogen."<sup>16</sup> In another sense, vaccine developers had limited ability in identifying, isolating, and producing all potential disease-producing strains of bacteria. Today's pneumococcal vaccine is protective against 13 serotypes, and the adult vaccine protects against 23 serotypes of that bacteria.<sup>16</sup>

There are similar concerns with the Ebola virus that, due to fulminant spread and viral replication, several serotypes of the virus may exist. When DNA is copied in a cell, enzymes called "polymerase" do the building, adding nucleotide after nucleotide until the DNA is copied. Normally, cellular machinery proofreads the DNA, getting rid most of the bad copies, and keeping the mutation rate very low. But, when a virus like Ebola or influenza hijacks the cell to make copies of itself, it uses the host RNA polymerases. RNA polymerases make copies of genes in the DNA in the form of RNA, which is then read by the cell protein factories (ribosomes) to assemble proteins. Unfortunately, RNA polymerases do not proofread well, so lots and lots of mutations slip through. That is the reason flu shots are administered yearly, because the influenza virus (RNA virus) mutates rapidly. The rapid spread of the Ebola virus gives it more opportunity to mutate rapidly. As a result, it becomes hard to treat it. That is why cures and vaccines are difficult to develop when the targets keep changing. Targeting one serotype may not provide the desired protection by vaccination.<sup>19</sup>

## ROLE OF GENERAL PREVENTIVE STRATEGIES

There is great interest among health-care professional to prevent and treat the current Ebola virus infection epidemic and to understand general preventive strategies that were effective in 1918–1919 and how they can be applied in current settings. However, such a search may be not a rewarding one.

In Philadelphia after the second wave in late 1918, new flu case appearances dropped abruptly to almost nothing.<sup>10</sup> Most people would like to believe that medical professionals improved strategies in preventing and treating the bacterial pneumonia that developed along with the viral infection, and therefore,

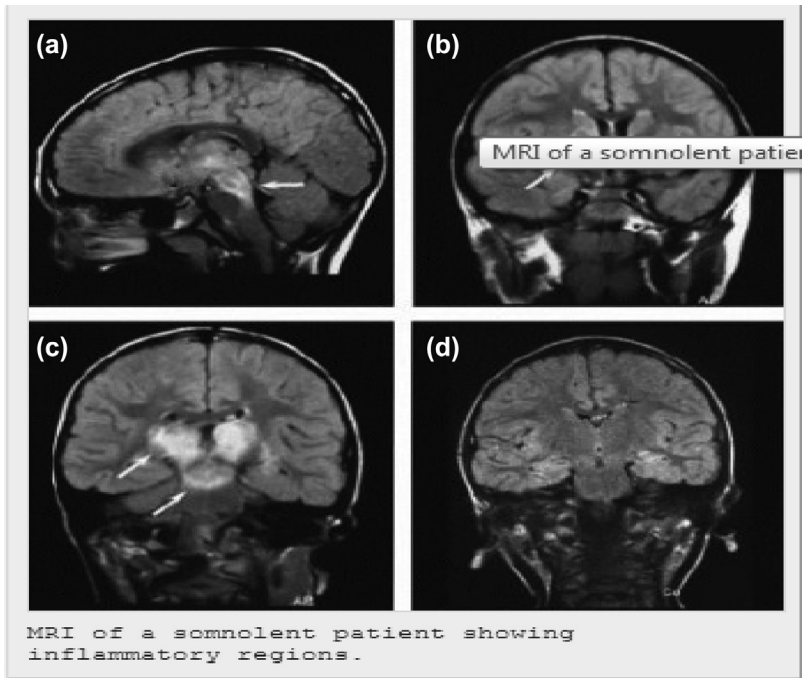
the fatality was substantially reduced. In the United States, spitting was banned in public places, and covering mouth was made mandatory while sneezing. Cities and counties began to recommend that citizens should wear masks, but influenza cases continued even in the communities wearing the masks. In 1918, during an epidemic to slow the transmission of the flu epidemic, the New York commissioner ordered that businesses should be opened and closed on staggered shifts to avoid subways overcrowding. People seen spitting on the street were approached by Boy Scouts in New York City who gave them cards reading “You are in violation of the Sanitary Code.”<sup>20</sup>

To prevent disease from spreading, quarantine was imposed in many communities in the United States. Theaters, schools, saloons, pool halls, and churches were closed. Some physicians suggested that drinking alcohol could prevent infection, which caused a high demand on supplies of alcohol. Public health officials censored newspapers and simple directives to stop the rising panic about influenza disease, but posters and cartoons were allowed to warn people about influenza. The posters, however, were exclusively printed in English despite knowing the fact that much of the nation’s large population did not speak or read English. Even the native speakers found posters and directions confusing. Many folk healers prescribed to wear a special amulet type or a small bag of camphor as preventive measures against influenza. None of these practices proved to be beneficial in preventing a pandemic.<sup>21</sup>

## **ENCEPHALITIS LETHARGICA (VON ECONOMO’S ENCEPHALITIS) EPIDEMIC (1915–1926)**

Encephalitis lethargica literally means “inflammation of the brain that makes you tired.”<sup>22</sup> Encephalitis lethargica has also been known as von Economo’s encephalitis, lethargic encephalitis, sleeping sickness, epidemic encephalitis, sleepy sickness, von Economo’s disease, Schlämmerkrankheit, Schlafkrankheit, or simply Economo’s disease. Kinnier Wilson and Bernard Sachs named the disease on the basis of the brain region involved such as mesencephalitis and basilar encephalitis, respectively. This illness spread through Europe in a manner consistent with an epidemic, beginning in the winter of 1916–1917. Sporadic appearances of cases continued till 1930.<sup>22</sup>

Doctors Russell Dale and Andrew Church reported that the disease was related to a particular strain of bacteria called diplococcus, a known cause of sore throat. The actual neurological manifestations were thought to be due to exaggerated immune responses to the bacteria particularly targeting neural tissue (cross reactivity). Other researchers, however, believe that the cause of the disease is a viral infection or post-viral disease.<sup>22</sup> There was no evidence that the disease spread by direct contact. The cases were isolated and seemed to appear simultaneously. Most of the physicians did not consider the disease as being contagious. Children and adults were affected and died at the same ratio of 1:2. Only 2% of cases were over the age of 60 years in one report.<sup>23</sup>



Ref. 22.

Young people are most vulnerable to the disease, though it infects people of all ages. The disease typically manifests as sore throat, headache accompanied by fever, double vision, and severe weakness. Within hours, it will progress to episodes of tremors, intense myalgias, involuntary movements, and fatigue. Behavioral changes included psychosis and hallucinations, followed by steadily increasing lethargy and drowsiness. Many patients will eventually become completely unresponsive and comatose. Survivors tended to remain in a vegetative state or coma. Many of those who were affected with the disease, even after some recovery time, continue to experience vision problems, personality changes, difficulty swallowing, and intermittent psychosis.<sup>22</sup> Symptoms and signs of Parkinsonism or persistent catatonia with varying severity of cognitive deficits may be seen in postinfectious period.<sup>22</sup>

The disease was first reported at the beginning of 1917 in Austria by von Economo. One case was noted in each of the months of January, February, and March of that year. In spring of 1918, the disease reached France and England and the following winter, cases were reported in Italy. In February 1919, the disease first appeared in Portugal, in November in India, and in early part of 1920 in Spain. In the United States around the end of 1918, disease first appeared on the Atlantic Coast and in October 1919, on the Pacific Coast. The first case of that year occurred in New York. Subsequently, there were 3 cases in October,

7 cases in November, 10 cases in December 1919; and during 1920, there were 19 cases in January, 35 cases in February, 61 cases in March, 12 cases in April, 5 cases in May, and no reported cases in the month of June. In all of the United States, Public Health Service (PHS) received notification of 222 cases. After the investigation, 39 cases were eliminated as unrelated to the disease.<sup>23</sup>

Cases were reported in South America and Uruguay. The disease was also reported in Australia in March 1919.<sup>23</sup> A short-lived outbreak occurred in three communes of Western Flanders, Belgium, during summer of 1919. In Denmark, from July 1919 to April 1920, 58 cases were reported along with 13 deaths. In England and Wales during 1919, 535 cases were reported, and another 202 cases were reported up to April 10, 1920. Most of the cases occurred during the winter in England, suggesting a seasonal pattern of the disease. A majority of the cases occurred in individuals under the age of 35 years. It was rare for cluster of cases to occur in the same household.<sup>23</sup> In Peru, three cases were reported in 1919. In Poland, cases of encephalitis lethargica were reported in February 1920 when disease notification was made compulsory by the Ministry of Health. Two suspected cases and one confirmed case were reported from Tunis.<sup>23</sup> Since January 1, 1919, encephalitis lethargica has become a notifiable disease in England and Wales.<sup>23</sup>

Netter reported the occurrence of the disease in France at the end of 1918. Since that time, the number of cases started to increase, especially during the winter of 1919–1920 according to French delegate, Dr Pean. In about 2 months, 321 cases were reported out of which 100 died with an estimated case fatality rate of about 30%. During 1918 in Italy, sporadic cases were registered and a considerable number of cases occurred from 1919 to 1920. The greatest number of the cases were reported from the Central and North Italy, while south of the country remained entirely disease-free, suggesting that the maritime climate conferred a certain immunity.<sup>23</sup>

In 1928, the encephalitis lethargica epidemic disappeared with the complete absence of any new cases. Previously affected patients required institutionalization and constant care. In 1969, over 40 years after the occurrence of infection, some catatonic patients showed dramatic improvement in their mobility when treated with levodopa. But recovery was short-lived and most patients deteriorated into catatonic states with repeated or increasing dosages being ineffective.<sup>22</sup>

## **EBOLA-LIKE HEMORRHAGIC FEVERS IN MEXICO**

Another epidemic in the sixteenth-century Mexico bore similar characteristics to the hemorrhagic variant of the Ebola virus disease. In 1545, after 24 years of Spanish rule over the Aztec empire, a disease appeared in the highlands of Mexico that had never been seen before. The disease was characterized by an acute fever, dizziness, severe headaches, bleeding from nose, mouth, and ears along with yellow color of skin (jaundice), and chest pain. The disease persisted

for 3–4 days and led to death in a high proportion of the affected persons. The disease only afflicted the native population, sparing the Spanish population for reasons that no one understood until the present day. The Spanish had not experienced any disease like the one that was rampant in Americas, but nonetheless had immunity to the disease. The epidemic of 1545 in Mexico caused about 800,000 deaths in Mexico Valley alone and lasted for 4 years. At that time, the population of Mexico was about 6.6 million. The epidemic was so severe that about 80% of the native population died by the time the disease outbreak had ended.<sup>24</sup>

The disease was named *cocoliztli*, a word for pestilence in Nahuatl, a Uto-Aztec language widely spoken in Central and Western Mexico. The epidemic of hemorrhagic fevers was the first in a series of epidemics that devastated Mexico from 1545 to 1815, a period that coincides with Spanish colonial period in Mexico. Such temporal coincidences implicate the Spanish invaders as the harbinger of the disease, although, in the absence of previous exposure, no such association can be confirmed. Another group that could have carried the disease was slaves transported from Africa into the Americas. The inevitable question is whether the disease was a precursor or variant of Ebola hemorrhagic fever seen in Africans in current times. Eleven more outbreaks of *cocoliztli* were reported, but information about them is scarce. They occurred in 1555, 1559, 1566, 1587–1588, 1592–1593, 1601–1602, 1604–1607, 1613, 1624–1631, 1633–1634, and 1641–1642.<sup>24</sup>

## THE EPIDEMIC OF COCOLIZTLI IN 1576

One of the largest epidemics of *cocoliztli* occurred in 1576 from a population of 4.4 million, causing 2 million deaths in Mexico and a mortality rate to 45% of the entire population. At this time, there were intense changes taking place in Mexico. Diseases like smallpox, measles, mumps, and typhus were taking their toll in the native population. Slaves were being brought from Africa; hard work and high taxes were being imposed on native population; deforestation was intense for the construction of Spanish cities; the Spanish introduced new industries like silver mining, domestic animals, and crops; and constant wars were waged with Indians of the North and conversion to Catholicism was an ongoing process. Under these circumstances, *cocoliztli* reappeared 31 years after the first outbreak.<sup>24</sup>

The presence of hemorrhagic fever was first reported in June 1576 and quickly became a source of death in just 3 months all over the country. Tepeaca, a city 150-km southeast Mexico City with a preepidemic population of 60,000 was converted into an 8000 postepidemic population and lost 86% of its citizens. Cholula, 95-km east of Mexico City, saw a decline from 15,000 inhabitants to 9000 with a 40% death rate. Nochistlan, a town, 450-km northwest of Mexico City suffered from 66.7% loss in its inhabitants secondary to the disease. The overall mortality caused by this epidemic was a loss of about 2 million people from its original 4.4 million. Young indigenous adults suffered the most

during this epidemic. The data from the census of Cholula epidemic indicate that 75% of deaths were among individuals 25 years or older. The infant mortality remained unchanged from previous years. In regards to population segment afflicted, the disease shared features with flu and Ebola virus disease epidemics that came five centuries later. During this epidemic, weather remained cloudy, cold, and foul; the rainy season started 2 months earlier than it was expected and was intense.<sup>24</sup>

Fray Juan de Torquemada, a Franciscan historian, described epidemic of 1576 in Mexico City magnitude as follows.

*In the year 1576, a great mortality and pestilence that lasted for more than a year overcame the Indians. It was so big that it ruined and destroyed almost the entire land. The place we know as New Spain was left almost empty. It was a thing of great bewilderment to see the people die. Many were dead and others almost dead, and nobody had the health or strength to help the diseased or bury the dead. In the cities and large towns, big ditches were dug, and from morning to sunset the priests did nothing else but carry the dead bodies and throw them into the ditches without any of the solemnity usually reserved for the dead, because the time did not allow otherwise. At night, they covered the ditches with dirt... It lasted for one and a half years, and with great excess in the number of deaths.<sup>24</sup>*

Martin Enriquez wanted to know the number of missing people in New Spain. After searching in towns and neighborhoods, it was found that the number of deaths was more than 2 million.<sup>24</sup>

Dr Francisco Hernandez, the protomedico (physician-in-chief) of New Spain and former physician of King Phillip II of Spain wrote:

*The fevers were contagious, burning, and continuous, all of them pestilential, in most part lethal. The tongue was dry and black. Enormous thirst. Urine of the colors sea-green, vegetal-green, and black, sometimes passing from the greenish color to the pale. Pulse was frequent, fast, small, and weak—sometimes even null. The eyes and the whole body were yellow. This stage was followed by delirium and seizures. Then, hard and painful nodules appeared behind one or both ears along with heartache, chest pain, abdominal pain, tremor, great anxiety, and dysentery. The blood that flowed when cutting a vein had a green color or was very pale, dry, and without serosity. In some cases gangrene and sphacelus invaded their lips, pudendal regions, and other regions of the body with putrefact members. Blood flowed from the ears and in many cases blood truly gushed from the nose. Of those with recurring disease, almost none was saved. Many were saved if the flux of blood through the nose was stopped in time; the rest died. Those attacked by dysentery were usually saved if they complied with the medication. The abscesses behind the ears were not lethal. If somehow their size was reduced either by spontaneous maturation or given exit by perforation with cauteries, the liquid part of the blood flowed or the pus was eliminated; and with it, the cause of the disease was also eliminated, as was the case of those with abundant and pale urine. At autopsy, the*

*liver was greatly enlarged. The heart was black, first draining a yellowish liquid and then black blood. The spleen and lungs were black and semi-putrefacted. The bile was observed in its container. The abdomen dry. The rest of the body, anywhere it was cut, was extremely pale. This epidemic attacked mainly young people and seldom the elder ones. Even if old people were affected they were able to overcome the disease and save their lives. The epidemic started in June 1576 and were not over in December, when I am writing these lines. Of all New Spain, the disease invaded cold lands (highlands) in the perimeter of 400 miles, and had a lesser effect in lowlands. The disease attacked primarily regions populated by Indians here and there, then regions of mixed population of Indians and Spaniards, later the Ethiopians, and now, finally the Spaniards. The weather was dry and quiet, and disturbed by earthquakes, the air was impure, filled with clouds but without resolving into rain... Very few with abdominal distention were saved. In the beginning, the blood was expelled by some without severe disease, then by very few. Vital energy was consumed quickly.*<sup>24</sup>

Dr Hinojoso made some additional observations, mentioning that the disease lasted 3–4 days from onset to death and that on the second or third day the patient became insane and irritated, eyes were red, thirst was insatiable, and nodules behind the ears and neck were so big that they covered entire neck and half of face. Patient fevers were very high, and autopsies showed extremely large and hard livers and also identified the splenomegaly.<sup>24</sup>

The striking aspect of this epidemic was its selective vulnerability of the native population. The selective vulnerability of the indigenous people was not limited to cocoliztli, but also seen with smallpox, chicken pox, measles, and mumps infections. With those diseases, however, an explanation was more forthcoming. The Spanish population had acquired a protective immunity to these diseases due to exposure in Europe at a young age. The native population developed some degree of immunity to those diseases about 20 years later.<sup>24</sup>

In 1576, the time of the second epidemic of cocoliztli, many of the Spanish settlers who helped the sick natives were then between 0 and 54 years, but none of them died of disease. Why did the Spaniards who grew up in the new colonies continue to manifest immunity seen in those who had come from Europe? Immunity is not inherited and therefore it is unlikely that, 55 years later, the immune status of Spanish immigrants played any role in epidemic selection. A possible explanation for this selection could lie in the socioeconomic status of that indigenous and colonizing Spanish population as the majority of the native population lived in poverty and were undernourished.<sup>24</sup>

Cristobal Godinez, a government official, reporting on the epidemic wrote:

*The reason so many Indians die of the pestilence is a God secret. I do not find any better answer than that in the past the Indians were not as badly mistreated and oppressed as they are today with heavy workloads. They are skinny and delicate, the disease finds them overworked and without resistance, so they are finished.*<sup>24</sup>

Under those conditions, the pattern of cocoliztli epidemic is well explained by the presence of an infectious agent favored by poor living conditions or nutritional deficiencies.<sup>24</sup>

## HOW COCOLIZTLI DIFFERED FROM OTHER MAJOR DISEASES

What was cocoliztli? It was a disease that does not exist today or a variant of the present diseases. Cocoliztli differed from epidemic typhus (tabardete) in that rashes were absent. The lack of respiratory symptoms in cocoliztli resulted in the dismissal of influenza, pertussis, or diphtheria infection. Fever caused by malaria runs in spikes, whereas a cocoliztli fever ran continuously high. Symptoms in intestinal anthrax infections predominantly consisted of gastrointestinal tract symptoms such as diarrhea and vomiting, while in cocoliztli there were no such symptoms. Patients of cocoliztli had severe yellow discoloration of the skin (jaundice), severe bleeding, and injected eyes, which are not classical description of bubonic plague. The absence of rash, high fever, and high prevalence of enlarged liver and liver failure in cocoliztli made the possibility of infection by filoviruses such as Ebola and Marburg virus less likely but certainly a possibility. The true etiological agent for cocoliztli is still unknown. The illness ran uncontrolled and caused devastating damage to Indian population for about a century.<sup>24</sup>

## EPIDEMICS IN MODERN TIMES

### Severe acute respiratory syndrome (SARS) in Southeast Asia

#### *Introduction*

Severe acute respiratory syndrome (SARS) is a highly infectious disease caused by coronavirus. This previously unknown virus was first identified in Asia in early 2003 and named as “SARS-associated coronavirus” or SARS-CoV. Since October 2012, SARS-CoV has been under the care of National Select Agent Registry that monitors the handling and possession of bacteria, viruses, or toxins that have the potential to be a severe threat to public health and safety.<sup>25</sup> The initial cases of SARS appeared in last part of 2002 in Guangdong Province of China. The contagious nature of the disease and delayed public response caused the epidemic to spread around the globe very rapidly.<sup>25</sup>

Disease manifestations varied considerably depending on the age and physical status of the patient. Fever and dry cough are the most common symptoms although not specific to SARS.<sup>1</sup> At the beginning of the third week, young patients especially did improve from infection. About a fifth of all patients would have progressive pulmonary involvement requiring mechanical ventilation and 10% of affected patients would die. Deaths, far more prevalent in those aged over 65 years of age, might be due to SARS virus alone or in combination with secondary infections. Investigators also imply a role of exacerbated immune response in pulmonary injury.<sup>1</sup>



## **“A walk through the course of the SARS epidemic”**

The first known case appeared on November 16, 2002, in Guangdong Province, China. On February 13, 2003, 300 cases including five deaths in Guangdong Province due to “acute respiratory syndrome” were reported by the Chinese Ministry of Health. On March 11, an outbreak of SARS among hospital workers was reported in Hong Kong. On March 15, SARS was confirmed as a “worldwide health threat” by World Health Organization (WHO). Possible cases were identified in Canada, Indonesia, Philippines, Singapore, Thailand, and Vietnam. WHO issued an advisory for travelers going to Southeast Asia about the SARS. By March 19, SARS cases emerged in the USA, UK, Spain, Germany, and Slovenia. On March 27, WHO recommended the screening of travelers arriving from worst-affected areas. On March 29, Carlo Urbani, one of the WHO officials who identified SARS, died from the disease. On April 2, WHO recommended the postponement of all nonessential travel to Hong Kong and Guangdong Province of China. By April, the slow response and release of only selected information by Chinese officials became apparent, leading to a public apology. On April 9 and 17, the first SARS cases were reported in Africa and India, respectively. On April 14, Canadian scientists confirmed that they had sequenced the genome of the SARS virus. On April 23, WHO recommended postponement of nonessential travel to Toronto, Canada.<sup>26</sup>

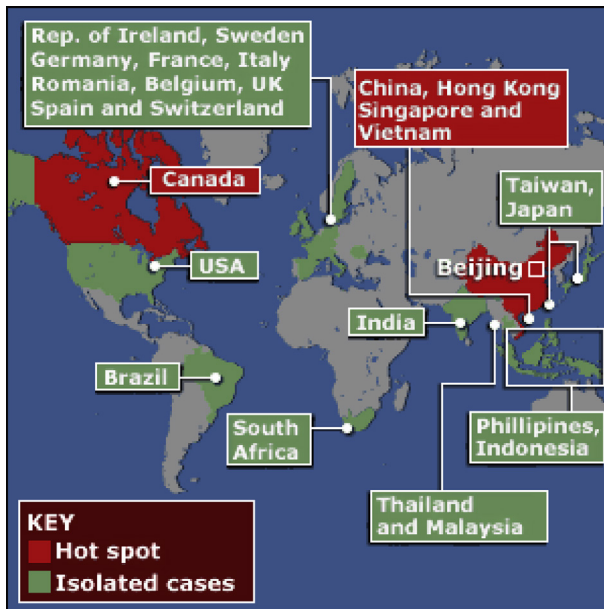
As the infection spread, more radical measures were put into place. All schools are shut down in Beijing for 2 weeks to halt the spread of the disease. On April 26, 13 East and Southeast Asian countries’ health ministers met in Malaysia to call for all international travelers to be screened for SARS. On April 27, all entertainment venues, including theaters, cinemas, and karaoke bars, were ordered by the Beijing authorities to be closed down until the outbreak was determined to be an end. On May 5, 10,000 people were quarantined in eastern city of Nanjing, China, by authorities. On May 11, spitting was banned in public places in southern Chinese city of Guangzhou to control SARS. On May 15, in China anyone who broke the quarantine rules was threatened with execution or imprisonment for life. On May 22, the infection reached its peak in Taiwan, with emergence of 65 new cases in one day.<sup>26</sup>

The first hope of epidemic control appeared on April 28, when Vietnam was deemed to have contained the spread of infection with no new cases reported for 20 consecutive days. On May 31, WHO declared Singapore SARS-free. On June 5, WHO announced that the outbreak had peaked the World including China. On June 13, WHO withdrew its travel warnings for Chinese provinces of Hebei, Inner Mongolia, Shanxi, and Tianjin but maintained the warning for Beijing. On June 17, the travel advisory was removed for travel to Taiwan. On June 23, China and Hong Kong were removed from the WHO list of SARS-infected areas. On July 2, after 20 consecutive days without SARS new cases, Toronto was declared SARS-free by the WHO. On

July 5, Taiwan was the last country to be removed from WHO list of SARS-infected areas.<sup>26</sup>

Sporadic cases of SARS reemerged in Asia. On September 9, Singapore announced a new SARS case, but was never confirmed by WHO. On December 17, a medical researcher at Taipei military hospital contracted the virus, according to Taiwan health officials. On January 5, 2004, a 32-year-old man in southern Guangdong Province had developed SARS as confirmed by Chinese health officials. On January 16, 2004, WHO said that it found the evidence suggesting that civets do carry SARS. Plans were announced to slaughter thousands of civet cats to prevent the spread of the disease. On January 17, 2004, Chinese authorities confirmed two new cases in Guangdong Province. On April 26, 2004, the Chinese health officials said that it was investigating at least four new suspected cases and all new cases are connected to a confirmed patient who worked at a SARS research laboratory. On May 19, 2004, the WHO had declared that China had contained the latest outbreak of SARS.<sup>26</sup>

The political ramifications continued in the months that followed. In July 2004, Li Liming, the director of China's main disease control center resigned over the April outbreak, which happened at one of its laboratories. On July 7, 2004, Yeoh Eng Kiong, the Hong Kong health secretary at the time, resigned after being criticized over his handling of the 2003 SARS crisis. He was accused of paying too little attention to SARS when it first appeared in China and about issuing the misleading statements to Hong Kong public.<sup>26</sup>



Geographic distribution of SARS occurrence.<sup>27</sup>

## **FACTORS THAT PROMOTED THE GLOBAL SPREAD OF SARS**

There are two main reasons why SARS spread in China. First, is because of the close interaction of Chinese people with wildlife. Second, in many parts of China, people's diets are selenium-deficient and this deficiency may play a role in the emergence of new viral strains. A team led by Melinda Beck of the University of North Carolina at Chapel Hill observed very high mutation rates of flu viruses when they infected selenium-deficient mice. Beck issued a statement saying that "The fact that China has widespread selenium-deficient areas, may play a role in the emergence of new viral strains."<sup>25</sup> SARS spread to Hong Kong when a doctor from Mainland China visited there. Unfortunately, he brought the infection from China, and the infection spread to seven other people who had been staying at the same hotel. Out of these seven people, three were from Singapore, two were from Canada, one was from Vietnam, and one was a local person. Each of these people carried the virus to their respective countries.<sup>28</sup>

## **STEPS THAT WERE EFFECTIVE IN CONTROL OF SARS EPIDEMIC**

### **Preventive and control measures in China**

The government got involved by sending supervisory teams to all 31 provinces to examine the implementation of local control measures. Thus, SARS control measures got incorporated into the legal framework through these legislative efforts. After April 20, 2003, SARS data were reported, analyzed, and managed through national disease reporting and management information system. Close contacts of SARS-infected patients were put under medical observation for 2 weeks to ensure early detection, reporting, isolation, and treatment. In all provinces, special fever clinics and designated SARS hospitals were set up and medical and technical expertise were improved.<sup>29</sup>

A central budget was allocated to treat the farmers and urban residents who had financial difficulties. SARS patients' feces, secretions, dead bodies, and other medical wastes were disinfected diligently. Passenger observation, monitoring, registration, and follow-up systems were set up in civil aviation, railway, long-distance bus, boat, and other public transport systems. The Ministry of Science and Technology coordinated national scientific research into SARS to improve knowledge and understanding of the disease.<sup>29</sup>

### **Preventive and control measures in Hong Kong**

The Department of Health of the Hong Kong Special Administrative Region Government passed legislation making SARS a notifiable infectious disease. SARS patients were isolated in hospitals and family or close contacts were kept under surveillance. Public health workers undertook investigations to identify the source of infection, tracing the contacts, and promoting application of control measures. The government, in May 2003, established three committees: one

responsible for the overall cleansing campaigns; one to revitalize city economy including tourism, employment, and trade one to devise ways to promote community involvement in improving the physical, social, and economic environments of the city. The government strengthened collaboration and communication with Mainland China and WHO. Funds were approved to support research on diagnosis, treatment, and SARS vaccine development.<sup>28</sup>

## DENGUE FEVER IN ASIA AND SOUTH AMERICA

Dengue fever is a mosquito-borne virus disease that has rapidly spread to several regions in recent times.<sup>30</sup> Dengue fever presents with high-grade fever, headache, mouth nose bleeding, muscle joint pains, vomiting, rash, diarrhea, gastrointestinal bleeding, altered consciousness, seizures, and itching.<sup>31</sup> The disease spread throughout the tropics with local variations, influenced by rainfall, unplanned rapid urbanization, and temperature. In 1950s, during dengue epidemic in the Philippines and Thailand, a severe form, known as dengue hemorrhagic fever, was first recognized, and has become a leading cause of death among children in Asian and Latin American countries.<sup>30</sup> Unlike the Ebola virus infection, which causes a depletion of coagulation proteins by affecting the liver, dengue fever causes hemorrhages by depleting the platelets within the circulation.<sup>32</sup>

About 500,000 dengue fever cases require hospitalization worldwide each year with large proportion of whom are children. Close to 2.5% of those affected with dengue fever will die from the disease.<sup>30</sup> There are four serotypes of dengue fever virus. Recovery from one serotype does not provide complete immunity against other serotypes. A subsequent infection by the other serotype increases the risk of developing dengue hemorrhagic fever.<sup>30</sup>

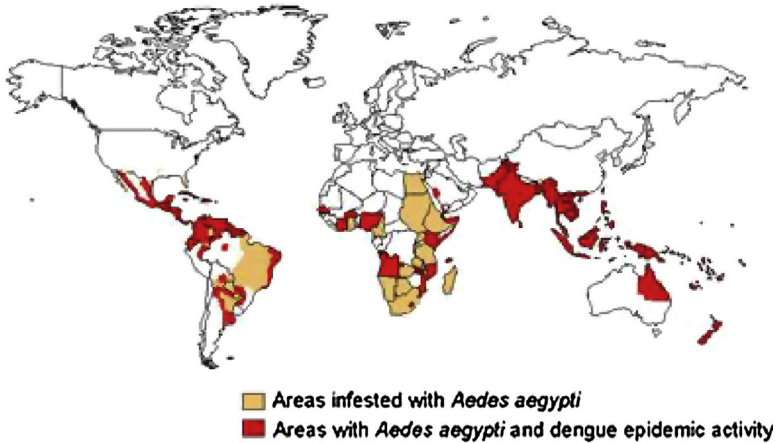
## TRANSMISSION AND SPREAD OF DENGUE FEVER

The virus gets transmitted by female mosquitoes, mainly by the species *Aedes aegypti* and, to a lesser extent, by *Aedes albopictus*. Infected humans are the main multipliers and carriers of the virus, a source of acquisition of the virus for uninfected mosquitoes. After the first appearance of their symptoms, the patients can transmit the infection for 4–5 days (maximum of 12 days) through *Aedes* mosquitoes. The *A. aegypti* mosquito breeds mostly in man-made containers and lives in the urban habitats. It is a daytime breeder and its peak biting periods are early morning and in the evening before dusk. During each feeding period, female *A. aegypti* bites multiple people. *Aedes albopictus* is the secondary dengue vector in Asia.<sup>30</sup>

International trade in products like lucky bamboo led to the spread of *A. albopictus* from Asia to North America and Europe. *Aedes albopictus* is highly adaptable and able to survive in cooler, temperate regions of Europe. It can tolerate temperatures below freezing by hibernation and can shelter in microhabitats.<sup>30</sup>

## GLOBAL BURDEN OF DENGUE FEVER

### Geographic Distribution of Dengue Fever Cases Occurrences – 2005



Ref. 33.

The dengue fever incidence has recently increased dramatically. There appears to be a slowly increasing incidence with intermittent outbreaks consisting of large regional clusters of cases. The actual number of cases is underreported and many are misclassified. One recent estimate shows that 390 million dengue virus infections occur per year, of which 96 million infections have clinical manifestations. In 2013, 37,687 cases of hemorrhagic fever were reported within WHO member states across Americas, Western Pacific, and Southeast Asia, of which 2.35 million cases were related to the dengue virus.<sup>30</sup>

Local dengue fever transmission was reported in France and Croatia in 2010 for the first time, and, in three other European countries, new cases among immigrant populations were detected. In 2012, dengue fever outbreak on the Madeira Islands of Portugal resulted in over 2000 cases. Cases among immigrants were detected in mainland Portugal and 10 European countries.<sup>30</sup> New cases were identified in Florida (United States of America) in 2013 and Yunnan (a province of China). South American countries, importantly Costa Rica, Mexico, and Honduras, also identified new cases. After a lapse of many years, Singapore also reported an increase in new cases, and Laos reported an outbreak. Trend analysis in 2014 indicated an increase in the number of cases in Pacific Island countries notably the People's Republic of China, Fiji, Malaysia, Vanuatu, and the Cook Islands. After a lapse of 70 years, dengue fever was reported in Japan.<sup>30</sup>

## THE STORY OF QUARANTINE

Quarantine is a state of enforced isolation used to separate and restrict the movements of persons who may have possibly be exposed to a communicable disease.<sup>34</sup>

The concept of quarantine can be seen as early as the Old Testament. Under the Mosaic Law among the Israelites, as recorded in the Old Testament, infected people were separated to prevent the spread of disease.<sup>35</sup> The quarantine period could be very long such as Mary Mallon (also known as Typhoid Mary, a typhoid fever carrier who spent the last 24 years of her life under quarantine), or it could be very short, such as in the case of suspected anthrax attack (the person is allowed to leave as soon as he or she sheds his or her potentially contaminated clothes and undergoes a decontamination shower).<sup>36</sup>

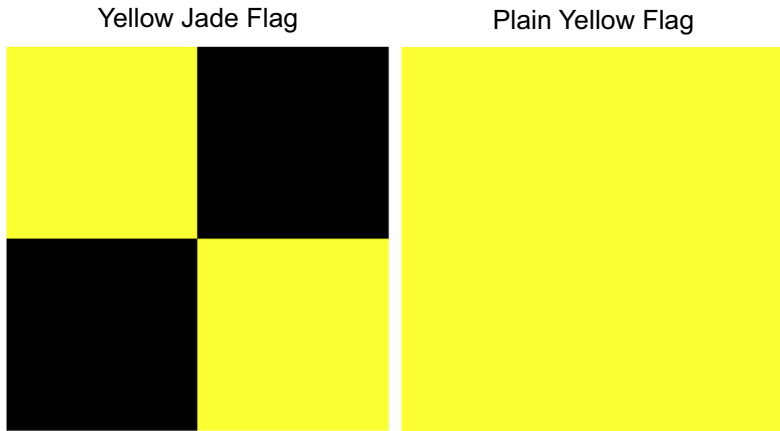
The Italian words *quaranta giorni* meaning “40 days” gave origin to quarantine. To protect coastal cities from plague epidemics, this practice began during the fourteenth century. Ships arriving from infected ports to Venice were bound to sit at anchor for 40 days as a quarantine measure.<sup>36</sup>

The Black Death annihilated about 30% of Europe’s population along with a significant percentage of Asia’s population between 1348 and 1359. Newcomers entering the city had to spend 30 days (a *trentine*) in an isolated place (nearby islands) waiting to see if the symptoms of Black Death would appear, as stated in the original document from 1377 kept in the Archives of Dubrovnik. Later on, it was prolonged to 40 days, changing the term from “*trentine*” (30 days) to “quarantine” (40 days).<sup>37</sup>

At the start of Black Death in 1348, three guardians of public health were appointed in Venice, Italy, to check the spread of plague. The next record of preventive measures comes from Reggio in Modena in 1374. Venice founded the first lazaret (quarantine station for maritime travelers) on a small island adjoining the city in 1403. The old leper hospital of Marseille was converted into a plague hospital when Genoa, Italy, followed Venice’s example in 1476. Perhaps a complete lazaret of kind, “The great lazaret of Marseilles” was founded on the island of Pomègues in 1526. At all the Mediterranean lazarets, the practice did not differ from the English procedure in the Levantine and North African trade. In 1831 at the western ports, new lazarets were set up during the approach of cholera in 1831, showing the continued use of this system for disease outbreaks.<sup>36</sup>

## **SYMBOLS OF QUARANTINE**

To represent disease, green, plain yellow, and even black flags have been used on ships and ports. The yellow color has longer historical precedent as being a color for marking houses of infection and maritime marking color for disease. The present flag used is the “Lima” (L) flag, mixture of yellow and black flags, also called “Yellow Jack.” The disease yellow fever probably derived its name from the flag not from the color of the victim. The plain yellow flag (“Quebec” or Q) probably derived its letter symbol from its initial use in quarantine, but, in present times, it means the opposite, declaring a ship free from quarantinable disease and requesting boarding and routine port inspection. The signal flag “Lima” also called the “Yellow Jack” showed that ship is under quarantine.<sup>36</sup> The simple yellow now indicates that ship is free of a disease.<sup>37,38</sup>



Refs. 36 and 38.

## GLOBAL FACES OF QUARANTINE

With the aim of keeping infection out of east and preventing its spread within Europe, many conferences involving the European Powers have been held since 1852. All these conferences were primarily focused on limiting the spread of cholera, but that of 1897. Conferences at Paris (1852), Constantinople (1866), Vienna (1874), and Rome (1885) were fruitless. Each international sanitary convention aimed to make governments follow a uniform set of minimum of preventive actions. The individual countries could have further restrictions.

### 1. Quarantine rules in Australia

There are many pests and diseases present in Southeast Asia and the Pacific not present in Australia. Due to its proximity to these regions, quarantine is very important in Northern Australia. For this region to protect all Australians, quarantine activation is very important in the region from Cairns to Broome—including the Torres Strait. Due to being isolated geographically for millions of years from major continents, Australia has a distinct ecosystem devoid of many pests and diseases present in other parts of the world. Border inspection of any products that might damage the Australian environment is the responsibility of the Australian Quarantine and Inspection Service. Visitors are bound to fill out the card correctly to declare what food and any other products they bring back with them. Failure to do so will result in quarantine fine of 220 Australian dollars or facing criminal convictions of fining 100,000 Australian dollars and 10 years of imprisonment.<sup>39</sup>

### 2. Quarantine rules in Canada

Canadian Parliament has passed three quarantine acts: Quarantine Act (humans), Health of Animals Act (animals), and Plant Protection Act (vegetation). In the case of health emergency under the Quarantine Act, the council governor is empowered to block the importation of unnecessary items. If border

service officers have reasonable belief that a traveler might be a source of communicable disease or is refusing to answer to necessary questions regarding the public safety, a quarantine officer must be called to isolate that person. In the case of a refusal to be isolated, any peace officer can arrest without a warrant. A quarantine officer who has sufficient belief that traveler might be a source of communicable disease can order treatment after medical examination and detain any traveler who refuses to comply with his or her orders under the law.<sup>40</sup>

### 3. Quarantine rules in Hong Kong

Health officers may hold the articles he or she believes to be infectious or contain infectious agents under the Prevention and Control of Disease Ordinance (HK Laws. Chapter 599). Failure to submit themselves to a health officer when requested is against the law and will result in arrest and prosecution. The health officer is legally allowed to detain, isolate, and quarantine anyone or anything he or she believes to be infected and restrict any article from leaving the designated quarantine area. Prohibition of the landing or leaving, embarking or disembarking of an aircraft through Civil Aviation Department can also be ordered by him or her.<sup>41</sup>

### 4. Quarantine rules in the United Kingdom

The quarantine rules in the United Kingdom require that dogs and most other animals must spend 6 months at an HM Customs and Excise pound in quarantine in order to reduce the risk of introduction of rabies from continental Europe. This practice was abolished in 2000 in favor of documentation known as pet passports. Under this scheme, if there is documented proof of animal vaccinations, quarantine can be avoided.<sup>42</sup>

### 5. Quarantine rules in the United States

The rules imply that, if a disease gets traced back to a particular shipment or product, the United States can put quarantines into effect immediately. In the case of disease outbreak in other countries, all imports will be quarantined. At a number of US ports, small quarantine facilities are operated by the Division of Global Migration and Quarantine (DGMQ) of the Centers for Disease Control and Prevention (CDC). It includes one land crossing (El Paso, Texas) and 19 international airports such as Anchorage, Atlanta, Boston, Chicago, Dallas/Ft. Worth, Detroit, Honolulu, Houston, Los Angeles, Miami, Minneapolis, New York JFK, Newark, Philadelphia, San Diego, San Francisco, San Juan, Seattle, and Washington, D.C. (Dulles). Other ports of entry are also responsible to quarantine potentially infected travelers in their assigned regions.<sup>43,44</sup>

## EARLY AMERICAN QUARANTINE

In 1878, continued outbreaks of yellow fever finally pushed Congress to pass quarantine legislation. This paved the way for federal involvement in quarantine activities while conflicting with states' rights.<sup>45</sup>



## LATE NINETEENTH CENTURY

Reinterpretation of the law happened in 1892, providing federal government the liberty to impose quarantine requirements following cholera outbreaks from passenger ships arriving from Europe. Control of local quarantine stations was handed over to the US government. Following this, the government built additional federal facilities and increased the number of staff to provide a better coverage. Transferring control of the last quarantine station to the US government in 1921 made the quarantine system fully nationalized.<sup>44</sup>

## PUBLIC HEALTH SERVICE ACT

In 1944, the Public Health Service (PHS) Act fully implemented the federal government's quarantine policy for the first time. This gave the U.S. PHS responsibility to prevent the introduction, transmission, and the spread of communicable diseases from foreign countries to the United States.<sup>45</sup>

## REORGANIZATION AND EXPANSION

In 1967, quarantine was transferred to an agency known as CDC. The consists of 55 quarantine stations, located at every international airport, port, and a major border station with 500 staff members.<sup>45</sup>

## FROM THE INSPECTION TO INTERVENTION

In 1970, the CDC trimmed the quarantine program by changing its focus from routine inspection to enhanced surveillance system based on monitoring the onset of epidemics abroad and modernizing the inspection process for meeting the changing needs of international traffic.<sup>45</sup> In 2003, after the SARS epidemic, the CDC upgraded the quarantine system with 18 stations and greater than 90 field employees.<sup>45</sup>

## SOCIAL IMPLICATIONS OF QUARANTINE

Quarantine and other public health practices have always been perceived as intrusive and accompanied by suspicion, distrust, and riots in every age and under all political regimes despite being effective and valuable ways to control the communicable diseases. Standard-Times senior correspondent Steve Urban describes such temporary quarantine powers, "Civil rights activists in some cases have objected to people being rounded up, stripped and showered against their will. But Capt. Chmiel said local health authorities have 'certain powers to quarantine people.'"<sup>46</sup> Political, economic, social, and ethical issues are always being raised by these strategic measures. Individual rights have often been trampled in the name of public good. The liberty of outwardly healthy persons from lower classes has frequently been violated by isolating or segregating persons suspected of being infected. Marginalized groups of different ethnicities and

ances have been stigmatized and discriminated against. Quarantine has a line of continuity from the time of plague to the influenza A pandemic in 2009.<sup>46</sup>

During plague and cholera outbreaks, the fear of discrimination and mandatory quarantine pushed the lowest social class and minorities to flee from affected areas. This contributed to a more rapid and wider spread of the disease as this regularly occurred in towns affected by deadly disease outbreak. In this global world, the fear caused by mass media can spread the disease farther and faster, playing a larger role than in the past. Entire populations or segments of populations are at the risk of being stigmatized. In the light of new challenges posed by twenty-first century that can lead to the spread of infectious diseases, quarantine, along with other public health tools, retains importance for public health preparedness. Vigilant attention is required to avoid the intolerance and injustice while implementing these measures. Regular, transparent, and comprehensive communications should be used to gain the public trust. Valuable lessons from the past must lead to successful responses to public health emergencies.<sup>46</sup>

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