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VIRAL PANDEMICS

(Exclusive Student's Volume)

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From the Principal's Desk

I would like to congratulate the entire team of Department of Microbiology for their wonderful though very strenuous attempt to publish a journal exclusively for the students. Presently the e-version of the journal is going to be released on auspicious day of 5th September, i.e. the Teacher's Day. I hope, later on the print version will be published. In my perception it is a tribute to the entire faculty members by the students because these write ups simply say that how much they assimilate from their teachers in this subject.

We all know and still experiencing a very stressful as well as fearful daily life due to the pandemic. We came to know many information regarding this covid-19 virus from many microbiologists not only from India but also from other countries like Canada, USA and many more. The Department of Microbiology, Vijaygarh Jyotish Ray College produced many students who are pursuing their research in India as well as abroad. In response to the call from their teachers they shared their knowledge with us in many webinars organized by the department. In my perception all the students of this department are budding scientist of future. No one knows it may so happen that we come to know that one of our students succeed to be associated with the invention of any life-saving drug or vaccine.

Once again, I want thank all students and faculties for initiating this attempt and hope that this will continue to publish.

Rajyasri Neogy

Dr. Rajyasri Neogy,

Principal, Vijaygarh Jyotish Ray College

Contents

H1N1 SWINE FLU PANDEMIC 2009: SPREAD AND EFFECT ON HUMANS

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ABSTRACT: Not all infectious organisms are spread equally, so different diseases are classified under various scientific terms, such as 'epidemic' and 'pandemic'. It is seen that the terms are often interchanged mistakenly. An 'epidemic' is a disease which affects a large number of people within a community or region. On the other hand, a 'pandemic' is an epidemic that spreads over multiple countries or continents. The term 'pandemic' and 'epidemic' are used to describe the rate and distance of the disease not by the severity of the disease. This article highlights every basic detail about the H1N1 Swine Influenza Pandemic of 2009, starting from the genetic material of the virus to statistical representation of the pandemic, and finally discussing about the social conditions during and before the pandemic.

Keywords: Epidemic, Pandemic, Influenza.

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1.1 INTRODUCTION:

A viral pandemic was observed during 2009-2010 due to the spread of H1N1 Swine flu virus, which is believed to have started in pigs. As a result, people in close contact with pigs were the first to get infected, but later it spread to different countries such as Mexico, USA and parts of Western Australia. The world experienced an influenza pandemic beforehand in 1918, during the spread of Spanish flu. In 2009, a new influenza strain led to the spread of Swine flu, which was labeled as a 'pandemic' by the World Health Organization (WHO).

2009	Novel Influenza A(H1N1) Outbreak and Pandemic Milestones
17 March	First case (Mexico) in the world, which was later identified as swine flu
28 March	First case in the US, which was later identified as swine flu
12 April	First known death in Mexico due to swine flu
24 April	First Diseases outbreak of the swine flu notified by the WHO
27 April	First case confirmed in Canada, United Kingdom & Spain
28 April	First death confirmed in the USA; First case confirmed in New Zealand
30 April	First case confirmed in Hong Kong, China
7 May	First death confirmed in Canada
8 May	First case confirmed in Japan
9 May	First case confirmed in Australia
10 May	First case confirmed in China
16 May	First case confirmed in India
22 May	First case confirmed in Russia
26 May	First case confirmed in Singapore
3 June	First case confirmed in Saudi Arabia
11 June	The WHO raises it's Pandemic Alert to Phase 6
Current WHO[83] Update* as of 6st July 2009	• 135 countries have officially reported 94,512 human cases of influenza A (H1N1) infection, resulting in 429 deaths in 19 countries (Fig. 3). • The USA has reported the largest number of laboratory confirmed human cases (33,902) with death of 170 persons, the highest reported mortality among countries • Mexico has reported 10,262 human cases with a casualty amounting up to 119. • Other countries experiencing sizeable number of human cases but with fewer deaths are Canada (7983 – 25 deaths/), UK (7447 – 3 deaths), Chile (7376 – 14 deaths), Australia (5298 – 10 deaths), Argentina (2485 – 60 deaths), Thailand (2076 – 7 death), New Zealand (1059 – 3 deaths), Uruguay (195 – 4 deaths), Costa Rica (277 – 3 deaths); and China (2040) and Japan (1790) but with no human casualty. • Countries reporting 1-2 human casualties of swine flu include Philippines (1 death/ 1709 cases), Spain (1 death/ 776 cases), Brazil (1 death/ 737 cases), Guatemala (2 deaths/ 286 cases), Paraguay (1 death/ 106 cases), Dominican Republic (2 deaths/108 cases), Colombia (2 deaths/118 cases), and Honduras (1 death/123 cases).

*As per CDC Atlanta 436 deaths and 99,222 human cases.(http://en.wikipedia.org/wiki/2009_flu_pandemic_by_country as on 08 July 2009).

Fig. 1) Cases of Novel Influenza A (H1H1) outbreak and pandemic milestones 2009. (Image courtesy: www.who.int)

1.2 GENETIC VIEW AND PATHOGENESIS OF THE VIRUS:

Influenza viruses are categorized into three groups: Influenza A, Influenza B and Influenza C. Among these, Influenza A is the causative organism for diseases in humans. Also, they are classified into different strains according to the proteins, HA and NA, present on their surface. One of the strains, H1N1 Influenza A, causes 'Swine Flu', which was found to be originated in pigs.

The H1N1 influenza virus belongs to the family of orthomyxoviridae. Generally, they produce virions which vary between 80 nm to 120 nm in diameter. It has been observed that their RNA genome size is approximately 13.5 kb. [Jilani et al., 2019]

Influenza viruses are normally round in shape, but during some observations, their amorphous or long, string-like filaments are also noted. As stated earlier, there are two surface proteins present, namely, HA and NA. Among them, the protein HA, also called Hemagglutinin, allows the virus

to bind to the cells in respiratory tract by interacting with the Sialic acid on the cell surface. NA (Neuraminidase), on the other hand, cuts off the Sialic acid and thus, helps the newly produced viruses to get released from the affected cells.

Since the virus enters the lung through the airways, thus it affects a variable percentage of lungs. Generally, the incubation period of H1N1 swine flu ranges from 1 to 4 days, but in some cases, it may nearly take 7 days.

It is observed that the viruses primarily infect the epithelial cells lining of the respiratory tract surface. After the end of the incubation period, the onset and progression of bronchial inflammation has been observed. After a few days, intra-alveolar hemorrhage and thrombosis of capillary have been found. As a result, signs and symptoms such as fever, chills, cough, sore throat and shortness of breath were observed. During the 2009 H1N1 pandemic, reports also stated vomiting and diarrhea as other symptoms. [Al-Muharrmi, 2010]

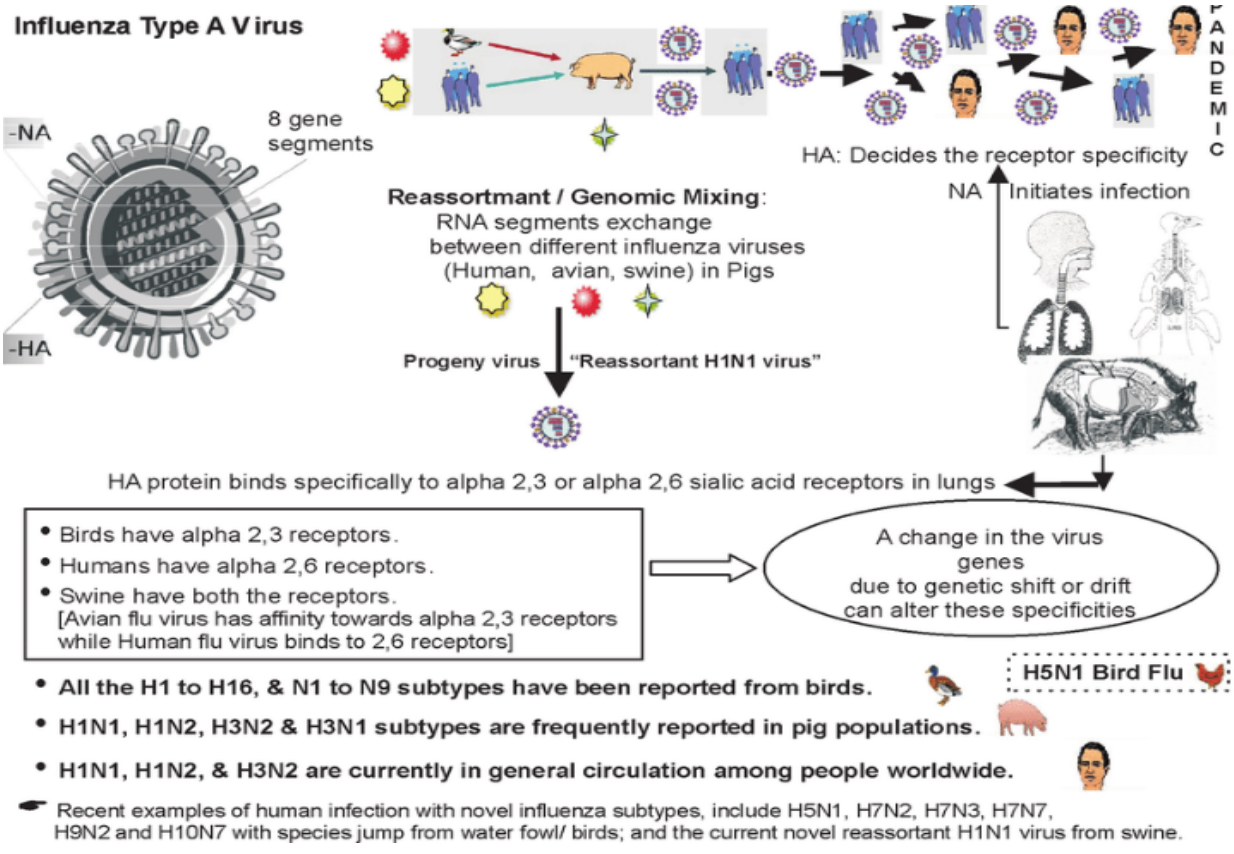

Fig. 2) Genomic representation of Influenza H1N1 virus. (Image courtesy: www.researchgate.net)

1.3 COMPARISON OF DEATHS BETWEEN PANDEMIC AND SEASONAL INFLUENZA

1.3.1 BACKGROUND:

Every winter, millions of people encounter with a viral infection of the airways and hundreds to thousands people die (mainly elderly) due to low immune response. The severity of H1N1 influenza pandemic sometimes can be compared by the confirmed cases of deaths in Seasonal Influenza. These comparisons are either done nationally or worldwide.

As Seasonal Epidemic frequencies are low but frequent changes in the Virus genome challenges the immune system of the host. Due to memory response of immune system caused by previous infection the host is partially protected from next year's Virus encounter.

Somehow, the comparison between Pandemic and Seasonal Influenza can be misleading. The mortality rates of Seasonal Epidemic can be estimated. A statistical model has been designed to calculate the rates "EXCESS MORTALITY" during a period of time when the infectivity of the virus is at peak in a given population. [WHO]

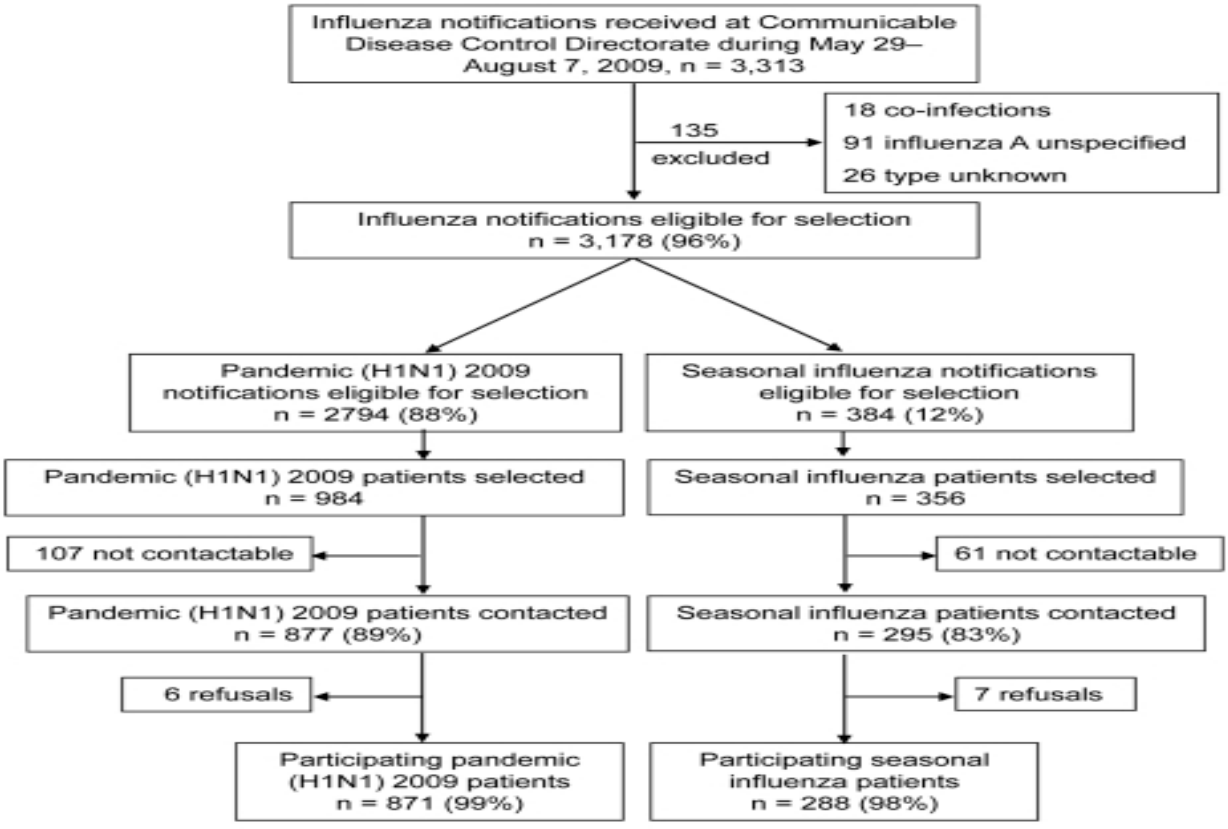

Fig. 3) Recruitment of pandemic and seasonal influenza study participants,Western Australia 2009. (Image courtesy: www.researchgate.net)

1.3.2 ESTIMATING NUMBER OF MORTALITY CASES IN ALL-CAUSE:

The way of estimating "excess mortality" were introduced in 19th century to capture the Influenza related deaths otherwise the recorded data would be misplaced.

The statistical model uses data to estimate death as recorded in death certificate and medical records. These records give us a baseline data on comparing Pandemic and Seasonal Influenza.

As stated by WHO, the studies of comparisons between Influenza A H1N1 and seasonal Influenza A are based on estimates and relative differences in mortality rates. These comparisons may be inaccurate and misleading. However, the present study doesn't conclude any of these factors, but the main attention is to draw the differences between socio-demographic and clinical differences of both Influenza A infections. [WHO]

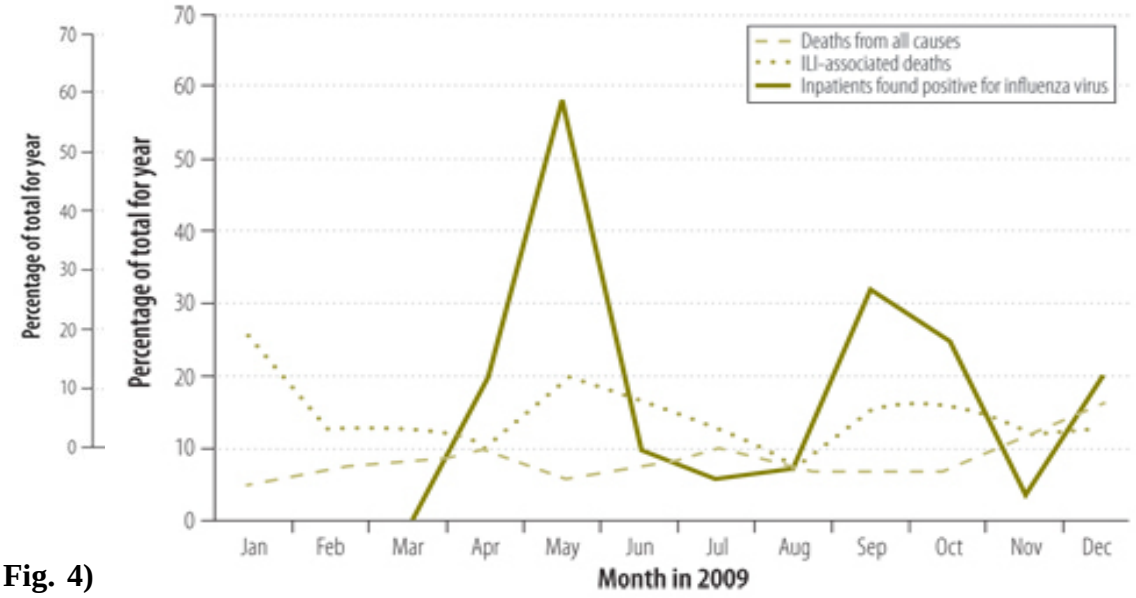

Fig. 4) s found positive for influenza virus 2009. (Image courtesy: www.who.int)

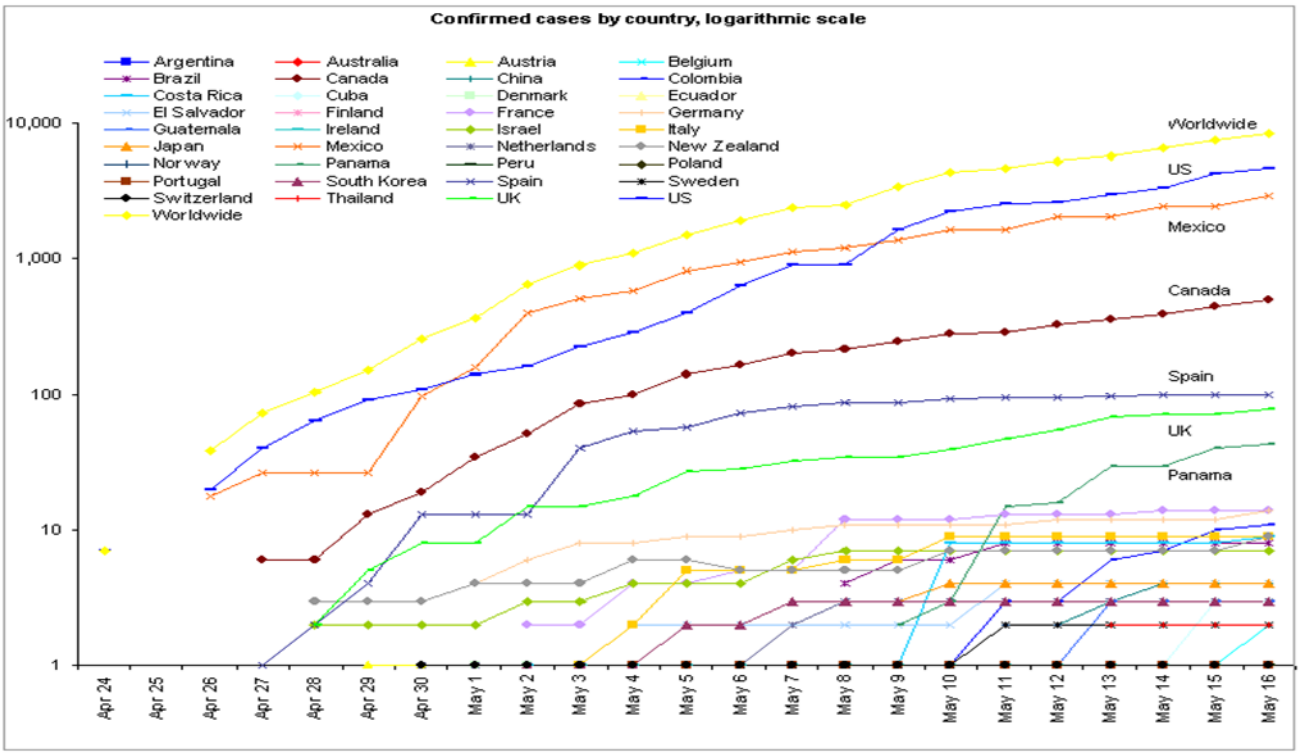

Fig. 5) Confirmed cases of different countries using the Statistical method. (Image courtesy: www.researchgate.net)

1.3.3 COMPILATIONS OF RECORDS THROUGH LABORATORY CONFIRMED DEATHS:

The number of deaths from pandemic Influenza is not an estimate guess but laboratory confirmed report. These are notified by national laboratories and tabulated by WHO. However, the confirmed cases do not give the true picture of mortality and can be substantially higher. The figures may indicate only minor groups of Influenza related deaths which are definitely diagnosed and confirmed in lab. [WHO]

As pandemic Influenza mimics with signs and symptoms of other infectious disease, doctors do not suspect H1N1 infection and do not test. This picture is true for developing countries where respiratory diseases like Pneumonia are common. Moreover, the routine testing for pandemic Influenza is costly, demanding and beyond reaches of many countries. If the testing is done and confirms H1N1 infection, doctors record the infection as underlying medical condition not due to

pandemic Influenza. In many cases these records are not found and are misplaced. [Al-Muharrmi, 2010]

Moreover, in a large number of developing countries the systems for registrations are either poor or non-existent, leading to no investigation of deaths nor certified in terms of the cause.

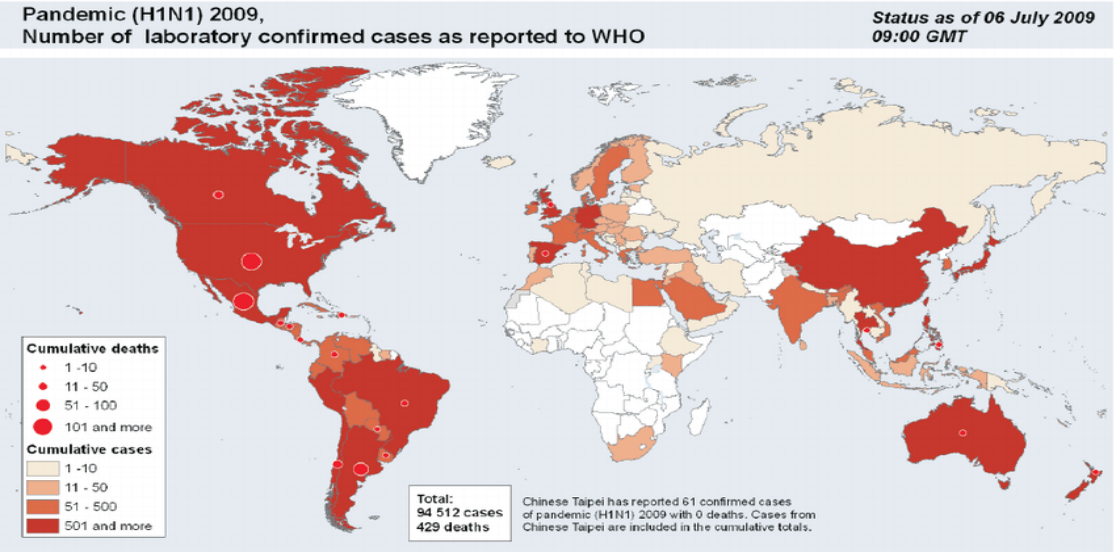

Fig. 6) Pandemic H1N1 2009, Number of laboratory confirmed cases as reported by WHO. (Image courtesy: www.researchgate.com)

1.4 SURVEILLANCE

1.4.1 WORLDWIDE SPREAD OF THE NOVEL H1N1 INFLUENZA VIRUS

The H1N1 Influenza virus that emerged in 2009 was novel by its nature, i.e., the world encountered the reported virus for the first time. Generally when a novel virus emerges, it spreads very rapidly because most of the people are not immune to it. Same issue was observed during the spread of the novel H1N1 virus.

The first identified case of H1N1 pandemic was reported in April 2009, in the city of Veracruz, Mexico. Beginning of June 2009, more than 70 countries had reported cases of novel H1N1 infection, and WHO declared it as a ‘pandemic’ on June 11, 2009 and raised its pandemic alert level to the highest phase. During the next few months, the disease had spread to over 213 countries and territories of the world. This was the ‘first wave' of the Swine flu pandemic. By the end of

October, countries like USA had reported the start of the ‘second wave’ of the spread of H1N1 influenza A virus. Multiple waves of the spread of the disease were observed in the countries with a significant cattle population. [Carcione et al., 2010] [CDC, 2009]

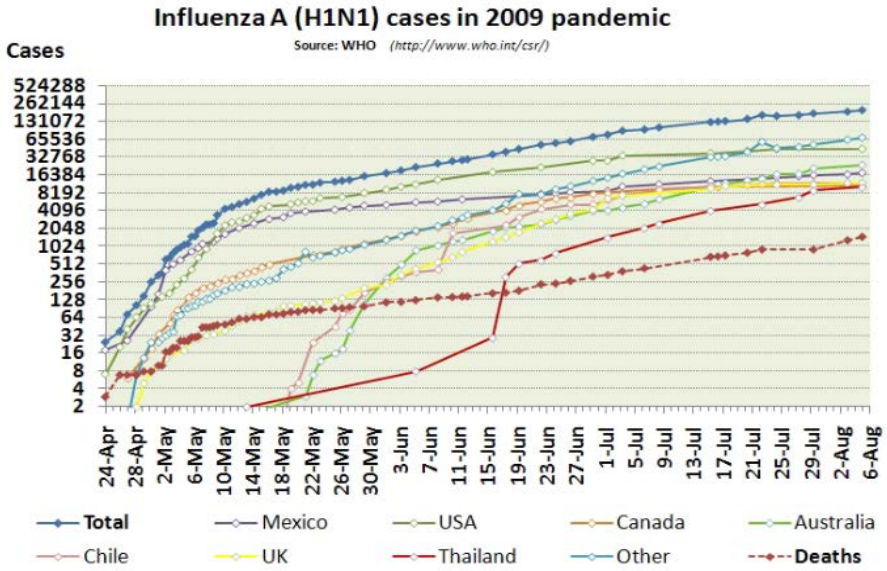

Fig. 7) Influenza A (H1N1) cases in 2009 pandemic. (Image courtesy: www.who.int/csr)

1.4.2 HIGH RISK OF VIRUS IN SPECIFIC GROUPS

People with illness suffering from 2009 H1N1 virus has ranged from mild to severe. While most of the people have recovered without special medical treatment, hospitalizations and deaths from infection have occurred.

In Seasonal Influenza certain groups of people are at ‘High Risk’ with serious complications. A pediatric representation of H1N1 2009 can be atypical. The severity of infection is often attributed as underlying disease cause and rates of secondary bacterial infections are low. [Simonsen et al., 2013]

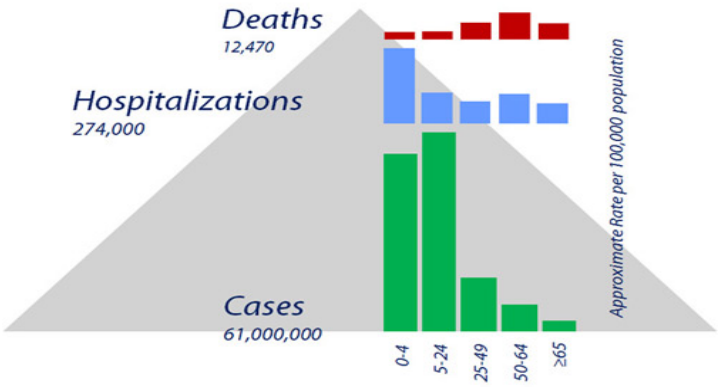

Fig. 8) Approximate rate per 100,000 population. (Image courtesy: www.cdc.gov)

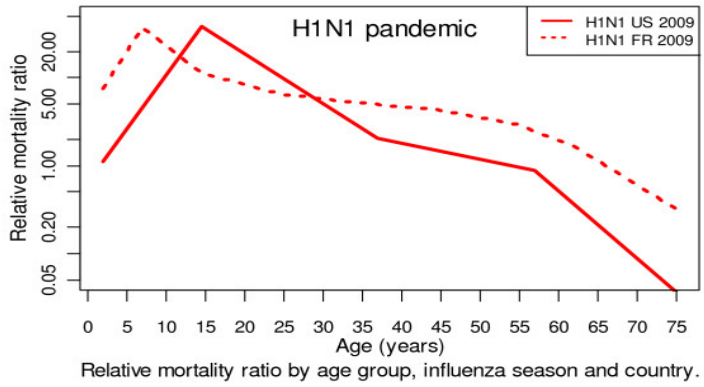

Fig. 9) Relative ratio by age group, influenza and country. (Image courtesy: www.researchgate.org)

1.4.3 TYPES OF COMPLICATIONS OBSERVED

Most people who get flu (either seasonal or 2009 H1N1) will have mild illness and do not require medical help or antiviral drugs. They are likely to be recovered within two weeks. However, some people tend to have serious health complications that results in being hospitalization, intensive care and occasionally results in death.

Some reported cases of health complications shown by both children and adults are –

1. Pneumomediastinum.

2. Seizures.

3. Altered mental illness.

4. Pneumonia.

5. Bronchitis.

6. Sinus infection.

7. Ear infection. [Simonsen et al., 2013]

The flu can also make chronic health problems worse. The list below includes the groups at higher risk of severe influenza (H1N1 2009).

1. Children younger than 5, but especially children younger than 2 years old.
2. Adults 65 years of age and older.
3. Indigenous populations.
4. Pregnant women.

Possible risk groups –

1. Obesity (Body mass index >35).

2. Extreme/ Morbid obesity (Body mass index >40) are also at higher risk because they have one of the higher risk conditions. [Lemaitre and Carrat, 2010]

Table 2. Underlying Medical Conditions among the Patients, According to Age Group.*

Medical Condition	All Patients (N=272)	Patients <18 yr (N=122)	Patients ≥18 yr (N=150)
		number (percent)	
Any one condition	198 (73)	73 (60)	125 (83)
Asthma	76 (28)	35 (29)	41 (27)
Chronic obstructive pulmonary disease	22 (8)	0	22 (15)
Diabetes	40 (15)	3 (2)	37 (25)
Immunosuppression	40 (15)	11 (9)	29 (19)
Chronic cardiovascular disease	35 (13)	5 (4)	30 (20)
Chronic renal disease	25 (9)	7 (6)	18 (12)
Neurocognitive disorder	20 (7)	14 (11)	6 (4)
Neuromuscular disorder	19 (7)	13 (11)	6 (4)
Pregnancy	18 (7)	1 (1)	17 (11)
Seizure disorder	18 (7)	13 (11)	5 (3)

* Patients who are pregnant, who have immunosuppression (from either medications or immune disorders, including human immunodeficiency virus infection), or who have chronic pulmonary disease (e.g., asthma or chronic obstructive pulmonary disease), cardiovascular disease (excluding hypertension), or renal, hepatic, hematologic, neurologic, or metabolic disease (e.g., diabetes) are considered to be at high risk for influenza-related complications. For additional clinical characteristics of the patients, see Table 1 in the Supplementary Appendix.

Fig. 10) Underlying medical complications among the patients according to age group. (Image courtesy: www.nejm.org)

Table 1. Characteristics of 272 Hospitalized Patients Who Were Infected with the 2009 H1N1 Virus in the United States (April–June 2009).

Characteristic	No. (%)
Female sex	132 (49)
Age group*	
0–23 mo	23 (8)
2–4 yr	20 (7)
5–9 yr	29 (11)
10–17 yr	50 (18)
18–49 yr	104 (38)
50–64 yr	32 (12)
≥65 yr	14 (5)
Race or ethnic group†	
Hispanic	83 (30)
Non-Hispanic white	73 (27)
Black	53 (19)
Native Hawaiian, Asian, or Pacific Islander	15 (6)
Native American	9 (3)
Multiracial, not further defined	2 (1)
Unspecified	37 (14)

* The median age of the patients was 21 years (range, 21 days to 86 years). Percentages may not total 100 because of rounding.
† Race or ethnic group was reported in the clinical chart.

Fig. 11) Characteristics of hospitalized patients who were infected with the 2009 H1N1 Virus in USA. (Image courtesy: www.nejm.org)

Table 4. **Characteristics of Hospitalized Patients Who Were Not Admitted to an Intensive Care Unit (ICU) and Survived and Patients Who Were Admitted to an ICU or Died.***

Characteristic	Patients Who Were Not Admitted to an ICU and Survived (N=205)	Patients Who Were Admitted to an ICU or Died (N=67)
Age		
Median — yr (range)	19 (21–80)	29 (1–86)
<18 Yr — no. (%)	98 (48)	24 (36)
Shortness of breath — no. (%)	104 (51)	58 (87)
Neurocognitive disorder — no. (%)	11 (5)	9 (13)
Neuromuscular disorder — no. (%)	10 (5)	9 (13)
Pneumonia seen on chest radiography on admission — no./total no. (%)	51/182 (28)	49/67 (73)
Antiviral treatment — no./total no. (%)		
Any — no./total no. (%)	144/203 (71)	56/65 (86)
≤2 Days after onset of symptoms — no./total no. (%)	62/139 (45)	13/56 (23)
Days from onset of symptoms to initiation — no. (range)	3 (0–29)	5 (0–24)
Antibiotic treatment — no./total no. (%)	144/195 (74)	62/65 (95)
Corticosteroid treatment — no./total no. (%)	57/183 (31)	29/56 (52)

* For all variables listed here, the comparisons between hospitalized patients who were not admitted to an ICU and who survived and patients who were admitted to an ICU or died were significant on bivariate analysis ($P<0.05$). The chi-square test was used to compare categorical variables, and the Wilcoxon rank-sum test was used to compare continuous variables. For additional clinical characteristics of the patients, see Table 2 in the Supplementary Appendix.

Fig. 12) Selected Laboratory abnormalities in the patients. (Image courtesy: www.nejm.org)

1.5 POST-PANDEMIC EFFECT

The H1N1 swine flu was declared as a pandemic in June 2009. After that, the world witnessed more than 17000 deaths within a year and a half, until WHO declared the end of the pandemic in August 2010.

But like most of the viruses, the H1N1 swine flu virus took the behavior of a seasonal influenza, and circulated for sometime following the pandemic. Though the pandemic was declared to have been ended, still New Zealand reported cases of different localized transmissions for a few months. During the pandemic, the H1N1 Influenza A strain was observed to be the dominant strain over the other viruses. This was largely reduced over the following years, when some countries started to report Influenza cases caused by other seasonal Influenza strains. [WHO, 2010] [Fajardo-Dolci et al., 2012]

Many studies revealed that nearly 20-40% of the population in the infected areas had developed protective immunity. This was a sign of relief for the producers of vaccine. Within a significant

time span, different countries came up with a number of vaccines, which were later released in the markets worldwide. [Choudhary et al., 2012]

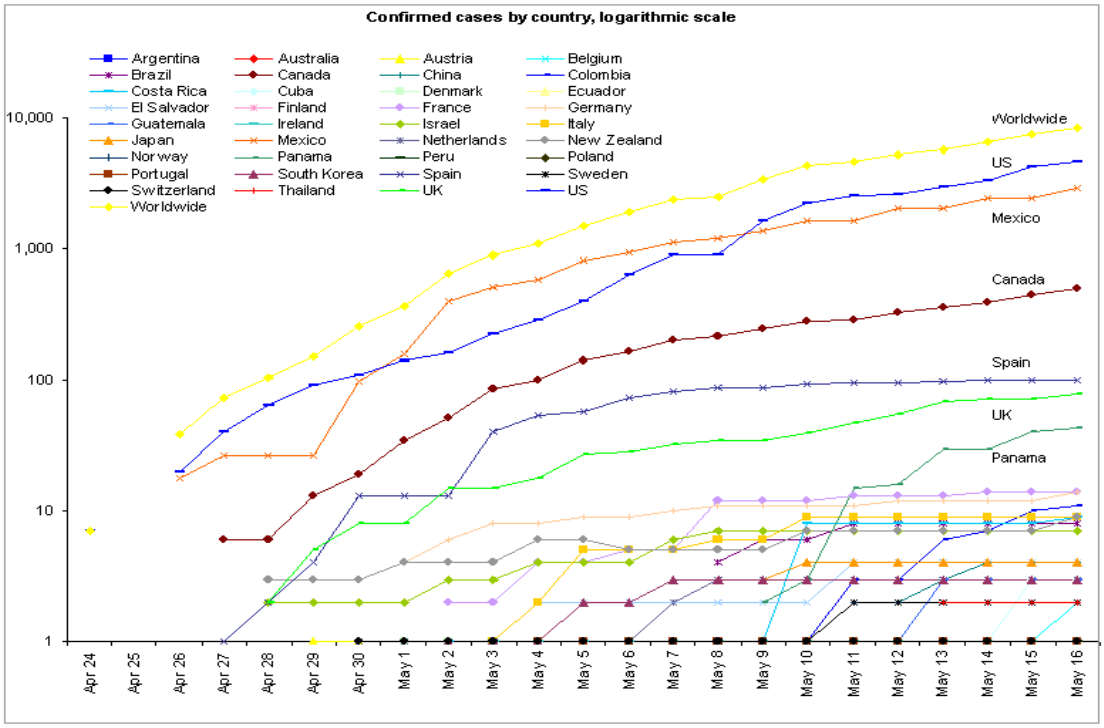

Fig. 13) Confirmed cases of countries in logarithmic scale. (Image courtesy: www.researchgate.net)

1.6 CONCLUSION

The world experienced a pandemic during 2009-2010, after nearly 41 years of the previous one. Though a large number of deaths were reported, some people developed self-immunity and many of them were provided with the vaccines. The main fear was the possibility of the rise of a new strain of the H1N1 influenza virus, leading to another wave of the disease. Fortunately, the mutations have not occurred rapidly, and no new strain of Swine flu with pandemic-potential has been reported till the beginning of July 2020.

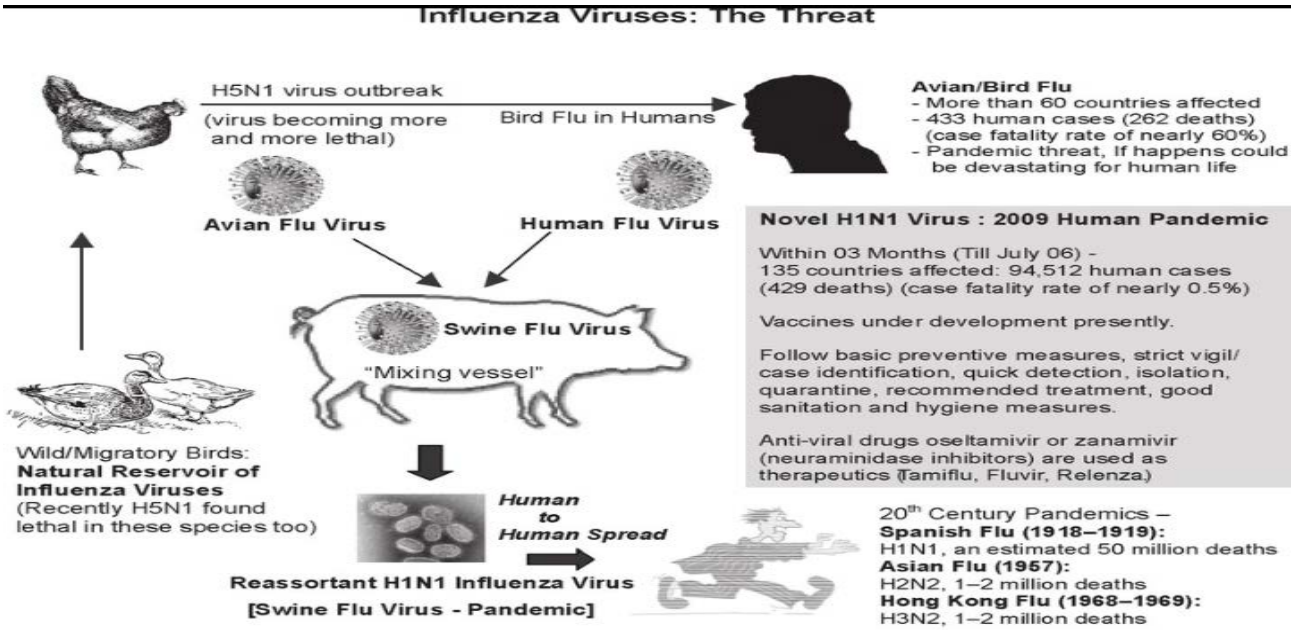

Fig. 14) Transmission of Influenza Viruses among different groups. (Image courtesy: www.researchgate.org)

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EFFECT OF VIRAL LEGACY ON HUMAN SOCIETY

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ABSTRACT

A pandemic is the larger form of epidemic occurring on a scale that crosses international boundaries, usually affecting people on a worldwide scale.It is evident that there are some basic differences between the terms ‘epidemic’, ‘pandemic’ and ‘endemic’. An epidemic is a disease or condition that affects many people within a community, population or region. Whereas a pandemic is an epidemic that spreads over multiple countries or continents, but not all epidemics turn into a pandemic.Endemics on the other hand, are something that belongs to the peoples of a specific location or a country. Such as malaria is endemic to some parts of Africa. Animals are silent carriers of many viruses that rarely spread to humans which when gets mutated become transmissible, contagious and highly harmful to humans. This article is mainly focused on the different viruses outbreaks that affected not only human health but also affected economy and effective vaccines present to defend us from this acellular particle. The WHO has a six phase program for identifying potential flu pandemics. This 2019 Novel corona virus pandemic taught us that prevention is better than cure and also we should all be conscious with our immune system and health.

The WHO's Pandemic alert system ranges from Phase 1(a low risk) to Phase 6(a full pandemic) …

Phase 1: - A virus in animals has caused no known infection in humans.

Phase 2: - An animal virus has caused infection in humans.

Phase 3: - There are scattered cases or small clusters of disease in humans. If the illness isspreading from human to human, it is not broad enough to cause community level outbreak.

Phase 4: - The disease is spreading from person to person with confirmed outbreaks at thecommunity level.

Phase 5: - The disease is spreading between humans in more than one century of the oneof the WHO regions.

Phase 6: - At last one more country, in a different region from phase 5 has community-level outbreaks.

•The basic strategies in the control of an outbreak are: -

1) Containment

It includes contact tracing and isolating infected individuals to stop the disease from spreading to the rest of the population, other public health interventions on infection control, and therapeutic counter measures such as effective vaccinations if available.

2) Mitigation

When it becomes no longer possible to avoid the spread of the disease, a mitigation stage comes in the scene, in which measures are taken to slow the spread of the disease and mitigate its effects on society and the health care system. Containment and mitigation measures may be undertaken simultaneously.

• A key way to manage an infectious disease outbreak is to decrease the epidemic peak, known as "flattening the epidemic curve" which decreases the risk of health services being

overwhelmed, and provides more time for a vaccine and treatment to be developed. A broad group of the so-called non pharmaceutical interventions may be taken to manage the outbreak which include personal hygiene, wearing facemasks, self-quarantine, social distancing (closing schools and cancelling mass gatherings) and environmental measures (cleaning of surfaces). Another strategy to manage such a situation is suppression, in which entire cities are placed under lockdown, but such strategy knocks in social and economic costs.

Prominent Viral pandemics that haunted India: -

1) **The 1918 flu pandemic in India between (1918-1920):** It was a part of the worldwide Spanish flu pandemic, referred to as the Bombay Influenza or the Bombay Fever in India which had killed 14 -17 million people in the country. In India, the pandemic broke out in Bombay in June 1918, with one of the possible routes being via ships carrying troops returning from the First World War in Europe. The outbreak most severely affected younger people in the age group of 20 - 40, with women who were relatively undernourished and sick died more than men. The spread of the disease was exacerbated by a failed monsoon and the resultant famine-like conditions that had left people underfed and weak, and forced them to move into densely populated cities. The commissioner's report for 1918 noted that all rivers across India were clogged up with bodies, because of a shortage of firewood for cremation. Hindi poet, SuryakantTripathi, wrote "Ganga was swollen with dead bodies." Mahatma Gandhi, the leader of India's independence struggle, was also infected by the virus. The healthcare system in the country was unable to meet the sudden increase in demands for medical attention.

2) **Smallpox (1974):** It is caused by infection with the Variola virus. 60% of the smallpoxcases globally were reported in India and were more virulent as compared to other parts of the world. Though India launched the National Smallpox Eradication Program (NSEP) and failed to get the desired results. However, WHO along with the Soviet Union sent some medical assistance to India and in March 1977 India was free from smallpox.

3) **SARS (2002-2004):** In the 21st century, the first severe disease was SARS whichbecame an epidemic throughout the country as it was transmissible from one person to another through coughing and sneezing. It was a severe acute respiratory syndrome (and the cause of SARS was like COVID-19, named SARS-CoV).

4) Dengue and Chikungunya Outbreak (2006): These are transmitted to humans bythe bites of infected female mosquitoes. Several parts of India were infected, and the highest numbers of patients were reported in Delhi. Globally, Chikungunya disease was first recognized in 1952 during an outbreak in southern Tanzania.

5) Swine flu outbreak (2014-2015): In the year 2014, states like Gujarat, Rajasthan,Delhi, Maharashtra and Telangana were among the worst affected states due to the virus. Swine flu is a type of influenza virus H1N1. Approximately 33,000+ cases were reported from all over the country and about 2000 people died.

6) Nipah Virus outbreaks (2018): In May 2018, an infection was caused by fruit bats it was being reported in Kerala which became an epidemic within a few days. There have been 17 deaths and 18 confirmed cases as of 1 June 2018. Due to the preventive measures, by the month of June, the outbreak was curbed within Kerala.

Globally highlighted most brutal viruses include: -

1) EBOLA VIRUS:- Ebola outbreaks in humans were the first ever recorded, struck simultaneously inthe Republic of the Sudan (mortality rate was 71%) as well as in the Democratic Republic of Congo in 1976 (mortality rate was 50%). Ebola is spread through contact with blood or other body fluids, or tissue from infected people or animals. The Western African Ebola virus epidemic (2013–2016) is regarded as the most widespread outbreak of EVD in human history with a mortality rate of 40%. The first case was recorded in Guinea (December 2013); later the disease spread on to neighboring Liberia and Sierra Leone. In December 2016, the WHO announced that a two-year trial of the rVSV-ZEBOV vaccine was appeared to offer protection from the variant of EBOV (Makonavariant) was responsible for the Western Africa outbreak. The vaccine is considered to be effective and is the only prophylactic and offers protection, rVSV-ZEBOV received regulatory approval in 2019.

2) HIV/AIDS PANDEMIC (AT ITS PEAK, 2005-2012):- It was one of the great pandemic in the second half of the twentieth century. AIDS is the result of an infection by the Human immunodeficiency virus (HIV). It passes from one infected person to another by infected blood, semen, vaginal secretion. It was first identified in Democratic Republic of the Congo in 1976, HIV/AIDS has truly proven itself as a global pandemic, that killed more than 36 million people in 1981. Currently there are between 31 and 35 million people living with HIV, The vast

majority of them are in Sub-Saharan Africa, where 5% of the population is infected, roughly about 21 million people. Between 2005 and 2012 the annual global deaths from HIV/AIDS dropped from 2.2 million to 1.6 million due to the latest advancement in medical facilities.

3) FLU PANDEMICS:- FLU PANDEMIC (1968)/ THE HONG KONG FLU Mortality rate:0.5 % it was actually caused by the H3N2 strain of the Influenza A virus, which was a genetic offshoot of the H2N2 subtype. In Hong Kongon July 13, 1968the first reported case was found. Within 17 days' cases were reported in Singapore and Vietnam, and within a time span of three months it had spread to The Philippines, India, Australia, Europe, and the United States. Almost 15% of the population residing in Hong Kong was killed due to this disease.

4) ASIAN FLU (1956-1958):- Mortality rate 0.67%. It was a pandemic outbreak of Influenza A of the H2N2 subtype, thatwas originated in China in 1956 and lasted until 1958. Within two years it went down to Singapore, Hong Kong, and the United States from the Chinese Province. Approximately 2 million deaths were officially reported.

5) FLU PANDEMIC (1918):- There is no universal record that was found in mortality rate where thevirus was first originated, it spread worldwide during 1918- 1919. In the United States, it was first identified in the military personnel in spring 1918. It infected over third of the world's population and ended the lives of 20 – 50 million people out of the 500 million people in the pandemic of 1918. What separated the 1918 flu pandemic from other influenza outbreaks were actually the types of victims; nevertheless, influenza had always previously killed juveniles and the elderly or patients with pre medical conditions, it had begun striking down hardy and completely healthy young adults, while leaving children and those with weaker immune systems still alive.

6) SWINE FLU (2009):- Mortality Rate from 0.001 percent to 0.007 percent of the world's population died due to the respiratory complications associated with (H1N1) pdm09 virus infection in the spring of 2009, a novel influenza A (H1N1) virus emerged in US which spread quickly throughout the world. This new H1N1 virus contained a unique combination of influenza genes that was not previously identified. This virus was designated as influenza A (H1N1) pdm09 virus. Only one-third of older people, more than 60 years old had previous exposure to (H1N1) virus already developed antibodies to fight against any further exposure of the virus. Unlikely to the fewer younger population with an existing immunity to the (H1N1) pdm09 virus.

Emergence of effective vaccines:-

1) Edward Jenner in 1716 developed the first successful vaccine which is small pox virus. While he observed he found that the milkmaids who were previously caught by the cowpox did not catch smallpox and showed later that inoculated vaccines protected against inoculated variola virus. (WHO Small Pox Vaccines, 2014)

2) A member of the paramyxovirus family is Nipah virus, which was first isolated and identified in 1999 the virus crossed the species barrier from the fruit bats to pigs and then infected humans, inducing an encephalitis with up to 40% mortality. (Science Daily Nipah Virus,2019)

3) One of the major medical breakthroughs of the 20th centurywas the development of effective vaccines which would prevent the paralytic polio. There are two different kinds of vaccine, an inactivated (killed) polio vaccine (IPV) and a live attenuated oral polio vaccine (OPV). (WHO Poliomyelitis, 2020)

4) Inactivated influenza vaccines (and live attenuated influenza vaccines (LAIV) were the two types of influenza virus IIV) which was found widely available.To protect against this 3 different seasonal influenza viruses,traditionally influenza vaccines (both IIV and LAIV) have been produced which are also called as trivalent viruses. (WHO Influenza virus, 2014)

In the recent decade, the corona virus disease 19 (COVID-19) is a highly transmittable and pathogenic viral infection caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which emerged in Wuhan, China and spread around the world. The disease is caused by a new strain of coronavirus where 'Co' stands for corona and 'Vi' stands for virus and 'D' stands for disease. It is referred to as 2019 novel coronavirus or 2019 ncov. Virus is transmitted through direct contact with respiratory droplets of an infected person through coughing and sneezing. People can also infect through contaminated objects and then touch their faces, as the virus can enter through eyes, nose or mouth. The symptoms of this disease are similar to flu or the common colds like fever, cough, and shortness of breath etc. In more severe cases infection can cause pneumonia or breathing difficulties. More rarely this disease can be fatal especially for older people and people with chronic medical conditions such as diabetes, cancer, heart disease etc. It can affect people of any age but relatively chances of affecting young people are less than the older. As this is a new virus scientists are still learning about it. There is no currently available vaccine for Covid- 19. However many of the symptoms can be treated and getting early care from a health care provider can make the disease less dangerous. There are several clinical trials in many countries that are being conducted to evaluate potential therapeutics for Covid-19. Till then we should try to slow the spread of this disease, maintaining some common and general habits like staying home when sick, covering mouth and nose when coughing or sneezing, washing hands with soap and water or using sanitizer, wearing a mask and maintaining social distance.

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PANDEMIC: A TERROR

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ABSTRACT:

Pandemics have a long history, but the term “pandemic” is still not been defined by many medical texts. This current pandemic situation of Novel Corona Virus (Covid-19) is not a new thing in the history of humanity. Many pandemics have occurred over ages and affected the lives of thousands of people. From the Plague of Athens to the current Novel Corona Virus Situation, Pandemics have occurred overtimes and people have suffered because of it. There have been many significant pandemics recorded in the history of humans. The pandemics related crisis has caused huge negative impacts on health, economics, and even the national security of the world. This article will explore about the concept of history of pandemics that have occurred since the early ages. Through this we come to know that pandemics have occurred in the past and they will be occurring in the future, we can’t do anything about it but to be mentally and physically prepared. We should not only pause to remember and reflect but to seek lessons from them, these lessons can help us prevent, control, and limit future tragic pandemics.

Keywords: Pandemic

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1.1 Introduction

A **pandemic** is generally an outbreak of a disease that spreads across countries or continents. It affects a larger amount of people and takes more lives than an epidemic. The amount of lives lost in a pandemic depends on: -

- How vulnerable certain groups of people are
- How many people are infected

- Prevention efforts and how effective they are
- How severe an illness that the virus causes

The WHO's pandemic alert system ranges from phase 1(a lower risk) to Phase 6(full pandemic)

- Phase 1-
  An animal illness causing virus has caused no known infections in humans.
- Phase 2-
  An animal virus has caused infections in humans.
- Phase 3-
  There are scattered cases of disease in humans. If the illness is spreading from human to human, it's not wide enough to cause community level outbreaks.
- Phase 4-
  The disease is spreading from human to human with confirmed outbreaks at the community level.[1]
- Phase 5-
  The disease is spreading between humans in more than one country of one of WHO regions.
- Phase 6-
  At least one more country that is in a different region from phase 5 has community level outbreaks.

Like human beings, infectious diseases are also spreading across the world. Even in these modern ages, outbreaks are nearly constant, though not every outbreak reaches pandemic level as Covid-19 (Novel Corona Virus). Today's visualization outlines some of history's most deadly pandemic from the Antonine Plague to the current Novel Corona Virus event. [2]

Disease and illness have plagued humanity since the first days, our mortal flaw. However, it was not until the mark shift to agrarian that the scale and spread of these diseases increased adequately. [2]

Widespread trade created new opportunities in human being and animal interactions that sped up such epidemics. Influenza, Tuberculosis, Leprosy, Smallpox, Malaria, and thousands of others, first appeared during these early years.

The more developed humans become with larger cities, more exotic trade roots and increased contact with different populations of people, ecosystem and animals-The more likely pandemics would occur.

1.2 Here are some of the major pandemics that have occurred over time [3]

1. Plague of Athens; 430 BC
2. Antonine Plague; A.D 165-180
3. Plague of Cyprian; A.D 250-271
4. Plague of Justinian; A.D 541-542
5. The Black Death; 1346-1353
6. Cocoliztli epidemic; 1545-1548
7. American Plagues; 16th century
8. Great plague of London; 1665-1666
9. Great Plague of Marseille; 1720-1723
10. Russian Plague; 1770-1772
11. Philadelphia yellow fever epidemic; 1793
12. Flu pandemic; 1889-1890
13. American Polio epidemic; 1916
14. Spanish Flu; 1918-1920
15. Asian Flu; 1957-1958
16. AIDS pandemic and epidemic; 1981-present day
17. H1N1 Swine Flu pandemic; 2009-2010
18. West African Ebola epidemic; 2014-2016
19. Zika Virus epidemic; 2015-present day
20. Novel Corona Virus; 2019-Till date

The **Novel Corona Virus** has taken just a few months to sweep the globe. How many will die, how society will change- these questions are impossible to fathom as the disease rages [4]. But history shows that past pandemic has reshaped societies in many ways. Thousands of millions of people had died, Governments have cracked and generations have been wiped out. Here is a look at how pandemics that remade the world.

- Antonine plague (165-180 A.D)
  Deaths: 5 million **Cause:** Measles and smallpox
- Plague of Justinian (541-542 A.D)
  Deaths: 30-50 million **Source:** Rats and fleas
- Black Death (Mid-14th century)
  Death: 75-200 million **Source:** Rats and fleas
- New world smallpox (1520-unknown)

Deaths: 25-55 million**Cause:** Variola Virus

- Great Plague of London (1665)
  Death: 7 5,000 – 100,000 **Source:** Rats and flea
- The Cholera pandemics (1817-1923)
  Deaths: 1 million **Cause:** V. Cholerae bacteria
- Yellow fever (Late 1800s)
  Deaths: 150,000 **Source**: Mosquito
- The 1918 flu (1918-1920)
  Deaths: 5.0 million **Cause:** H1N1
- Asian Flu (1957-1958)
  Deaths: 1 million **Cause:** H2N2
- Swine flu (2009)
  Deaths: 200,000 **Cause:** H1N1

The Novel Corona Virus, **Covid-19** pandemic is a worldwide health problem of our time and the greatest challenge we have faced since World War II. The virus has spread to every continent excluding Antarctica.

This pandemic situation leads to health crisis; an unprecedented socio-economic crisis which emphasized everyone. It has the potentiality to create devastating economic, social, and political effect that will leave a long-lasting scar.

Each day people are losing jobs and income with no way of knowing when normality will return [5]. **The International Labor Organization** estimates that more than 195 million jobs could be lost; 800 million people will not be able to meet their basic needs.

Drawing experiences from other outbreaks such as, SARS, HIV, Ebola, TB, and Malaria, UNDP will help countries to urgently and effectively respond to Novel Corona Virus as part of its mission to eradicate poverty, reduce inequalities and build resilience to crisis and shock. [5]

We must also find out ways that will prevent a similar pandemic recurring. In the longer term, UNDP will look at ways to help countries to prevent crisis situations ensuring that the world makes full use of what we will learn from this.

The practice of quarantine began during the 14^{th} century, in an effort to protect coastal cities from plague epidemic. Cautious port authorities required ships arriving in Venice from infected ports to anchor for forty days before coming to land [5]. The origin of the word quarantine is

from the Italian word ‘quarantagiorni’ meaning forty days. It’s difficult to calculate and forecast the actual impact of Covid-19, as the outbreak is still ongoing, and researchers are still learning about this new form of corona virus.

1.3 Urbanization and spreading of diseases

We arrived at where we began, with an increasing global interactions and connections as a driving force behind all pandemics. From small hunting and gathering to metropolis, humanity’s dependence on one another has also made opportunities for disease to spread.

Urbanization in the developing world is bringing more and more rural residents into denser neighborhoods, while increasing population are putting great pressure in the environment. These macro trends are having an intense impact on the spread of infectious disease.

As governments and organizations around the world ask citizen to practice social distancing to help reduce the rate of infections, whereas the digital world is helping people to maintain connections among each other.

An effective and efficient emergency response can reduce avoidable mortality and morbidity and reduce the types of economic and social impacts. How to have an effective and efficient emergency management will be a critical task of governments to deal effectively with disease outbreak and a pandemic. At last it can be concluded that pandemic can be fought only when a combined global response is received which is an investment for our future.

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AN IN DEPTH STUDY OF VIRAL PANDEMICS OCCURING WITHIN THE PERIOD OF 1956-2012

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Abstract: Significant viral pandemics have been recorded in human history, and the diseases caused by the viruses have had a disastrous impact on health, economy and even national security in the world. Pandemics are an outbreak of diseases caused by a microorganism which affects people all around the globe and this article will explore some of the worst global pandemics within the history of mankind from the 1950s to 2012 owing to which variant lives have been lost and which had a negative impact on the economic conditions of the infected countries. This article explores viral pandemics like the Asian Flu(1956-1958), Hong Kong Flu (1968),Swine Flu Influenza pandemic (2009) and the HIV/AIDS Pandemic (2005-2012 at its peak).These are some of the viral pandemics that have caused innumerable deaths and this article discusses the origin of the viral strain responsible for the outbreak, the maximum number of people affected, how the virus was transmitted, the symptoms shown by the infected individuals , the treatments undertaken and how the pandemic came to an end.

Keywords: Virus, pandemic, diseases, treatment, deaths

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1.1 INTRODUCTION:

An epidemic spanning over an outsized scale crossing geographical boundaries and affecting people on a worldwide scale is understood as an outbreak (pandemic) (CDC Bulletin, 2019).

The following article is a study of the worst global viral pandemics within the history of mankind from 1950 to 2012, owing to which variant lives have been lost.

1.2 ASIAN FLU (1956-1958)

1.2.1 ORIGIN:

Originating from a mutation in wild ducks combining with a pre-existing human strain in 1956, the Asian flu was an outbreak of Influenza A of H2N2 subtype that spread from the Chinese province of Guizhou to Singapore, Hong Kong, and also the U.S. of America infecting a complete of 5.5 million (CDC Bulletin, 2019).Roughly 2 million deaths occurred, 69,800 of them died within the US alone (WHO Bulletin, 2020).

1.2.2 SYMPTOMS:

The elderly were particularly affected to the flu (WHO Bulletin, 2020). The symptoms included:

- Fever
- Body aches
- Chills
- Dry Coughs
- Weakness and loss of appetite
- Raw throat
- Breathing Issues

Recovery from the H2N2 virus took many weeks and several other complications like pneumonia, seizures, and heart disease were also reported (WHO Bulletin, 2020).

1.2.3 SPAN:

The Asian flu falls under one among the categories of the two flu pandemic outbreaks of avian influenza that originated in 1956 in China and lasted till 1958. A vaccine for the H2N2 flu was

introduced in 1957 causing the pandemic to curtail. But there was a second wave in 1958, then it became part of the regular wave of seasonal flu (Cox et al., 2003). In 1968, the H2N2 Asian Flu is claimed to have completely disappeared from the population. HA proteins, referred to as Hemagglutininin proteins, these are homotrimers having receptor binding pockets on the globular head of a monomer. They have 18 antigens H1 to H18 and have two functions, one is that the recognition of target vertebrate cells and the other is to ease the entry of viral genome into the target cells by fusion of host endosomal membrane with the viral genome. For viral activation, HA is cleaved by a Trypsin like Serine endoprotease between HA1 and HA2 domains of the protein (WHO Bulletin, 2020).

1.3 THE HONG KONG FLU (1968)

1.3.1 ORIGIN AND DEATH TOLL:

One among the two Flu pandemics is "the Hong Kong Flu". This flu pandemic originated in 1968 and was caused by the H3N2 strain of the Influenza A. The initial case was reported in Hong Kong on 13th July 1968, and it took only 17 days before outbreaks of the virus were reported in Singapore and Vietnam (Snacken et al., 1999). Within 3 months the flu had spread to The Philippines, India, Australia, Europe, and also the US. This Pandemic had a fatality rate of 0.5% but still resulted the deaths of quite 1,000,000 people, including 500,000 residents of Honk Kong, which was almost 15% of its total population at the time (Cox et al., 2003).

1.3.2 NEW SUBTYPES:

The H3N2 strain of the influenza a deadly disease, descended from H2N2, through the antigenic shift, a genetic process during which genes from multiple subtypes are assorted to make a replacement virus. The H3N2 virus struck again during the subsequent 1960/1970 flu season, leading to a second, more drastic deadlier wave of deaths. It remains prevalent and in circulation, even today as a strain of seasonal flu. Both the H2N2 and H3N2 pandemic flu strains had derived genes from the avian influenza viruses (Snacken et al., 1999). The new subtypes arising in pigs infected with the avian and human viruses were swiftly transmitted to humans. (WHO Bulletin, 2020).

1.3.3 SYMPTOMS:

- Upper respiratory disorders
- Chills
- Fever
- Muscle pain
- Fatigue.

The symptoms usually persisted between four to six days (WHO Bulletin, 2020). Maximum deaths occurred in those 65 and older. However, fewer people died during this pandemic than the previous viral pandemics for several factors. Some immunity had been retained in populations against the H2N2 flu virus during the Asian flu pandemic in 1957 (Snacken et al., 1999).The spread of the infection had been limited because the flu had hit during the winter school vacations and therefore the availability of higher medical facilities and antibiotics was effective to supply ample support to the ill. The Hong Kong flu H3N2 strain shared the identical internal genes and neuraminidase with the Asian flu. So the previously-stored antibodies to the neuraminidase, aided greatly in this pandemic (WHO Bulletin, 2020).

1.4 2009 SWINE INFLUENZA PANDEMIC (2009-2010)

In April 2009, the Influenza A/H1N1 virus, termed as the swine flu, which originated from animal influenza viruses began to spread alarmingly (Guan et al, 2010).

1.4.1 TOTAL POPULATION INFECTED:

Approximately 151,700 to 575,400 deaths were reported globally within the first year of the disease caused by the H1N1 (H1N1) pdm09 virus. Within the U.S. about 43.3-89.3 million cases and 8868-18306 deaths were confirmed within one year of the virus spread (Taubenberger et al., 2008).

1.4.2 MORTALITY RATE AND THE MOST AFFECTED GROUP:

About 80 percent of deaths occurred within the age below 65. Children and middle-aged adults instead of the aged were mainly victimized by the pandemic. It is a big feature of this strain of Influenza that differentiates it from other strains of Influenza, especially the everyday seasonal cases of flu which primarily affects the population above the age of 65 years. (Iwasaki et al., 2014). When compared with other pandemics this was rather less severe as about 0.001%-0.007% of

individuals died globally owing to the respiratory complications caused by H1N1 infection from April 2009 to April 2010 (Guan et al., 2010).

1.4.3 HOW THE DISEASE SPREAD:

The H1N1 virus spread because of

- Close contact from person to the person.
- Exposure to infectious droplets released within the air by the coughing/sneezing of infected (Lowen et al., 2007).

Hence social distancing was the key to tackle the virus (Guan et al., 2010).

1.4.4 MODE OF ACTION OF VIRUS WITHIN THE HOST:

- Upper tract and inflammation of the respiratory passages and trachea occurred.
- Total incubation period for the H1N1 flu virus was 1 - 4 days.
- Contagious period for healthy adults was 1 day before severe symptoms developed and lasted for 7 days.
- In case of youngsters or people with weakened system the contagious period was (10 - 14) days (Stertz et al., 2011).

1.4.5 SYMPTOMS:

- A state of Malaise
- Fever
- Cough
- Headache
- Joint pains
- Sore throat and runny nose
- Vomiting
- Diarrhea

• Shortness of Breath (Monto et al., 2000).

1.4.6 TREATMENT

Maximum people infected with this virus recovered properly without showing severe symptoms and with no intensive medical treatment (Guan et al., 2010).

Basic supportive home care like:

• Resting

• Using pain reliever for pain (Prescribed)

• Drinking adequate fluids throughout the day

People who had breathing issues or fever even after three days were asked to lookout for serious treatment (Couch and R. B, 2000).

1.5 HIV/AIDS PANDEMIC (AT ITS PEAK, 2005-2012)

1.5.1 HUMAN IMMUNODEFICIENCY VIRUS (Retroviruses)

The virus attacks CD4+ T cells, dendritic cells and macrophages directly/ indirectly. They're transmitted as single-stranded, positive-sensed enveloped RNA viruses and are of two different kinds, HIV-1 (LAV or HTLV-III) is more virulent and is the sole reason of the bulk of HIV infections round the globe. HIV-2 have lower virulence and fewer people exposed to HIV-2 are infected, due to its relatively poor capacity for transmission (WHO Bulletin, 2020). HIV destroys CCR5 proteins expressing CD4 T cells during an acute infection which activates immune cells releasing pro-inflammatory cytokines and a number of other HIV gene products. The breakdown of the system of the gastrointestinal mucosal barrier occurs by the depletion of mucosal CD4+ T cells during the acute phase of the disease (Kallings and L. O., 2008).

1.5.2 ACQUIRED IMMUNE DEFICIENCY SYNDROME:

It is a disease caused by the Human immunodeficiency virus (HIV). Initially, an individual might not have any symptoms, however after a chronic period the infection gradually interferes with the immune system, weakens it massively, increasing the chance of developing tuberculosis, and infections by opportunistic microbes (Kallings and L. O., 2008). The symptoms that occur after a

particular period are cited as acquired immunodeficiency syndrome (AIDS). (WHO Bulletin, 2020).

1.5.3 DEATH TOLL:

HIV/AIDS was first identified in the Democratic Republic of the Congo in 1976, killing approximately over 36 million people since 1981(Medical news today Bulletin, 2020). Presently there are between 31 and 35 million people affected by HIV. Precautions and awareness with the advancement of treatments have made the disease more manageable. The annual global deaths from HIV/AIDS dropped in 2005-2012 from 2.2 million to 1.6 million (WHO Bulletin, 2020).

1.5.4 TRANSMISSION OF HIV:

HIV is transmitted from one person to a different by close contact with certain body fluids including blood, Semen, Vaginal Fluid, breast milk of an HIV positive individual. HIV can only be transmitted if these bodily fluids are in contact with the mucosa of a healthy individual. However, it can even get transmitted by damaged skin tissue or via direct injection with a needle or a syringe. (WHO Bulletin, 2020).

1.5.4.1 HIV commonly spreads via:

• Reusing the identical needle or syringe that was used before by an HIV positive patient. HIV can stay viable for about 42 days on used needles however it varies on the environmental conditions it's exposed to.

• Having Unprotected Anal or Vaginal Sex with someone who is HIV positive (CDC Bulletin, 2020).

1.5.4.2 Extremely rare causes of HIV transmission:

• Via Oral sex.

• Blood transfusion or Organ donation

• Being bitten by someone with HIV (No risk of disease spread if the skin isn't broken) (CDC Bulletin, 2020).

1.5.4.3 HIV isn't transmitted by:

• Insects or Pets

• Air

• Water

• Saliva or Tears

• Sweat

• Public Toilet Usage

• Food and Drinks (WHO Bulletin, 2020).

1.5.4.4 MODE OF ACTION OF VIRUS WITHIN THE HOST:

1.5.4.5 INTEGRATION OF THE VIRUS:

After integration into the target cell, the viral RNA genome is reverse transcribed into double-stranded DNA by Reverse transcriptase. The resultant viral DNA is imported into the cell nucleus and is integrated into the cellular DNA by Integrase (WHO Bulletin, 2020).Then the virus may attain latency, to avoid being detected by the immune system. The virus may also be transcribed, to produce new RNA genomes and viral proteins that are packaged and released from the infected cell for a new replication cycle to do HIV infection and can also spread between CD4 cells via two parallel routes: In the cell-free spreading, virus particles bud out from an infected T cell, enter the blood and infects another T cell. In cell to cell spreading, HIV is directly transmitted from one cell to the other (CDC Bulletin, 2020)

1.5.5 TREATMENT:

Diagnosis is done by HIV-RNA/p24 antigen and positive results are also verified by different seroconverted antibodies or PCR (Kallings and L. O., 2008).Treatment of the virus is normally done by slowing the progression of the disease by highly active antiretroviral therapy (HAART) which consists of 3 antiretroviral agents. Initial, treatment is typically a non-nucleoside reverse transcriptase inhibitor (NNRTI) plus two nucleoside analog reverse transcriptase (NRTIs) such as (AZT) or tenofovir (TDF) and lamivudine (3TC) or emtricitabine (FTC) (CDC Bulletin, 2020). WHO in 2019 listed dolutegravir/lamivudine/tenofovir as the first-line treatment for adults, protease inhibitors (PI) are also used if the above combinations fail to work (WHO Bulletin, 2020).

1.5.6 BENEFITS AND SIDE EFFECTS:

The benefits of treatment include a decrease in the progression to AIDS, the risk of death and the chance of acquiring tuberculosis is reduced by 70%. Some side effects of the retroviral agents are lipodystrophy syndrome, diabetes mellitus, and increased risk of cardiovascular disease (Medicalnewstoday Bulletin, 2020).

Adults undergoing anti-retroviral therapy with no symptoms of active tuberculosis should receive isoniazid preventive therapy (IPT) and the tuberculin skin test is used to decide if IPT is needed (WHO Bulletin, 2020).Vaccination against hepatitis A and B is advised to all people who are at risk of HIV before they become infected.(Medicalnewstoday Bulletin, 2020). The prevention of PCP is advised when a person's CD4 count is below 200 cells. Patients with immunosuppression are advised to receive prophylactic therapy for toxoplasmosis. Influenza vaccination and pneumococcal polysaccharide vaccine have been beneficial to people with HIV/AIDS. Caution and proper measures and research reduced the rate of HIV infections by 50% between 1992 and 1997 and by 2020 two people have been cured of AIDS (WHO Bulletin, 2020).

1.6 CONCLUSION:

When a bacterium/virus can spread rapidly on a large scale, they cause an epic outbreak of diseases globally which is termed as a pandemic. Seasonal influenza flu epidemics take place because of an already circulated subtype of the virus among the population but on the other hand Novel subtypes cause Pandemics because they have not been circulated in the population previously (WHO Bulletin, 2020).

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On the brink of a new viral pandemic

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Abstract

As the world is still battling with SARS-CoV 2, the fact is becoming clear that the frequency of pandemics have increased over the past decade. Every pandemic extracts a heavy toll on humanity with a huge loss of life and widespread economic crisis.

It is needed for nations and their government to be aware that such a catastrophe should be prevented to a greater degree; if not totally averted with some stringent measures and planning beforehand. This article discusses some of the ways which might avert the threat of viral pandemic over humanity.

***Keywords**:* Pandemic, zoonosis, anthropogenic factors, , health infrastructure, research funding, vaccine funding, biosafety, surveillance.

1. Introduction

1.1. Impact of environment on viral outbreak

Anthropogenic factors are a major driver for pandemic. Most viruses originate from animals which act as a virus reservoirs. Due to rapid urbanization, deforestation and climate change the chances of virus spillover has increased significantly.(Johnson, C. K., 2020)

1.2. Zoonosis

A zoonosis is any disease or infection that is naturally transmissible from vertebrate animals to humans. Animals thus play an essential role in maintaining zoonotic infections in nature.(Wikipedia “Natural reservoir”, n.d.)

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1.3. Drivers of viral pandemic

Disease emergence or outbreaks often occur following a driver. Examples of such drivers include climate change, economic factors, war, famine, human–wildlife interactions, land use and ecosystem changes.(Johnson, C. K., 2020)

1.4. Animals as a virus reservoir

- The reservoir is any population of organisms (or any environment) which harbors the pathogen and transmits it to the target population. Reservoirs may comprise one or more different species, may be the same or a different species as the target. It may also include vector species, which are otherwise distinct from natural reservoirs.

- Animals such as bats, rodents and pangolins carry many viruses within them but rarely get infected by them since they have developed an inherent immune system against them. (Wikipedia “Natural reservoir”, n.d.)

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1.5. How does destruction of the environment trigger viral pandemics?

- In the last 50 years 60% wildlife was lost and in the last 60 years new infectious diseases have quadrupled.

- The host phylogenetic proximity to humans and increased urbanization within a host distribution has been shown to be positively correlated with the number of zoonotic viruses in a species.

- Logging, mining, road building in remote places, dam building, irrigation, coastal development, rapid urbanization, population growth or wildfire — all lead to biodiversity loss. In its aftermath, altered habitat can yield less food, sending foraging wildlife into contact with nearby humans, creating vectors for zoonotic bacteria, viruses and parasites.("Biodiversity, pandemics and the circle of life",2020)

  Example- Ebola outbreak in West Africa which was said to be the direct result of deforestation, leading to closer contact between humans and wildlife.

- Migration of people, animals, food and trade often provides favourable grounds for the emergence of infectious diseases, including zoonoses. This points to rapid demographic growth, migration, density, increased movement of people and animals, and changes in land uses as the main processes linked to the prevalence of zoonosis.

- Trading of wildlife and wet markets serves as a potential ground for emergence of viral outbreak. (Johnson C. K., 2020)

2. Precautionary measure

To prevent the next pandemic related to these interfaces, research and implementation is needed in :

- **Surveillance activities** include monitoring animals and humans in close contact situations to advance outbreak preparedness.

- **Longitudinal field studies** needed to understand epidemiological patterns invirus transmission.

- **Optimizing disease prevention actions** Informed mitigation efforts aimed at ensuring biosafety in livestock production, minimizing interactions between wildlife and domesticated animals and limiting close contact with wildlife are especially needed given global trends in urbanization and food production.

Strict limitations on the animals sold in those markets should be introduced by the respective governments to reduce the risk of viral transmission.
(Smith, K. M., 2012)

2.1. Strengthen Health Systems

In some countries less than 50% of the required staff is available to serve rural populations, while at most of the times care is provided by non-qualified staff (WHO, 2006). Even a single

mistake can lead to a big epidemic. Eg : Nurses in the Yambuku mission hospital reportedly used five syringes for 300 to 600 patients a day which is the big cause of the Ebola pandemic in 2014-16 (CDC, 2018).

Following these steps will strengthen health systems-

i. Macro level, or the overall health system, such as resources
allocation, planning, deploying health workers, current regulatory framework, communication, decision-making processes, and accountability mechanisms.

ii.**Micro level, or the workplace itself** such as availability of equipment,drugs supply, teamwork and human resources management activities.

iii. Develop a global public health service: To make a successful globalhealth system, more medical and nursing schools particularly in rural areas will need to be set up
(WHO, 2006).

2.2. Funding to Research on Vaccine Programs

Outbreaks often take place in poor countries and/or remote rural areas, and are usually contained quickly. As a consequence, market mechanisms provide too little investment in R&D for new medicines, diagnostics and the vaccines for these pathogens.

Challenges faced in funding vaccine programs:

1. Complexity of the most challenging targets, which necessitates substantial investment of capital and human expertise.
   Only about 7% of vaccine development projects reach the preclinical development phase resulting in a licensed vaccine. With few exceptions, the scores of biotechnology companies and government and university laboratories lack the necessary resources for vaccine discovery and development.

2.The prevailing business model prioritizes the development of vaccines with a large market potential.

3. There are many viral disease targets for which vaccines are both badly needed and feasible but which are not being developed owing to either lacking governmental prioritization or lacking incentives because the market has been considered too small to justify the capital investment, to allow development costs and to reward the required investment risk.

(U.S Institute of Medicine,2003)

2.2.1. Ways to curb monetary challenges:

i. Merging public and private sectors to discuss and fund strategies for immunisation.

ii. Creating an insurance mandate which will require the public and private sectors to cover all recommended vaccines.

iii. Creating a more pluralistic market for vaccines would encourage healthcare providers and health plans to purchase vaccines.

iv. Improve incentives for the development of new vaccines by providing manufacturers with assuring adequate pricing and returns for those vaccines confer substantial public benefit.

v. In addition money should also be utilized to improve old vaccines. External funding could permit exploring ideas for improving partially effective vaccines.

(Plotkin, et al.,2015)

2.3. Biosafety and Bioterrorism

2.3.1. Biosafety

Biosafety is the prevention of large scale loss of biological integrity focusing both on ecology and human health. (Wikipedia, n.d.).

Accidental lab releases do happen. One even triggered a pandemic: An influenza strain surfaced in 1977 was linked to strains in Russian labs collected 2 decades earlier.

Maintaining Biosafety in laboratory

Biosafety level refers to the stringent biocontainment precautions deemed necessary by CDC for laboratory work with infectious materials.

2.3.2. Bioterrorism

Bioterrorism is the possible use of biological agents from laboratories as agents for warfare and public danger.

Measures against Bioterrorism :

A plan to respond to biosecurity should be developed to deal with specific incidents such as containment breaches, unauthorized access and removal of pathogens from a facility.

National and international laboratory response networks to efficiently and effectively manage bioterrorism incidents are being developed.

Traditional emergency response plans for biosafety practitioners have included response to spill of infectious materials, laboratory accidents/exposures, and containment breaches.

Finally, a noteworthy impact of bioterrorism on biosafety is the increased collaboration and cooperation at the national and international level with biosafety specialists, first responders (police, fire, medical authorities), laboratory staff those who design and construct containment facilities, and security experts.
(Best, M., 2003).

2.4. Better surveillance for monitoring and controlling the growth of viral pandemic

The early and accurate diagnosis of an infectious agent is essential for successfully treating individual patients and is even more important at the population or global level. The ability to identify quickly the causative pathogen of an emerging epidemic or pandemic markedly increases the chances of success of any countermeasures to contain the disease. Many countries together with WHO have made great efforts to develop integrated surveillance networks for tracking candidate pathogens and to keep tabs on their genetic structure, geographical distribution and host populations (Hunter, P., 2008).

The basic processes that are followed for surveillance are:

2.4.1. Identification of individual cases -The definition of a case for a surveillance system has important implications for the design and performance of the system. In settings where a surveillance system is intended to follow cases of a well-understood disease, it may be possible to make the case definition highly specific. Public health agencies in many developed countries conduct routine surveillance for communicable diseases. As a result, communicable disease surveillance systems tend to rely upon data from laboratory testing as opposed to data from clinical examinations. By monitoring information sources such as the internet, posts to electronic discussion boards, etc. this problem can be tackled.

2.4.2. ***Detecting population patterns among cases of infection***-The detection of population patterns among cases generally refers to the detection of unexpected patterns in the incidence of cases. Surveillance analysts are interested usually in detecting an unexpected increase in overall incidence or an increase in incidence in a population subgroup or in a geographic region. There is a close relationship between the characteristics of the case definition and the detection of population patterns. When a case definition is highly specific, a large proportion of identified cases will be true cases.

2.4.3. Convey information to decision-makers about population health patterns. This can be achieved by the following ways:

2.4.3.1.Information surveillance:The Internet has enabled novel approaches to collect public health data, both passively and actively.

Passive approaches rely on submission of disease reports, usually via email, to a single location; active approaches involve searches of the Internet for posted information about disease outbreaks. These systems conduct 'information surveillance', that follow information about outbreaks, as opposed to relying on the case definitions traditionally used in disease surveillance.

2.4.3.2. Syndromic surveillance: Advances in the electronic capture of health data have led to surveillance using data generated through the routine administration of health care services. This practice is known as 'syndromic surveillance' because cases are defined in terms of non-specific administrative codes or conditions, which can be thought of as syndromes. Syndromic surveillance is a novel technique that relies on the automated capture, transmission, and analysing non-specific information patterns in pre-diagnostic health data.

It will detect outbreaks earlier because the incidence of pre-diagnostic events, such as purchase of over-the-counter medications, will increase before the incidence of diagnoses.

2.4.3.3. Surveillance of animals and the environment: This method can only be performed after the health and research personnel know more about the epidemiology and genetics of an emerging virus.

2.4.3.4. Laboratory-based surveillance:After diagnostic methods are available, surveillance of positive laboratory tests becomes possible. This approach to surveillance is highly specific, but it will identify only those cases that are tested at laboratories participating in the surveillance system. Automated surveillance of
positive laboratory test results and monitoring the incidence of emerging pathogens through laboratory methods can be an effective form of surveillance.

(Buckeridge, D., and Cadieux, G., 2006)

3. Discussion

The emergence of pandemics must be viewed as part of a larger evolutionary trend involving myriad interconnected biological, chemical, physical, and social processes. The ultimate scientific challenge of the 21st century—understanding how earth and the society that inhabits it co-evolve—will require development of broader research perspectives, transcends the reductionist approach to science characterized most of the previous century("Pandemics and the global environment", 2020). In addition, all nations must commit to policy decisions consistent with the outcomes of such research if we hope to optimize public policy in a way that ensures the long-term prosperity of human society.

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Welcome to the anthropocene: A look into *Homo sapiens'* contribution to climate change and new pandemics

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Abstract:

The most prominent and pressing issues of the current environmental scenario are global warming and climate change. Human activities and its effect on climate and environment cause remarkable animal and plant extinctions, loss in biodiversity and endanger animal and plant life on earth. People think of global warming and climate change as synonyms—we can say they are interrelated, but are not synonymous to each other—scientists use "climate change" when describing the complex shifts affecting our planet's weather and climate systems. Climate change encompasses not only rising average temperatures but also extreme weather events, shifting wildlife populations and habitats, rising seas and a range of other impacts. All of these

changes are emerging as humans continue to add heat-trapping greenhouse gases to the atmosphere.

Key words: Climate change, microorganisms, greenhouse gases, biodiversity, pandemics

1. Introduction:

Scientists 100 years ago would have been skeptical about the idea that by the 20th century, humankind would be affecting the stratosphere. Yet remarkably, after 8000 generations of *Homo sapiens*, human-induced depletion of stratospheric ozone has begun (WHO 2003). The earth is surrounded by a thick layer of gases (works like a blanket!) which keeps the planet warm and allows plants, animals and microorganisms to survive. Without this gaseous blanket, our earth would be 20 to 30 degrees Celsius colder and unsuitable for life. (Gupta et al., 2014) Anthropogenic activities result in increased atmospheric levels of the major greenhouse gases- carbon dioxide, methane, ozone, nitrous oxide-as a result, the layer of greenhouse gases around our earth is getting much thicker. This inspissated layer is trapping additional heat and causing our planet to warm up more than needed. Since 1906, the global average temperature has increased by more than 1.6 degrees Fahrenheit (0.9 degrees Celsius)—and the impacts of rising temperatures are not waiting for the future- the effects of global warming are appearing right now. Scientists have already documented frequent and deadlier disease outbreaks, melting glaciers, especially at the poles, contributing to sea-level rise, with global sea-levels rising 3.2 millimeters an year, occurring at a faster rate in recent years. Rising temperatures (due to global warming) are affecting wildlife and their habitats, forcing many species to migrate to a suitable region where they can survive—even pushing many on the verge of extinction, due to their inability to adapt to newer, alien environment. The predictions for our future are not bright either (unless we work on fixing our mistakes and find sustainable, eco-friendly ways to live)—by the end of the century, sea levels are expected to rise between 26-82 centimeters, hurricanes and storms are likely to become stronger, leading to floods and droughts becoming more common- we face higher risk of decades-long “mega droughts” by 2100. (“Global warming and climate change effects”, 2020)

Table 6.1: Examples of how diverse environmental changes affect the occurrence of various infectious diseases in humans (Refernce 5)

Environmental changes	Example diseases	Pathway of effect
Dams, canals, irrigation	Schistosomiasis	▲ Snail host habitat, human contact
	Malaria	▲ Breeding sites for mosquitoes
	Helminthiasies	▲ Larval contact due to moist soil
	River blindness	▼ Blackfly breeding, ▼ disease
Agricultural intensification	Malaria	Crop insecticides and ▲ vector resistance
	Venezuelan haemorraghic fever	▲ rodent abundance, contact
Urbanization, urban crowding	Cholera	▼ sanitation, hygiene; ▲ water contamination
	Dengue	Water-collecting trash, ▲ *Aedes aegypti* mosquito breeding sites
	Cutaneous leishmaniasis	▲ proximity, sandfly vectors
Deforestation and new habitation	Malaria	▲ Breeding sites and vectors, immigration of susceptible people
	Oropouche	▲ contact, breeding of vectors
	Visceral leishmaniasis	▲ contact with sandfly vectors
Reforestation	Lyme disease	▲ tick hosts, outdoor exposure
Ocean warming	Red tide	▲ Toxic algal blooms
Elevated precipitation	Rift valley fever	▲ Pools for mosquito breeding
	Hantavirus pulmonary syndrome	▲ Rodent food, habitat, abundance

▲ increase ▼ reduction

2. Microorganisms and climate change:

The microbial world holds great significance in their role with respect to climate change. To understand how the life forms on earth (including those yet undiscovered) can withstand anthropogenic climate change, we must learn not only how microorganisms affect climate change, but also how they will be affected by it. Microorganisms play a vital role as either generators or users of greenhouse gases as they are capable of recycling and transferring essential elements (they are actively involved in biogeochemical cycles) such as carbon and nitrogen that make up cells—which in turn are responsible for climate change. Photosynthetic microbes are consumers of atmospheric CO_2, whereas the heterotrophic microbes decompose organic matter to emit greenhouse gases. The main determinant of the net carbon flux (which differs between ecosystems) is the balance between the two processes. Greenhouse gases like CO_2, CH_4 and N_2O originate predominantly from microorganisms. During the course of history, in determining the atmospheric concentrations of greenhouse gases the activities of microorganisms have been critical. The atmospheric lifetime and global warming potential of CO2, N_2O and CH_4 emitted due to microbial activities are 100, 114, 25 years and 1, 298, 12 respectively. (Dutta et al., 2016) Shifts in climate can influence the structure and diversity of

microbial communities either directly (~seasonality, temperature) or indirectly (~root exudates, plant composition and plant litter). It was found that short-term and long-term (more than 50 years) natural geothermal warming initially increased the respiration and growth of soil microorganisms, leading to net CO_2 increase and subsequent depletion of substrates, however, it caused a decrease in biomass and reduced microbial activity. It implies reluctance of microbial communities to adapt to higher temperatures, therefore reducing overall carbon loss through effects on reaction rates and patterns of substrate use (Cavicchioli et al., 2019). While high mutation rates, horizontal gene transfer and short generation times, can produce fast evolution in microbes, it can still be hard for them to adapt- even if they adapt fast enough, entire suites of lifestyles may be lost as the environment that requires them disappear (Gupta et al., 2014).

The complexity of microbial communities and their associations with their surroundings make it difficult to pinpoint the various feedback responses that microorganisms have to global warming. The fact is—microbes can highly influence future climate scenarios and ecosystem-level responses to climate change. Due to the large amount of CO_2 and CH_4 emissions produced during respiration, reliance of carbon stocks in soil on rate of respiration and the initial sensitivity of soil respiration to increased temperatures, pivotal role of soil respiration are quite evident. Microorganisms can prove to be an effective tool in attenuating greenhouse gas emissions and adapt to predicted climate change for future changes at the macroscopic and even global scale (Gupta et al., 2014).

3. Anthropogenic epidemic:

“Climate change is the greatest threat to global health in the 21st century.” warned WHO in 2015. The majority of emerging zoonoses are driven by anthropogenic activities—an unknown diversity of viruses, bacteria and other microbial flora exist within wild animal populations just as with us humans. There are beneficial microorganisms and there are pathogens that are deadly to life forms. “Global warming is making it easier for some of these pathogens to spread, reproduce and persist in the environment” said Matthew Baylis, a health researcher at the University of Liverpool. A remarkable rate of emergence of new and spreading diseases affecting our food production, plants, animal health, and human health is seen rapidly.This is due to the industrial revolution that began from mid-18th century, which led to loss of biodiversity from their natural habitat for the sake of human development- and as we are well into the 5th

industrial revolution, we must ask ourselves- are we really heading towards development when our activities are such that will set us back decades in areas like health, food security and quality of life. According to the United States Agency for International Development, about 75% of emerging and re-emerging infectious diseases are zoonotic- meaning they come from animals. (Patsavoudi, 2020). Emerging infectious diseases (EIDs) are defined as diseases that have recently increased in incidence or geographic range, recently moved into new host populations, recently been discovered or are caused by old pathogens that have mutated to become novel. These include pandemic diseases causing high mortality (AIDS, the recent COVID-19, Cholera, malaria, Influenza etc), diseases caused by pathogens that have developed drug resistance (tuberculosis, *Staphylococcus aureus* infection etc) and pathogens that have caused local outbreaks, but form a public health threat due to their high cases of fatality rates or lack of preventive/therapeutic regimen- Ebola virus disease, hantavirus pulmonary syndrome, Hendra virus disease, Nipah virus disease and other such outbreaks that have been frequently terrorizing human populations worldwide. (Daszaket al., 2001) An increase in the spread of infectious diseases is seen with the loss of biodiversity. It is speculated that some species are better at 'buffering' disease transmission—simply put, the presence of these species in the wildlife or near the area of transmission will prevent a disease from becoming a pandemic—due to their low reproduction rates, therefore high investment in immunity, known as 'dilution effect.' (Patsavoudi, 2020) EIDs have quadrupled in the last half-century, largely because of increasing human encroachment into habitat, especially in disease "hot spots" around the globe, mostly in tropical regions. And with modern air travel and a robust market in wildlife trafficking, the potential for a serious outbreak in large population centers is enormous. Zoonotic transmission is the exchange of pathogens between wildlife and humans and can be bidirectional. Viral spillover happens more frequently than identified—human activities that alter the environment create circumstances that are opportunities for wildlife viruses to make the jump into new hosts (Epstein and Field, 2015).

Multiple examples of zoonotic outbreaks which have involved bats and their viruses have been associated with anthropogenic changes to the environment. In Africa and China, the hunting and wildlife trade—which involves either killing and butchering animals *in situ* or in central markets after they have mixed with other species—are activities that put the handlers who come in contact with the bodily fluids of these animals at increased risk of exposure to any potentially

pathogenic microorganisms that it carries—however, indirect contact with such bodily fluids is the most common route of exposure to such pathogens. Nipah virus, Hendra virus, Ebola virus, Marburg virus are each associated with fruit bat reservoirs and exposure to bat excreta has been hypothesized as the main route of spillover from bats to humans through consumption of infected animals. SARS CoV (2003, first global pandemic of the 21st century) and the current SARS-CoV-2 (speculated by WHO advisors to have met the requirements to be the first disease X) emerged from bats through live-animal markets of southern China. The emergence of Nipah virus in Malaysia in 1998 was due to the expansion and intensification of pig farming with larger pig farms facilitating the maintenance of the virus—with transmission from bats to pigs taking place through the presence of fruit orchards, allowing food debris from feeding flying foxes to drop into pig pens, making its way into the Malayan population (Epstein and Field, 2015).

Climatic factors are an important determinant of various vector-borne, enteric and certain water-related diseases. Relationship between year to year variations in climate and infectious diseases are most evident where climate variations are marked, & in vulnerable populations. Climate change is likely to increase the frequency and/or amplitude of the Pacific-based El Niño Southern Oscillation (ENSO), an approximately semi-decadal cycle, which influences much of the world's regional weather patterns—including India. Higher temperatures and/or rainfall associated with ENSO affects transmission of Dengue, Malaria, and Yellow fever by causing changes in water storage practices, surface water pooling- which are required by mosquitoes in order to breed, with the adults requiring humid conditions for viability. In temperate regions (following mild winters) proliferation of rodents is supported-which act as reservoirs for various diseases such as-leptospirosis, tularemia and viral hemorrhagic diseases (all associated with flooding), Lyme disease, tick borne encephalitis and Hantavirus pulmonary syndrome (associated with rodents and ticks). Climate change will affect the pattern of deaths from exposure to high or low temperatures. The overall current estimated burden is relatively small to other major risk factors—in contrast, risks associated with climate change are gradually increasing rather than decreasing. (WHO, 2003)

In conclusion, as highly intelligent, most dominant primate species on earth—the entire human population has the responsibility to act fast towards finding solutions to reach the sustainable development goals (SDGs)-set in 2015 by the UN general assembly- by the intended 'deadline'

of 2030. Otherwise the grave repercussions of climate change will be felt far ahead into the future even when our current generation of scientists, researchers and climate activists are working towards fixing the problem that has been predominant since decades.

"Sustainability is essentially about maintaining earth's ecological and other biophysical life-support systems. If these systems decline, human population wellbeing and health will be jeopardized. Technology can buy time, but nature's bottom-line accounting cannot be evaded. We must live within earth's limits. The state of human population health is thus a central consideration in the transition towards sustainability."- World Health Organization on climate change and human health.(2003).

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Viral Pandemics: Yesterday, Today and Tomorrow

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ABSTRACT

Viruses are the sub microscopic obligate intracellular parasites, intermediate between living and non living but once inside the host cell they start replicating using the host cell machinery. Once they reach the threshold titre value, the clinical manifestations related to the disease starts. Viral diseases are even difficult to control compared to bacterial or fungal disease because in such cases disruption of cell wall kills the pathogen. Since virus uses host machinery, any attempt to neutralize them can have side effect on the normal functioning of the body. A look at the subsequent pages of this article will reveal how many times the very existence of humanity has been threatened by viral pandemics. We should develop robust mechanism and techniques for the early detection and control of viral diseases because globalization can lead to widespread infection within a very short span of time. This article will teach about the pandemics of the past while comparing it with our present scenario giving a lesson for a better tomorrow.

Before we indulge into giving a vivid picture of the pandemics let us first discuss what actually is a pandemic? So a pandemic is usually an epidemic which is no longer restricted to a particular region that is its spreading throughout the globe with leaps and bounds. WHO has six phase programme for identification of a potential pandemic. An epidemic on the other hand is a spread of a contagious disease which is restricted to a particular region which is affecting majority of a population in that region and its basic reproduction number (R_0) is higher attributing to its higher transmissibility and so is the disease related fatalities. A point worth mentioning is that most of diseases which cause pandemics are having the younger and the older part of the population in its susceptible range. Since now we know what a pandemic is I would now like to draw your attention to what causes it.

How does a pandemic arise out of the blue suddenly, the answer to this is more than one, the first one worth mentioning is antigenic shift that is the pathogen undergoes structural changes which were previously not there. On encountering such a novel strain the body starts treating it as a completely new pathogen to which it has not had any previous encounter with, and this novel strain can be more virulent and more fatal. Another instance which can possibly explain is that the previously known antibiotic against the pathogen is no longer useful, that is the organism is now resistant to the antibiotic so its epidemic potential is enhanced. Alternatively a zoonotic spill over event as predicted in case of corona virus can also be responsible for a possible pandemic outbreak. A zoonotic spill over event is an occasion when a pathogen crosses a species barrier, that is, it jumps from one species to another as predicted in case of corona virus bat and pangolins are suspected to be primary reservoirs. These events are rare in nature but since we have no prior encounter with such pathogens they take us by surprise and our defence mechanism does not get appropriate time for proper redressal.

Now we know what a pandemic is, what causes a pandemic, so we will have a look at the pandemic of the past which have wiped almost more than half of the world population in the past.

The first ever recorded pandemic can be dated back to (165-180 AD) “Antonine Plague” which killed around five million people worldwide and was thought to be brought by soldiers coming from the East to the Italian region its suspected to be either small pox (caused by variola virus) or measles (caused by rubeola virus). Smallpox has wrecked havoc time and again causing around 500 million deaths during the 20th Century but due to the efforts of

WHO and better vaccination practices the disease is now considered to be eradicated officially, whereas measles has become an endemic disease as it is continuously present in the community and many of the individuals develop resistance. In populations where the disease has not happened before, it can prove to be lethal.

Since we are focusing our study on viral pandemics the next noteworthy mention is of Spanish flu also known as the 1918 flu pandemic, which was basically an Influenza pandemic (caused by H1N1 influenza A virus) with an R_0 of around 3. It was so severe that it had 4 waves that is it kept coming back after small intervals with a more lethal and virulent strain causing the death of more than 50 million people worldwide. The same virus is also responsible for 2009 Swine flu pandemic it's named so because it was initially found in pigs but due to zoonotic spill over event it started infecting humans. It caused death of around half a million people in just 19 months since the outbreak. A constant fear lingering around with Influenza virus is that they undergo rapid mutation and antigenic shifts making them more virulent more lethal so we have to be constantly on the lookout to avoid future pandemics else we will be caught off guard. There is a variety of probable combinations for Influenza virus as H (Hemagglutinin) can range from 1-16 while N (Neuraminidase) can range from 1-9. So the combinations which have not been encountered by our immune system don't have their corresponding antibodies hence the neutralization of the pathogen does not occur. Avian flu (H5N1), Hong Kong flu and Asian flu all are related to influenza virus so its pandemic potential should not be neglected.

The late December 2013 cases of Ebola Hemorrhagic fever caused by Ebola virus discovered in Africa had a fatality rate of 50% and bats are suspected to be the primary reservoir of the Marburg virus belonging to the same family as Ebola and causes hemorrhagic fever with a fatality rate of around 80%. Rousettus bats are primary hosts of the Marburg virus. These diseases are highly communicable spreading through bedding, clothing and direct contact. Even though these were just epidemics, restricted to a particular region but the fact that world is now a global village as a result of globalization means that nothing can be kept restricted for long if proper containment and screening measures are not taken when we have the time.

Worthy mentions with pandemic potential are Nipah virus infection which had spread through Malaysia, Singapore (1998), Bangladesh and India (2018) which was characterised by acute respiratory illness, bats and pigs are the primary hosts supposedly. Its reemergence after 20 years is enough to prove that it is undergoing mutation and antigenic shift waiting for

the right moment so precautions have to be taken before hand. Although vaccine development is under process, it needs to be hastened to avoid it from becoming a pandemic. Yellow fever caused by arbovirus transmitted by mosquitoes such as *Aedes* and Haemagogus is preventable on vaccination but in densely populated developing countries the disease can prove to be fatal as vector borne transmission will be higher, vaccination campaigns should be done for yellow fever to avoid the possibility of pandemic because a pandemic impacts all walks of life be it social, economical, physical and mental.

So now I will talk about the disease COVID 19, I can bet all of us are now sick of hearing it in the news and living the life in the lockdown with depleting resources and uncertain future. Corona virus can be taxonomically divided into 4 categories alpha, beta, gamma and delta corona viruses where alpha and delta are involved in infecting mammals while gamma and delta are related to birds. Beta corona viruses have been found to be responsible for the corona related pandemics be it be it SARS (Severe Acute Respiratory Syndrome), MERS (Middle East Respiratory Syndrome) or COVID-19. All of them have bats as primary reservoir or host and via zoonosis started infecting humans. The viruses are named so because of the surface projections which are bulbous or crown like. Their genetic material is single stranded positive sense RNA.

SARS was first reported in China in 2002, is caused by SARS CoV. Since its discovery it has spread to five continents and 26 different countries causing the first pandemic of the 21st century. Although the mortality rate is low but transmission is high around the 10th day of incubation, it causes severe respiratory ailment leading to death in severe cases. It has a basic reproduction rate ranging between 2.2 to 3.7. MERS (Middle East Respiratory Syndrome) caused by MERS CoV was discovered in 2012 in Saudi Arabia with an R_0 less than 0.7. The dromedaries are thought to be primary host, humans getting infected on contact with the diseased dromedaries. It has a mortality rate of 35% and undergoes rapid mutation. The infected individuals may remain asymptomatic contributing to its transmissibility. It has spread to 24 countries by the end of 2015. What can be inferred from these two incidents is that geographical barriers can no longer contain a disease as international travel is quite common.

First reported as unusual cases of pneumonia in China during November 2019, the disease has undergone a lot of mutations and naming procedures to be now finally known as COVID-19 caused by SARS CoV2. By the time of preparation of this article 13.5 million people have

been infected with half million deaths across 188 countries out of the seven continents COVID-19 has reached 6 continents except Antarctica. The race to find a cure and a vaccine is on but as we know it's a tedious process and cannot happen overnight meanwhile a lot of lives will be lost during that time frame. People with co morbidities are more prone to get infected. It is highly infectious even though the death rate is low. Governments throughout the world are trying their best to control the disease by enforcing the longest lockdown ever. This is worsening the situation with jobs being cut and people not being able to afford their meals. The mental and economical impact of the disease also cannot be neglected. Isolation and contact tracing are the steps taken but in a country like ours with over a billion populations it's becoming impossible to control the disease with under developed healthcare facilities. Life in the post covid era will never be the same where every sneeze and cough is scorned at with suspicion. But I hope we learn from this to avoid pandemics in the future by developing better screening techniques, maintaining social distance and practising respiratory hygiene.

So I would like to conclude by saying that we need to fund the development of vaccines and screening procedures before the next pandemic hits us because we cannot win a battle if we start preparing for it when it has already begun. Screening of international travellers and their quarantine should be strictly implemented. Containment and mitigation procedures to be strictly followed even on slight suspicion of a possible pandemic.

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THE RADIX, REVERBERATIONS AND PROPHYLACTIC MANOEUVRE OF COVID-19 , FUNDAMENTALLY EVINCING SUBSISTENCE AMIDST SARS-CoV-2.

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ALIVE IN COVID-19 PANDEMIC

ABSTRACT

Humanity is witnessing the worse possible crisis in conformation of the COVID-19 pandemic. Novel SARS-CoV-2, the causative agent of COVID-19 disease has emerged into the most contagious strain of Corona viruses. The virus has spread rapidly across the globe, creating havoc and claiming thousands of lives. Although there is no concrete corroboration to state the explicit origination of the SARS-CoV-2, but the foremost transmission was proclaimed in Wuhan, China. The inceptive manifestation of COVID-19 is mild but if proper medication is neglected, symptoms may augment and eventually become detrimental. Prophylactic proceedings are prompt and effortless and should be practiced consistently.

KEYWORDS

SARS-Cov-2, corona virus, COVID-19, home -quarantine.

INTRODUCTION

Ever since the genesis of life, humankind across the globe has encountered disparate viral pandemics, the most neoteric and contemporary being COVID-19. Novel Corona virus has halted business across the globe, impeding motility besides mobility. Twentieth century is in conflict with the most terrible and perilous humanitarian catastrophe in the conformation of COVID-19, where in millions are in affliction with death toll reaching its zenith .

Severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) commonly known as novel corona virus is the new strain of Corona viruses and the causative agent of the disease COVID-19 , which has currently emerged into an appalling viral pandemic. The definite provenance of this virus is still debatable but a majority of medical adept

believe it emanated from bats or pangolins , while a few trace its outset from a seafood market in Wuhan. The prime transmission to humans were reported in Wuhan, China followed by the eruption of COVID-19 pandemic throughout the sphere. Initial symptoms including mild fever, cough , loss of taste and smell, sore throat and headache commences within 14 days of contact with the virus and if left untreated it has a substantial prospect of fatality(Kandola, 2020).

The detrimental effects of COVID-19 on health is intensifying with the number of cases burgeoning each day. A research study conducted in Wuhan revealed post recovery ailments, for instance abject functioning of heart ,lungs and liver among many recuperated patients. The British physician Nicholas Hart who treated Boris Johnson, Prime Minster of the United Kingdom , named the virus “this generation’s polio” , as it has the competence of altering global health. Chronic fatigue and Impaired lung functioning were observed among patients affected by SARS (Severe Acute Respiratory Syndrome virus , from the corona viruses strain) in the outbreak of 2003even after four years of recovery, evidently portraying the long term effect of Corona viruses. Furthermore recent reports and medical research unveils the damaging effects of COVID-19 on discrete parts of the body including kidneys , eyes and even gut.Scrutiny of corona virus infected patients from Italy and China exhibited possible symptoms of Chronic Cardiac Complications even after recovery, due to sustained inflammation (Du, 2020).

Though the virus is lethal with intricate effects yet its preventive measures are effortless, economical and fundamentally a part of our quotidian sanitation regime. The most coherent, rational and manageable prophylactic initiative is to wash hands frequently using soap and water for at least twenty seconds as detergent molecules disrupt the viral lipid bilayer rendering the virus susceptible to environment. SARS-CoV-2 can remain active on surfaces for up to three days , hence we should elude touching our face to curb the entry of virus through eyes, nose or mouth and consequently mitigate its spread. Staying home or home quarantine is a really insightful choice as it fades contact with the outside world by terminating exposure to infected individuals and commodity. Going out is not recommend dedand if its unavoidable then a safe minimal distance of one meter needs to be maintained from all individuals , especially from those who are sick or coughing, as a single sneeze can release myriad aerosol droplets containing virulent viral particles which if inhaled by a healthy individual may lead to COVID-19. In accordance with the protocols delineatedby World Health Organization (WHO), the usage of mask should be practiced by the health care workers or an ailing individual and care should be taken to ensure that the mask conceals the nose and mouth without the existence of any aperture between the mask and face. By incorporation of these basic yet effectual measures into our everyday schedule, we can expect to keep healthy and safe (Sissons, 2020).

CONCLUSION

2020 is in the midst and grip of a lethal viral pandemic , with fresh cases elevating each day and individuals from all age group getting infected. The Earth appears to be in pause mode with Schools, Universities, offices and all probable liveliness adjourned. I guess this is the 'new normal' wherein we have to learn to adapt to co-exist with the virus in an invulnerable way until the development of a vaccine, whi ch is again a laborious milestone to achieve considering the potential mutations. Till then sanitization and self-isolation should be the prime priority to ensure safety of ourselves and all around us.

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VACCINE: THE FUTURE WEAPON AGAINST CORONA

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Abstract:

The root of immunology is based on the early vaccination trials of Edward Jenner and Louis Pasteur. Thereafter, vaccination is the major cost- effective way against various diseases. The differences of epitopes of various antigens recognized by B and T cells and the concept of MHCs (I and II) and antigen processing pathways (endogenous and exogenous) help to develop vaccines to induce both humoral and cell mediated immunity. On current corona pandemic situation, the antiviral vaccine will be the most powerful tool to save mankind. Scientists are trying to find an effective anti-corona vaccine.

Keywords: Vaccination, Antiviral, Corona, Pandemic.

1. Introduction:

Vaccine is the major weapon to prevent various antimicrobial (anti viral or anti bacterial) diseases. Several diseases, like- measles, polio, tetanus, diphtheria, meningitis, influenza, tetanus, typhoid, cervical cancer can be treated by using vaccines.It strengthens our immune systems to resist a specific infectionby creating antibodiesbecause itcontains killed or weakened

viruses or bacteria. Vaccines are given by injection, orally or sprayed into the nose. One or more doses of a vaccine can protect us against a disease for years, decades or even a lifetime. (WHO, 2020). WHO has stated that the ideal vaccine would have the following properties:

■ Affordable worldwide

■ Heat stable

■ Effective after a single dose

■ Applicable to a number of diseases

■ Administered by a mucosal route

■Suitable for administration early in life (WHO, 2020)

Recent advances in immunology and molecular biology have led to effective new vaccines against corona virus. The journey of successful vaccine development is costly, long, and tedious process. But the scientists throughout the world are trying to develop a low cost, easily deliverable vaccine against corona virus.The Human Trial is the most crucial part of a vaccine development process which should be undergone to 4 phases. Even those vaccines that pass the primary trial and are ready for human trials are not guaranteed to use further among common people.Here, we discuss about different types of vaccines, immunization and current situation of anti-corona vaccine.

Active and Passive Immunization:

Activeand passive immunization are two main ways to develop immunity against infectious microbes. It can be achieved either by natural processes (usually by) or by using vaccines. In case of naturally gaining immunity, it can be achieved by transfer from mother to foetus or by previous infection by the organism. Antibodies from humans or animals induce passive immunity. The type of immunity that is achieved by injecting the full or part of the antigenic component of the attenuated or heat- killed pathogen is called the active immunity. Passive immunization gives us the transient protection against an infection, but active immunization helps to gain protective immunity and immunologic memory by the proliferation of T and B cells. Successful active immunization strengthens our immunity to permanently eliminate the pathogen or the pathogenic component of microbes.

Type	Acquired through
Passive immunity	Natural maternal antibody
	Immune globulin*
	Humanized monoclonal antibody
	Antitoxin†
Active immunity	Natural infection
	Vaccines‡
	Attenuated organisms
	Inactivated organisms
	Purified microbial macromolecules
	Cloned microbial antigens
	Expressed as recombinant protein
	As cloned DNA alone or in virus vectors
	Multivalent complexes
	Toxoid§

*An antibody-containing solution derived from human blood, obtained by cold ethanol fractionation of large pools of plasma; available in intramuscular and intravenous preparations.

†An antibody derived from the serum of animals that have been stimulated with specific antigens.

‡A suspension of attenuated live or killed microorganisms, or antigenic portions of them, presented to a potential host to induce immunity and prevent disease.

§A bacterial toxin that has been modified to be nontoxic but retains the capacity to stimulate the formation of antitoxin.

Table 1:Acquisition of active and passive immunity (Kuby, 2000).

1.1 Classification of common vaccines for humans:

Disease or pathogen	Type of vaccine
WHOLE ORGANISMS	
Bacterial cells	
Anthrax	Inactivated
Cholera	Inactivated
Pertussis*	Inactivated
Plague	Inactivated
Tuberculosis	Live attenuated BCG†
Typhoid	Live attenuated
Viral particles	
Hepatitis A	Inactivated
Influenza	Inactivated
Measles	Live attenuated
Mumps	Live attenuated
Polio (Sabin)	Live attenuated
Polio (Salk)	Inactivated
Rabies	Inactivated
Rotavirus	Live attenuated
Rubella	Inactivated
Varicella zoster (chickenpox)	Live attenuated
Yellow fever	Live attenuated
PURIFIED MACROMOLECULES	
Toxoids	
Diphtheria	Inactivated exotoxin
Tetanus	Inactivated exotoxin
Capsular polysaccharides	
Haemophilus influenzae type b	Polysaccharide + protein carrier
Neissera meningitidis	Polysaccharide
Streptococcus pneumoniae	23 distinct capsular polysaccharides
Surface antigen	
Hepatitis B	Recombinant surface antigen (HBsAg)

*There is an now also an acellular pertussis vaccine consisting of toxoids and inactivated bacteria components.

†Bacillus Calmette-Guerin (BCG) is an avirulent strain of *Mycobacterium bovis*.

Table 2: Different types of vaccines (Kuby, 2000).

Inactivated (killed) or live but attenuated (avirulent) bacterial cells or viral particles are used as vaccines generally. The comparison between attenuated, inactivated and DNA vaccines (currently using for human) are shown in the next table.

Characteristic	Attenuated vaccine	Inactivated vaccine	DNA vaccine
Production	Selection for avirulent organisms: virulent pathogen is grown under adverse culture conditions or prolonged passage of a virulent human pathogen through different hosts	Virulent pathogen is inactivated by chemicals or irradiation with γ-rays	Easily manufactured and purified
Booster requirement	Generally requires only a single booster	Requires multiple boosters	Single injection may suffice
Relative stability	Less stable	More stable	Highly stable
Type of immunity induced	Humoral and cell-mediated	Mainly humoral	Humoral and cell-mediated
Reversion tendency	May revert to virulent form	Cannot revert to virulent form	Cannot revert

Table 3: Comparison between attenuated (live), inactivated (killed), and DNA vaccines (Kuby, 2000).

There are several risks for using attenuated or killed **wholeorganism vaccines** because either the microbe used to prepare the vaccine can be revert back and cause disease otherwise the killed whole organism generate a new immune response against itself which can cause a new disease. This problem can be overcomeusingvaccines that consist of specific, purified macromolecules, like- inactivated exotoxins, capsular polysaccharides, and recombinant microbial antigens derived from pathogens.

In case of **recombinant vector vaccine,** genes of major antigens of pathogens can be inserted into attenuated microbes which serve as the vector, replicating within the host and expressing the gene product of the pathogen. Example: vaccinia virus, canarypox virus, attenuated poliovirus, adenoviruses, attenuated strains of ***Salmonellasp***., BCG strain of ***Mycobacterium bovis***, and certain strains of ***Streptococcussp***. are used as recombinant vector vaccines. The figure of DNA vaccine development is shown on the next page.

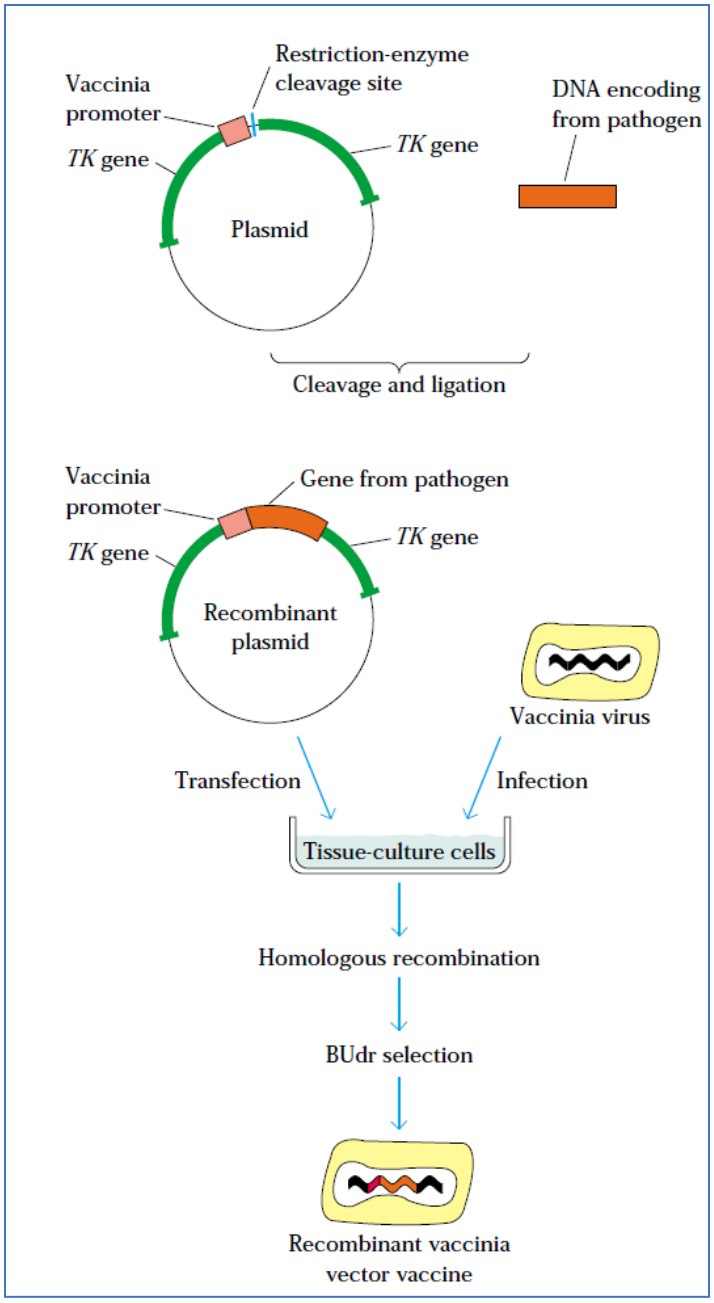

Figure1: Vaccinia vector vaccine development. The gene that encodes the desired antigen containing gene, the insert (orange), is introduced into a plasmid vector adjacent to a vaccinia promoter (pink) and flanked on either side by the vaccinia thymidine kinase (TK) gene (green). During tissue culture using vaccinia virus and the vector , the antigen gene and promoter are inserted into the vaccinia virus genome by homologous recombination.Bromodeoxyuridine (BUdr, which kills TK cells) is used for selection of the recombinant virus. [Moss et al.1985].

A recombinant plasmid having the DNA sequence of an antigen against a specific pathogen is used to develop **DNA vaccine**. By DNA vaccination, the human cells produce proper and significant response against a disease.

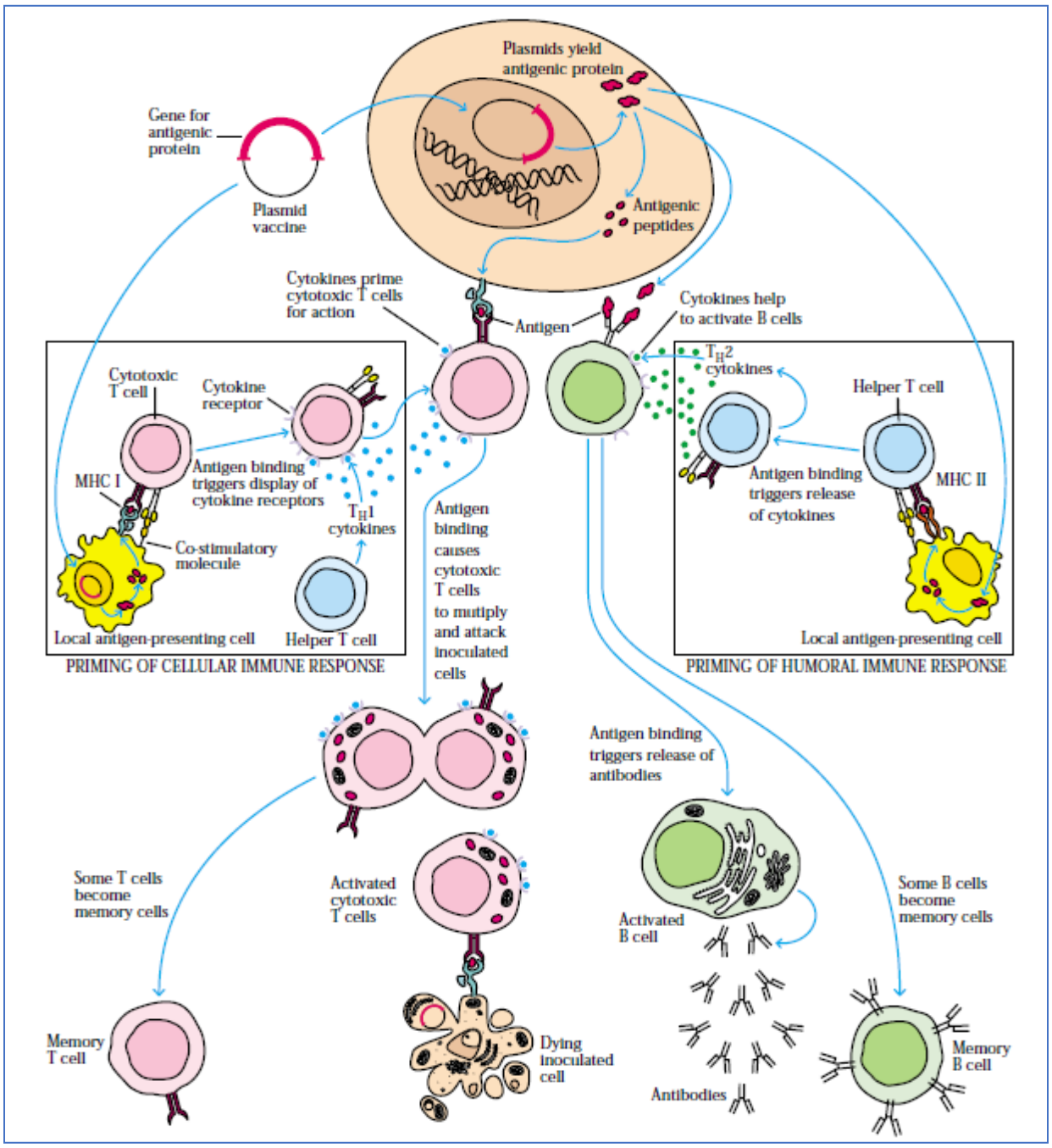

Figure2: Use of DNA vaccines:It induces both humoral and cell mediated immune response[Weiner et al.,1999].

1.1.a. Multivalent subunit vaccines - The synthetic peptide vaccines and the recombinant protein vaccines are poorly immunogenic as they induce only humoral response, a very minute or zero level cell mediated immune response. So it is necessary to prepare a synthetic peptide vaccine that has both B and T cell epitopes. To gain the response of cytotoxic T lymphocyte cells' response, the vaccine should be delivered in an intra cellular manner so that it can be processed by endocytic processing pathway and presented by MHC-I. Several techniques are used to develop such multivalent vaccines that can present multiple copies of the peptide(s) to generate immune response.

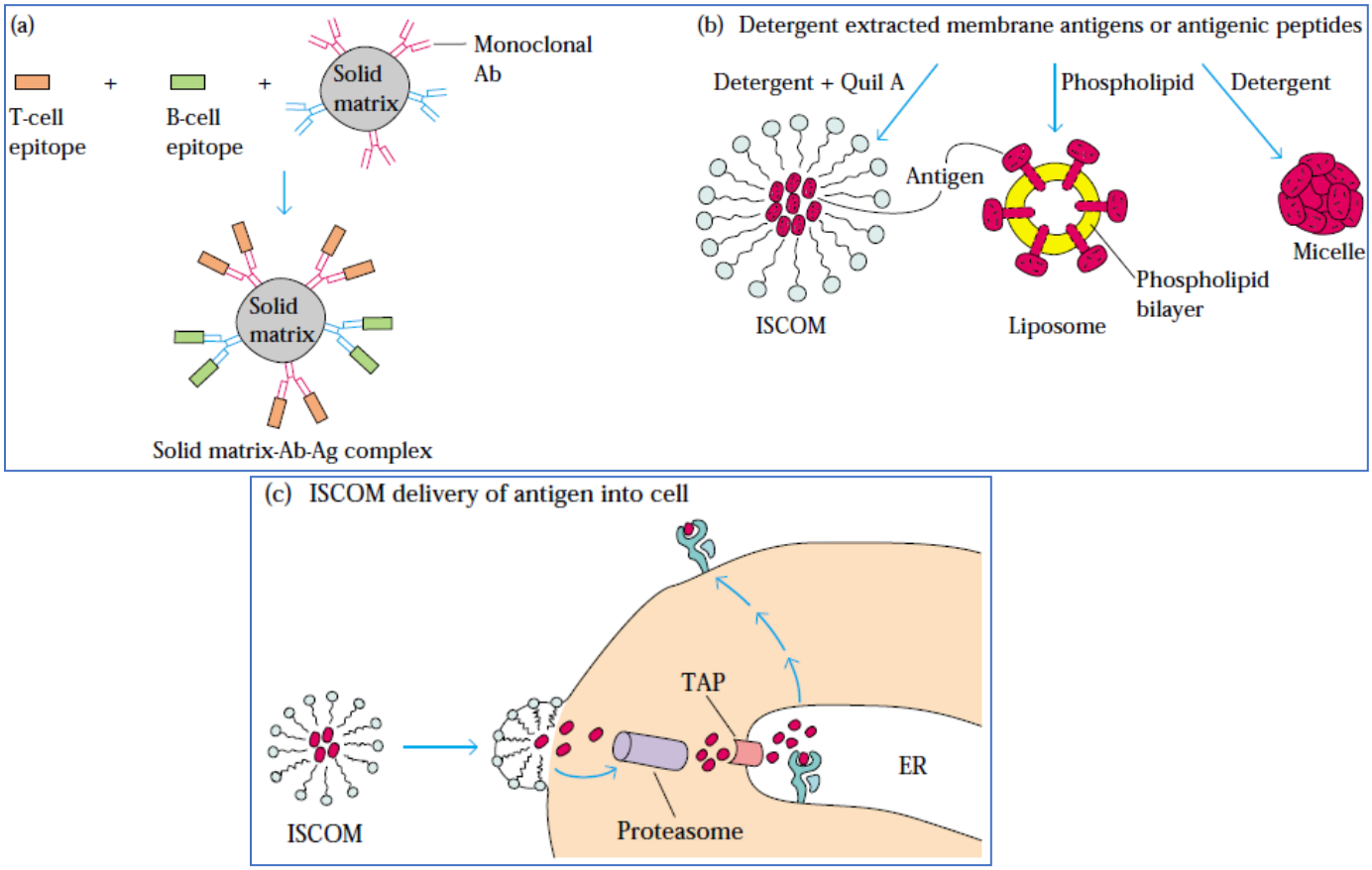

Figure 3: Different types of multivalent subunit vaccines(Kuby,2000).

1.1.b. Corona virus and vaccine:

Corona pandemic is a major disaster of this century. There are 7 structural proteins (spike protein, envelop protein, membrane protein, protease, nucleocapsid protein, hemagglutinin esterase, and helicase) and 16 nonstructural proteins which are potential targets for vaccine development. (Prajapat et al.,2020).

Researchers worldwide are working around the clock to find a vaccine against corona. Experts estimate that an effective vaccine can be development approximately within 12-18 months – if the tactic goes smoothly from conception to plug availability. (raps,2020)

The six steps for vaccine production are-

Exploratory: This research-intensive phase of the vaccine development process is designed to identify "natural or synthetic antigens that might help prevent or treat a disease." Antigens might include weakened strains of a particular virus.

Pre-clinical: During this phase, researchers, use tissue-culture or cell-culture systems and animal testing to determine whether the candidate vaccine will produce immunity. Many candidate vaccines don't move on to the next stage of development because they fail to produce that immunity or prove harmful to test subjects.

Clinical development: At this point, the company applies an Investigational New Drug (IND) to the recognized government organization (In India, it is ICMR and CDSCO). This summarizes findings to date and describes how the drug will be tested and created. An institution that will arrange the clinical trial will form a review board for approval of the application. Once the proposal gets approved, the vaccine then passes three trial stages of human testing:

Phase I introduces the candidate vaccine to a small group (less than 100 people) aiming to determine whether the candidate vaccine is safe and to learn more about the responses it .

Phase II includes hundreds of human test subjects, aims to deliver more information about safety, immunogenicity, immunization schedule and dose size.

Phase III includes thousands or tens of thousands of test subjects continues to measure the safety (little side effects sometimes don't appear in smaller groups) and effectiveness of the candidate vaccine.

Phase IV trial is the testing of vaccine in more number of human than phase III and after that; if the vaccine is approved by the corresponding government authority,it is ready to use among major population.

Regulatory review and approval: If a vaccine passes through all four phases of clinical development, the vaccine developer submits a License Application to the government organization.

Manufacturing: Major drug manufacturers provide the infrastructure,equipment and personnel necessary to create a huge quantity of vaccines.

Quality control: The approval and distribution is far from the end of the line. Stakeholders must adhere to procedures that allow them to track whether a vaccine is performing as expected. Multiple systems — including Phase IV trials (optional studies that can be conducted following the release of a vaccine). Then the vaccine is validated for safety issues with proper batch number and mfg and exp dates.

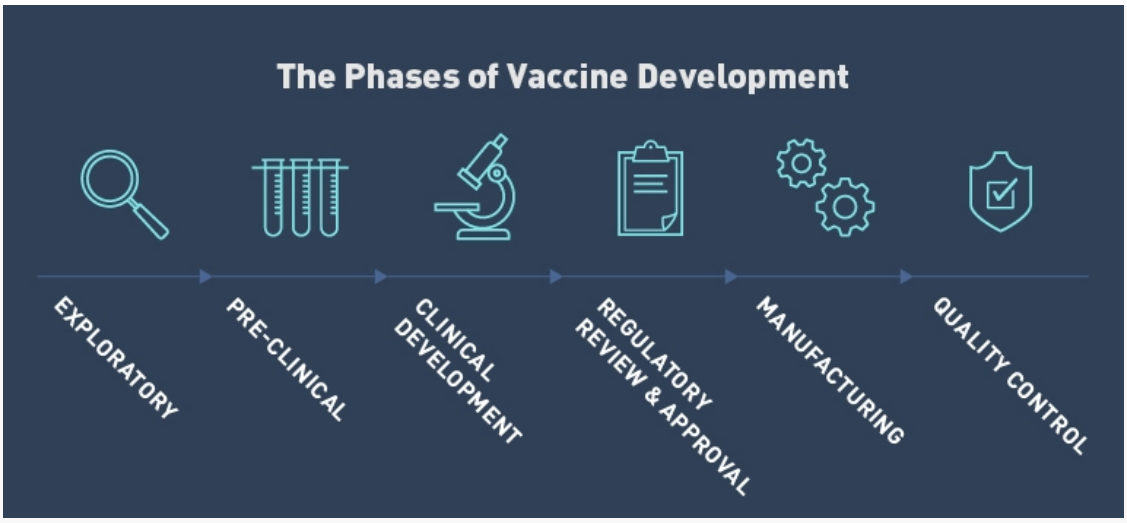

Figure 4: Phases of vaccine production. (publichealthonline,2020)

The US government is choosing three vaccine candidates to fund for Phase 3 trials for Covid-19 under Operation Warp Speed: Moderna's mRNA-1273 in July, The University of Oxford and AstraZeneca's AZD1222 in August, and Pfizer and BioNTech's BNT162 in September.

The list of various vaccine developers are on the next page.(raps,2020)

	Candidate	Sponsor	Trial Phase	Institution	Funding
	Bacillus Calmette-Guerin (BCG) live-attenuated vaccine	University of Melbourne and Murdoch Children's Research Institute; Radboud University Medical Center; Faustman Lab at Massachusetts General Hospital	Phase 2/3	University of Melbourne and Murdoch Children's Research Institute; Radboud University Medical Center; Faustman Lab at Massachusetts General Hospital	Murdoch Children's Research Institute; UMC Utrecht
	AZD1222	The University of Oxford	Phase 2/3	The University of Oxford, the Jenner Institute	Operation Warp Speed; UK Ministry of Health; The University of Oxford; BARDA
	mRNA-1273	Moderna	Phase 2	Kaiser Permanente Washington Health Research Institute	Operation Ward Speed; NIAID, BARDA ($483 million)
	BNT162	Pfizer, BioNTech	Phase 1/2	Multiple study sites in Europe	Pfizer; BioNTech
	Inactivated vaccine	Wuhan Institute of Biological Products; China National Pharmaceutical Group (Sinopharm)	Phase 1/2	Henan Provincial Center for Disease Control and Prevention	Ministry of Science and Technology, China
	BBIBP-CorV	Beijing Institute of Biological Products; China National Pharmaceutical Group (Sinopharm)	Phase 1/2	Henan Provincial Center for Disease Control and Prevention	Ministry of Science and Technology, China
	CoronaVac	Sinovac	Phase 1/2	Sinovac Research and Development Co., Ltd.	Sinovac Research and Development Co., Ltd.
	GX-19	Genexine	Phase 1/2		GenexineGenexine
	Gam-COVID-Vac	Gamaleya Research Institute, Acellena Contract Drug Research and Development	Phase 1/2	Various	Gamaleya Research Institute of Epidemiology and Microbiology, Health Ministry of the Russian Federation
	Ad5-nCoV	CanSino Biologics	Phase 1	Tongji Hospital; Wuhan, China	CanSino Biologics
	INO-4800	Inovio Pharmaceuticals	Phase 1	Center for Pharmaceutical Research, Kansas City. Mo.; University of Pennsylvania, Philadelphia	Inovio Pharmaceuticals
	mRNA-based vaccine	CureVac	Phase 1	CureVac	CureVac; German federal government

	SCB-2019	GlaxoSmithKline, Sanofi, Clover Biopharmaceuticals, Dynavax and Xiamen Innovax	Phase 1	Linear Clinical Research (Australia)	CEPI
	Adjuvant recombinant vaccine candidate	Anhui Zhifei Longcom Biopharmaceutical, Institute of Microbiology of the Chinese Academy of Sciences	Phase 1		
	bacTRL-Spike	Symvivo	Pre-clinical	Symvivo Corporation	Symvivo Corporation
	PittCoVacc	UPMC/University of Pittsburgh School of Medicine	Pre-clinical	University of Pittsburgh	CEPI
	Measles vector vaccine	University of Pittsburgh's Center for Vaccine Research	Pre-clinical	University of Pittsburgh; Themis Biosciences; Institut Pasteur	Merck
	NVX-CoV2373	Novavax	Pre-clinical	Novavax	Novavax, CEPI, Department of Defense ($60 million)
	Ii-Key peptide COVID-19 vaccine	Generex Biotechnology	Pre-clinical	Generex	Generex
	Recombinant vaccine	Vaxart	Pre-clinical	Vaxart	no information
	Self-amplifying RNA vaccine	Imperial College London	Pre-clinical	Imperial College London	UK Secretary of State for Health; UK Secretary of State for Business, Energy and Industrial Strategy
	Plant-based COVID-19 vaccine	Medicago	Pre-clinical	Medicago	Medicago
	DNA-based vaccine	Takis Biotech	Pre-clinical	Takis Biotech	Takis Biotech
	Ad26.COV2-S	Johnson & Johnson	Pre-clinical	Johnson & Johnson	Operation Warp Speed; Johnson & Johnson; BARDA
	AdCOVID	Altimmune	Pre-clinical	University of Alabama at Birmingham	Altimmune
	T-COVIDTM	Altimmune	Pre-clinical		Altimmune
	Protein subunit vaccine	University of Saskatchewan Vaccine and Infectious Disease Organization-International Vaccine Centre	Pre-clinical	University of Saskatchewan Vaccine and Infectious Disease Organization-International Vaccine Centre	no information

	LUNAR-COV19	Arcturus Therapeutics and Duke-NUS Medical School	Pre-clinical	Duke-NUS Medical School, Singapore	Arcturus
	Recombinant vesicular stomatitis virus (rVSV) vaccine	Merck; IAVI	Pre-clinical		BARDA
	Adenovirus-based vaccine	ImmunityBio; NantKwest	Pre-clinical		
	Molecular clamp vaccine	CSL; The University of Queensland	Pre-clinical		CEPI; CSL
	AAVCOVID	Massachusetts Eye and Ear; Massachusetts General Hospital; University of Pennsylvania	Pre-clinical		Wyc Grousbeck; Emilia Fazzalari
	Recombinant vaccine	Sanofi, Translate Bio	Pre-clinical		BARDA
	mRNA lipid nanoparticle (mRNA-LNP) vaccine	CanSino Biologics, Precision NanoSystems	Early research		
	Adenovirus-based vaccine	ReiThera; Leukocare; Univercells	Early research		
	gp96-based vaccine	Heat Biologics	Early research	University of Miami Miller School of Medicine	

- Hyderabad based Bharat Biotech, has successfully developed **COVAXIN**, India's first vaccine candidate for Covid-19, in collaboration with the Indian Council of Medical Research (ICMR) and National Institute of Virology (NIV). The SARS-CoV-2 strain, isolated from NIV Pune was transferred to Bharat Biotech to develop the vaccine. The Drug Controller General of India- Central Drugs Standard Control Organization and Ministry of Health & Family Welfare granted permission to initiate Phase I & II Human clinical trials after the company submitted results generated from preclinical studies, demonstrating safety and immune response. Human clinical trials begun across India in July 2020. (Prajapatet al. ,2020)

Conclusion:

With the world coming to a standstill after the spread of the Corona Virus, and with WHO recognizing it as a worldwide pandemic, it's apparent that the world will never be the same as before.When a disease is new, there is no vaccine until one is developed. It can take many years to develop an effective vaccine. There is no specific treatment for COVID-19. Developing a COVID-19 vaccine in record time will be tough. Manufacturingenough vaccines to end the pandemic will be the biggest medical manufacturing feat in history. Scientists are trying to find a new vaccine against this virus. But the random mutation of this RNA virus lowers the speed of vaccine development. Several factors must be kept in mind in developing a successful vaccine. Human subjects for clinical trial and cost of production are two major problems during this pandemic situation. The development of an immune response does not necessarily mean that a state of protective immunity has been achieved. But, the important partis,which branch of the immune system is activated. Vaccine designers must recognize the important differences between activation of the humoral and the cellmediated branches. The Corona Virus has forced us to retreat into our homes. This has been incredibly difficult for us who are used to working outside every day. From schools to offices, we have inculcated a routine for ourselves. Whether we like to abide by it daily or not, we have been following it religiously for at least a decade. This Virus suddenly forces us to stop and stare. This has been strenuous for our minds. The vaccine is the only ray of hope among the sickly and traumatized people, so we can expect that, we will get a vaccine soon to fight against corona. Thus, all we can do is to hope for a better and healthier future, and abide by the guidelines instructed by the Government due to COVID 19 pandemic, and help the world to end this pandemic soon.

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Consequences of Major Past Viral Pandemics in the last 200 years

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ABSTRACT

Communicable diseases came into existence since the days of hunter-gatherers. Epidemics started almost 10,000 years ago. Few of the epidemics which emerge during this period were Malaria, leprosy, influenza, etc. When an epidemic spreads to another country other than the one affected, it becomes a pandemic. In this article we focus on the major viral pandemics which occurred in the last 200 years and their consequences. The consequences include how the pandemics affected the world socially as well as economically. The information about the pandemics should be known in order to take proper precautionary measures in present and in future.

Keywords: Viral pandemics, Consequences.

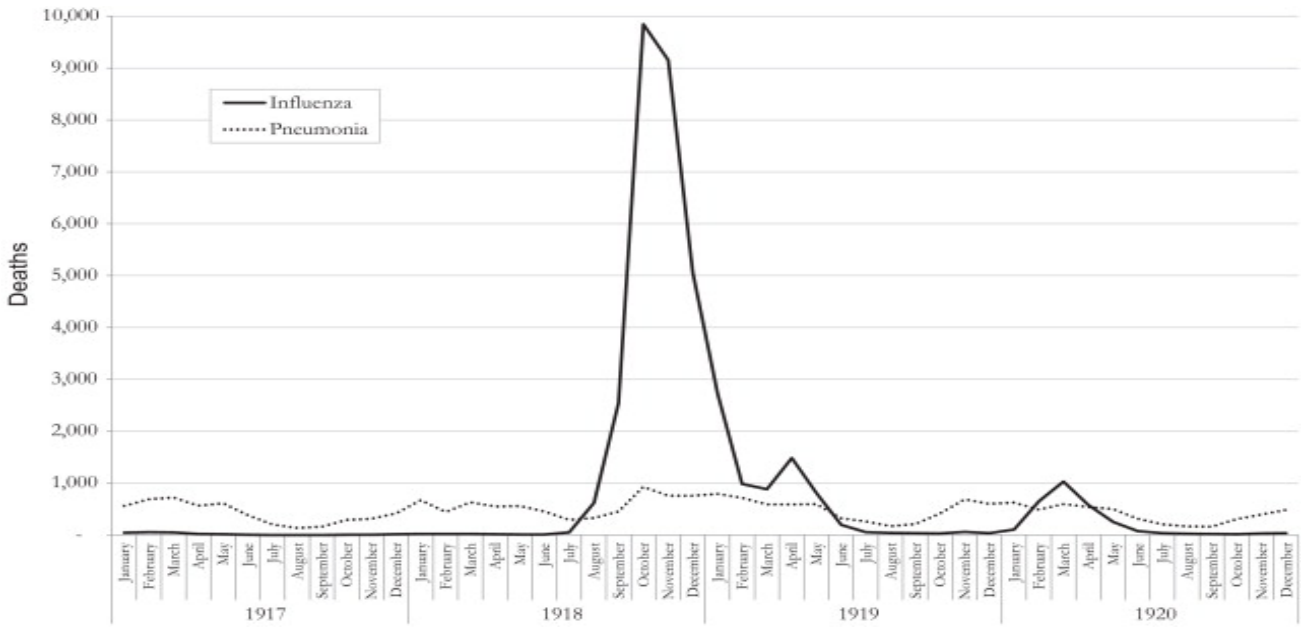
INTRODUCTION

The spread of a new disease worldwide is termed as pandemic. Many people lack the natural immunity to fight off the disease when it first emerges and might become sick as the disease spreads. This may sometimes cause a rapid spread of the disease between two people, across different communities or worldwide. (Lockett, 2020).

Many pandemics took over the world in the last 200 years namely Spanish Flu, HIV, etc. the most recent one being COVID-19.

1. Spanish Flu(1918)

Influenza is a respiratory disorder caused by a virus. The flu virus is very contagious: When an infected person coughs, sneezes or talks, respiratory droplets are produced and transmitted into the air, and can then be inhaled by anyone in the surrounding. A person who comes in contact with something with the virus on it and then touches his/her mouth, eyes or nose can become infected ("Spanish Flu," 2020).



Source: https://www.sciencedirect.com/science/article/pii/S0167629614000344

The Spanish flu being one of the deadliest attacked 500 million people worldwide, with the total count of morbidity being between 20 million to 50 million victims, including

675,000 Americans. People were advised to wear face masks.Schools, theaters etc. were shut down and bodies piled up in makeshift morgues before the virus ended its deadly global march (“Spanish Flu,” 2020).

Despite the fact that the 1918 flu was not isolated to one place, it became known around the world as the Spanish flu, because Spain was hit hard the most by the disease (“Spanish Flu,” 2020).

As time flew by, the community began to develop resistance against the virus. That is how the pandemic ended by 1920 (“Spanish Flu,” 2020).

2. Asian Flu(1958)

The Asian flu was caused by Influenza A virus subtype H2N2 which is a mixed strain of prevalent virus H1N1 and human genes. There was no previous immunity against this kind.

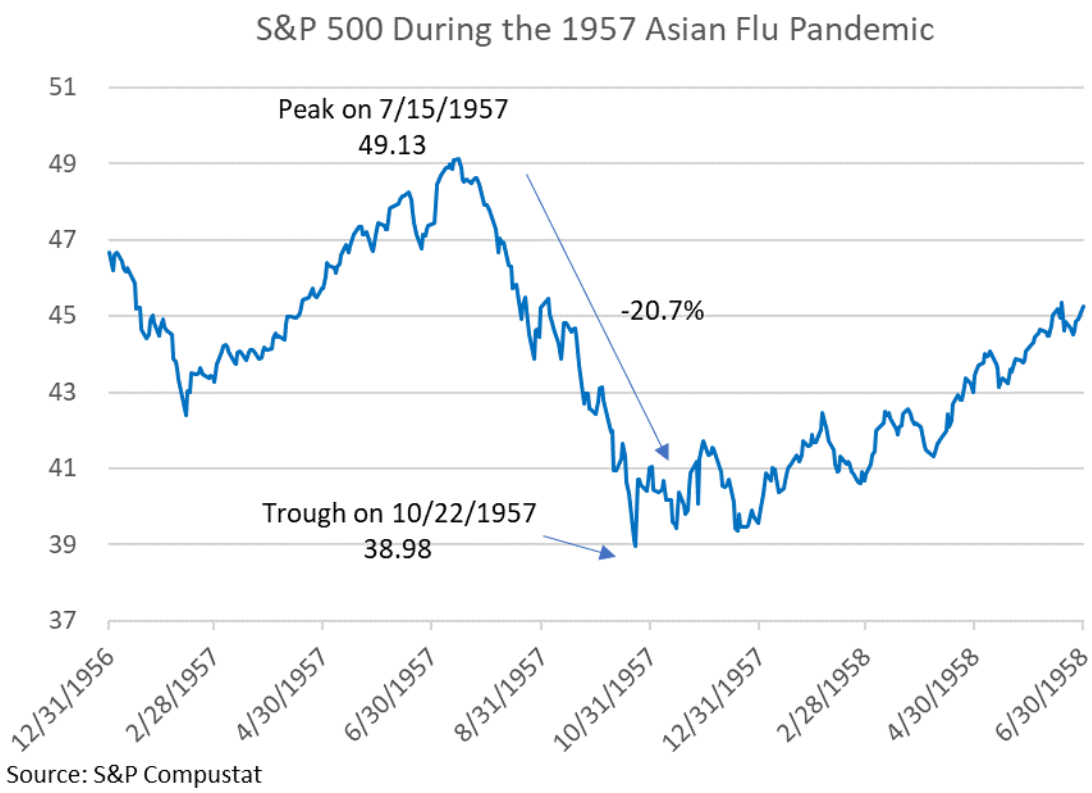
In 1956, the H2N2 virus infected an individual from Guizhou province in China. It started spreading across the Asian continent. The pandemic lasted till 1958, and finally vanished in 1968.

Children were extremely vulnerable to infection. This turned fatal for elderly, pregnant women in the third trimester and people with prevalent respiratory or heart diseases (Clark, 2008).

The death toll ranged between 2,000,000 to 4,000,000 globally (0.3% mortality rate) (Jackson, 2009).

In May, 1957 a vaccine was developed and healthcare facilities were improved reducing the mortality rate.

The pandemic led to economic crisis and schools being closed temporarily. This virus is believed to have been mutated to a H3N2 strain causing the Hong Kong flu pandemic (Clark, 2008).



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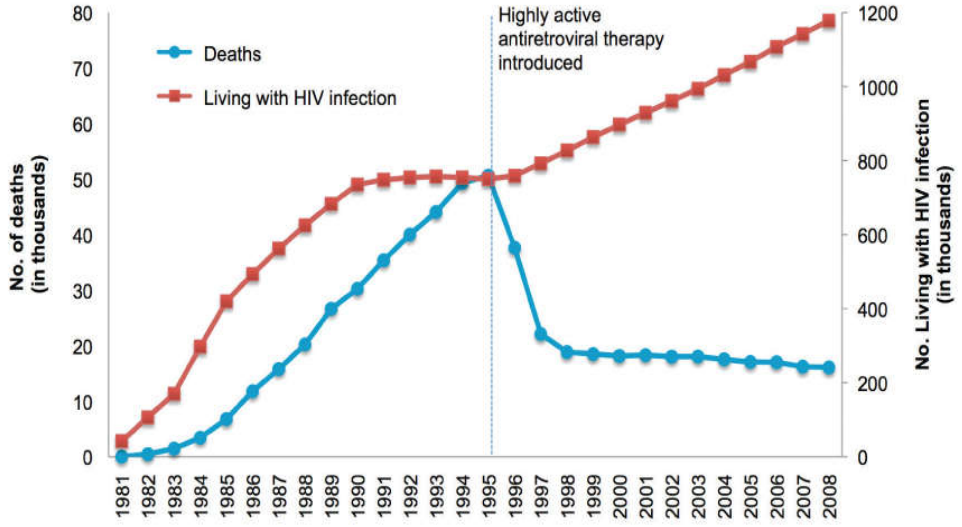
3. AIDS(1981)

HIV virus mainly attacks the immune system of an individual. The virus destroys a type of WBC in the immune system called a T-helper cell – also referred to as a CD4 cell – and uses these cells to make copies of itself and it gradually breaks down a person's immune system. This means that someone who has HIV, andif left untreated, will find it hard to fight off diseases and it might take up to 10 or 15 years for the immune system to be so damaged that it can no longer defend itself ("What are HIV and AIDS," 2020).

In some areas, HIV infection had spread quickly to the general population; in others, the infection had remained among higher-risk subpopulations, mostly amongst sex workers and their customers and intravenous drug users (IDUs). Worldwide, the adult prevalence rate is 1.07% of

the population, and 47% of infections occur among women. The AIDS pandemic drastically affected the economy nationwide. AIDS is by far the second leading cause of death among adults in developing countries. AIDS has hit the lower strata of the society drastically ("Social Impact of AIDS in the United States, 1993).



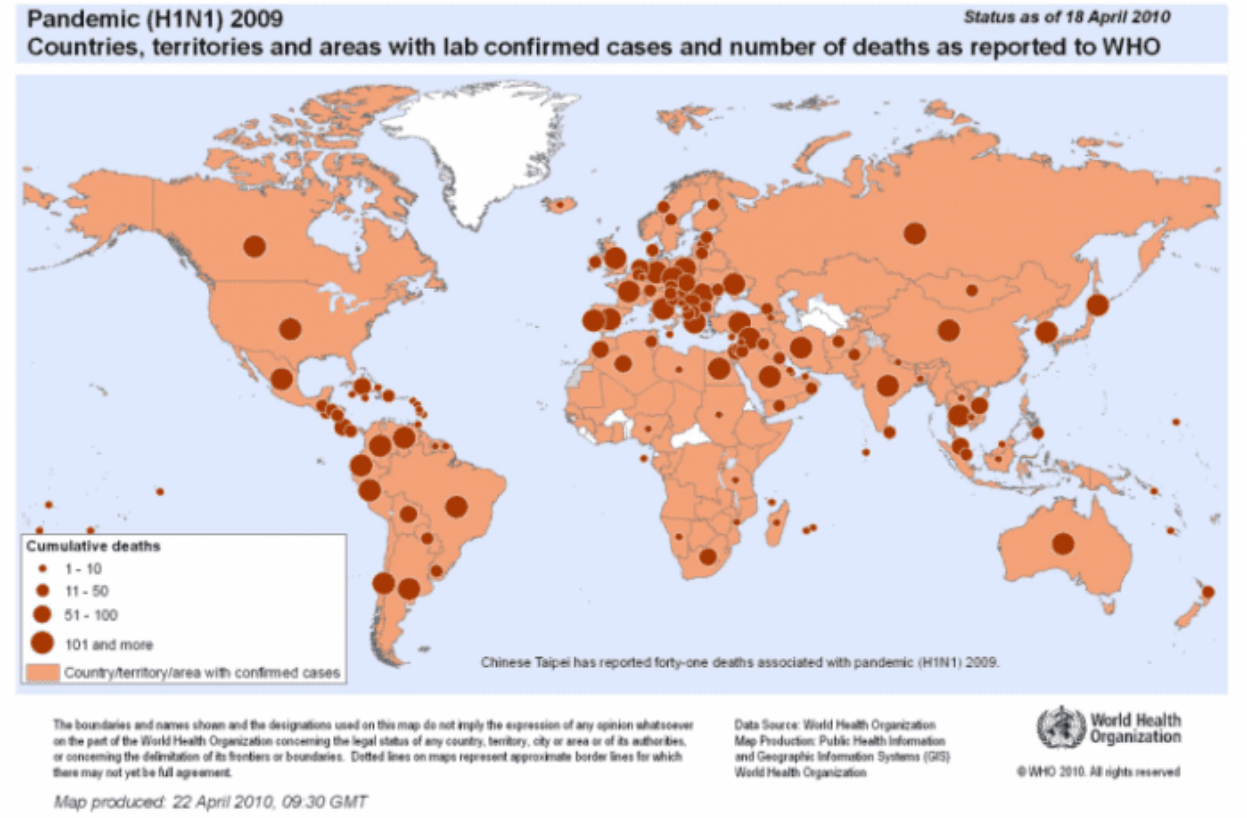
Source: https://www.drugabuse.gov/publications/research-reports/hivaids/how-does-abuse-affect-hiv-epidemic

Tuberculosis the most common infection and the leading cause of mortality among people with HIV in affected countries whereas industrialized countries *Pneumocystis carinii* pneumonia is the leading cause of HIV morbidity. Technological advancements have showed that controlled trial in TB preventive therapy prevents TB disease in persons co infected with HIV and TB. Before effective antiretroviral therapy was made available in developed countries, the survival of HIV-infected patients depended upon preventing infections by the use of antibiotic prophylaxis ("Social Impact of AIDS in the United States, 1993).

4. H1N1 Pandemic(2009)

The first case of H1N1 virus was identified in the USA("2009 H1N1 Pandemic (H1N1pdm09 virus) ", n.d.).

The number of lab-confirmed deaths which were reported to WHO were 18,449, though the H1N1 flu pandemic of 2009 is estimated to have caused almost 284,000 deaths. A follow up studydone in September 2010 showed that the risk of serious illness which developed from 2009 H1N1 flu was almost equal to that of yearly seasonal flu. 250,000 to 500,000 deaths occur due to seasonal flu annually as estimated by WHO (“2009 swine flu pandemic”, n.d.).



Source: https://reliefweb.int/map/world/world-pandemic-h1n1-2009-countries-territories-and-areas-lab-confirmed-cases-and-number-11

Due to this pandemic, the economy was affected on account of higher costs of healthcare, absenteeism and also due to effect on demand as people reduced their visit to crowded places (Chakravarty and Philipose, 2009).

A drug which prevents the infection of an individual with the influenza virus H1N1 strain is called Panvax which was approved for use in adults and children who are more than 10 years of age. This vaccine should not be used by individuals who have experienced an anaphylactic hypersensitivity previously to influenza vaccine, eggs or any other ingredients in the vaccine

("Panvax H1N1 Vaccine (Swine Flu Vaccine)", n.d.). On 15 September, 2009, the U.S. Food and Drug Administration approved the Swine flu vaccine for use ("Swine influenza", n.d.).

5. Western Africa Ebola(2013)

The causal organism for the Ebola outbreak was Ebola Virus (Zaire Species).

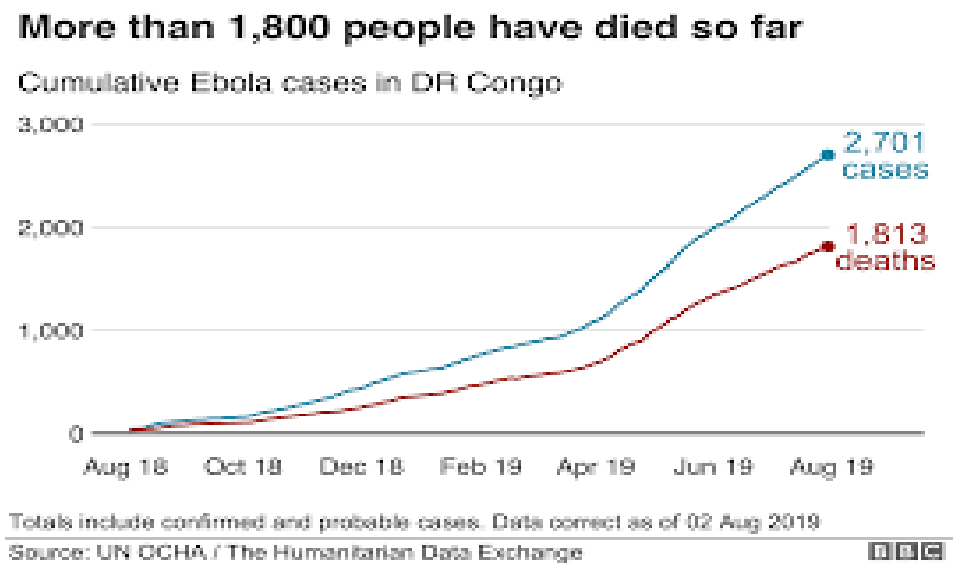
The most widespread Ebola Virus Attack affected a number of countries in Western Africa (2013-2016) taking away many lives and damaging the socioeconomic state highly. The disease was first reported in Guinea in December, 2013 and started spreading to Liberia, Nigeria, Senegal and Sierra Leone. Isolated cases were also reported from the United States, the United Kingdom, Spain and Italy (WHO, 2016).

The case count reached its peak in October 2014, and then started declining.

By May 2016, WHO (World Health Organization) reported approximately 28,646 suspected cases and 11,323 deaths, though the magnitude is believed to be even more (WHO, 2014)

Many survivors have reported post-Ebola syndrome, symptoms at times so severe that they require medical care for months to years. The virus may stay in dormant stage in many survivors for years till they again relapse, causing further deadly situation (Meltzar et al., 2014).

WHO, in December 2016, declared the rVSV-ZEBOZ vaccine, which was approved in 2019, had proven successful in prevention against the EBOV variant prevalent in Western Africa.Being the only effective and prophylactic vaccine to provide protection, 300,000 doses are stockpiled. (Geisbert, 2017).



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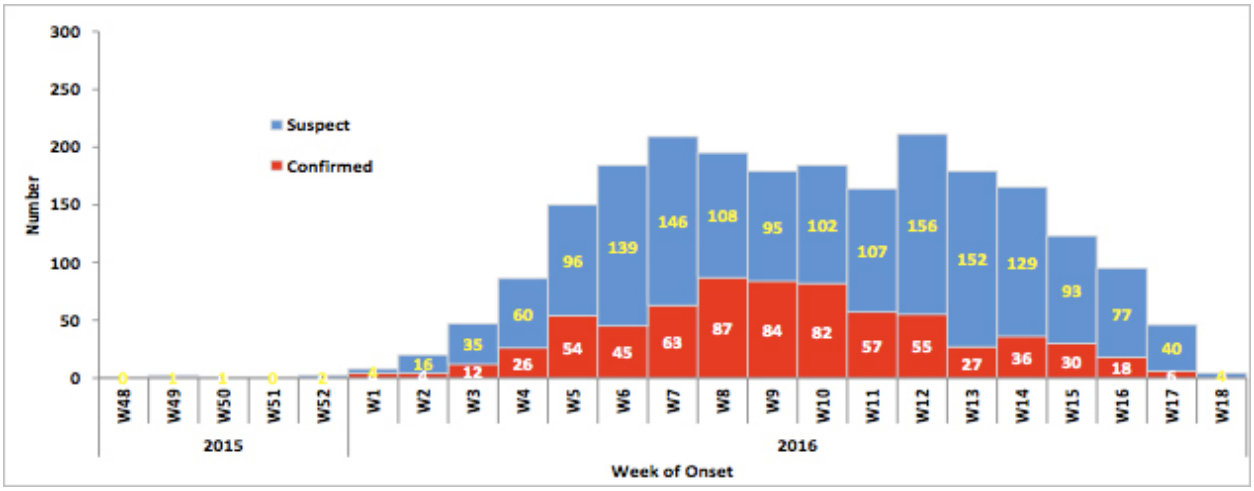
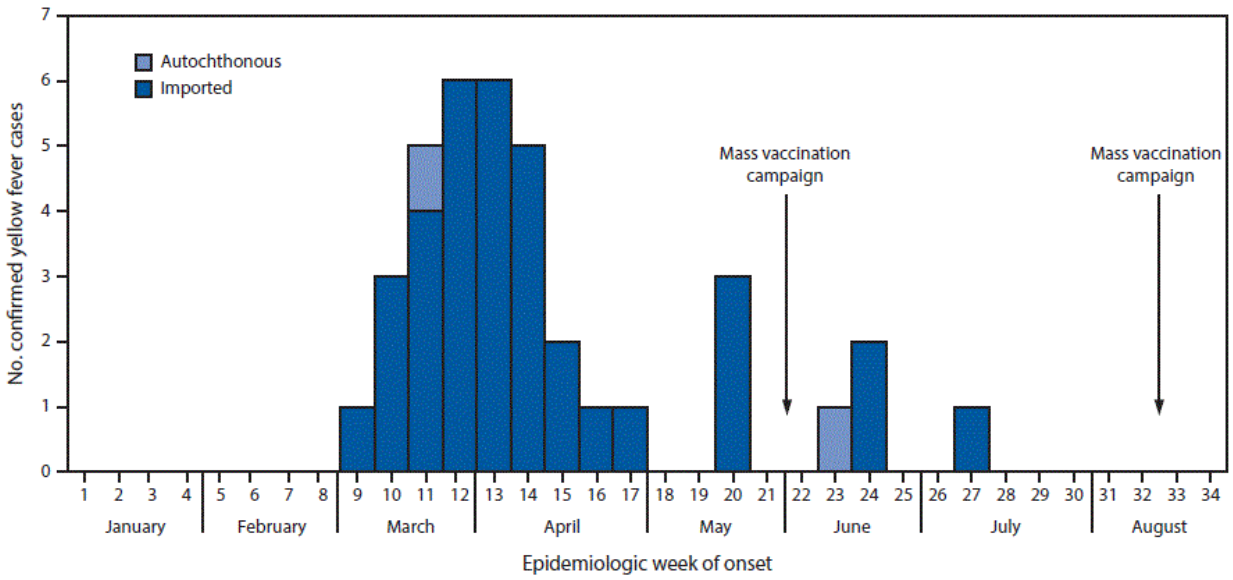
6. Yellow Fever (2016)

Yellow Fever virus belongs to genus *Flavivirus* of family *Flaviviridiae* which isarthropod-borne. Yellow Fever is a type of hemorrhagic fever usually occurring in South American countries and sub-Saharan Africa (Onyango et al., 2004).



Source: https://www.who.int/emergencies/yellow-fever/situation-reports/8-may-2016/en/

The outbreak of yellow fever started in December 2015 in municipality of Viana, Luanda province and spread to other parts of Angola. As of 28 October 2016, in Angola there were 884 confirmed cases among which 121 deaths were confirmed (case fatality rate, 13.7%) and 4347 suspected cases among which 377 deaths were confirmed (case fatality rate, 8.7%). In DR Congo, there were 78 confirmed cases (among which 57 cases were imported from Angola, 8 were sylvatic and 13 were autochthonous) 16 deaths were confirmed (case fatality rate, 21.1%). There were suspected 2987 cases among which 121 deaths were confirmed (case fatality rate, 4.0%) (Sylvatic cases were not considered a part of this outbreak) (WHO Bulletin, 2016).



Source: https://www.cdc.gov/mmwr/volumes/66/wr/mm6612a5.htm

Yellow Fever has caused hardship and despair among populations in the Americas, Europe, and Africa in the past. It brought economic disaster in its wake, and it acted as a stumbling block to development(Tomori, 1999).

The treatment for Yellow fever involves managing the symptoms and assisting the immune system in fighting off the infection by getting

- enough fluids and oxygen
- blood transfusions
- dialysis in case of kidney failure

- the other infections treated if present and maintaining proper blood pressure. (Colleen Story, 2019)

The only commercially available vaccine named17D vaccine, based on a live, attenuated viral strainwas discovered in the 1930s by microbiologist Max Theiler at the Rockefeller Institute in New York City (Norrby, E. (2007)) (WHO Bulletin, n.d.).

7. Dengue Fever(2019-2020)

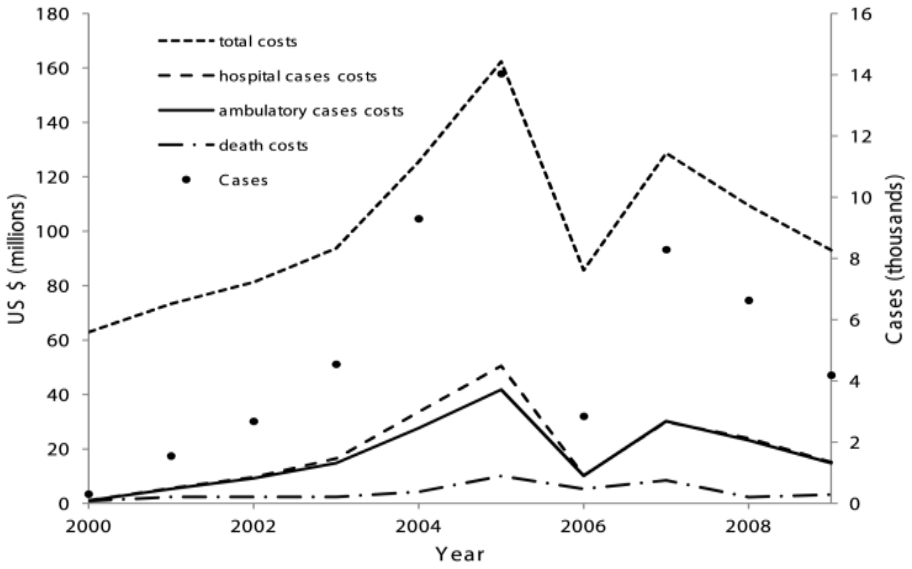
Dengue fever is a disease borne by mosquito. This disease is very painful and debilitating. Overall, there are four types of dengue viruses. Out of those four viruses, if any one infects an individual, the infected person ends up acquiring the disease. These viruses are similar to the viruses that cause West Nile infection and yellow fever. Dengue fever has been a significant arboviral disease borne by a vector since the beginning of the 21st century. More than 3.9 billion people are at risk of infection in 128 countries ("Dengue Fever," n.d.).

Worldwide, every year, approximately 400 million dengue infections occur. About 96 million results in illness. Most cases take place in tropical areas of the world. The greatest risk occurring in:

- The Indian subcontinent
- Southeast Asia
- Southern China
- Taiwan
- The Pacific Islands
- The Caribbean (except Cuba and the Cayman Islands)
- Mexico
- Africa
- Central and South America (except Chile, Paraguay, and Argentina) ("Dengue Fever," n.d.).

Dengue outbreaks caused a great financial impact on low-income families. Prevention and control campaigns were implemented between the periods of outbreak. In spite of that, it was reported by various stakeholders that dengue prevention and control efforts which were performed by municipal authorities were not sufficient. They also

suggested that efforts should be strengthened and coordination should be improved by governmental authorities, particularly during the periods of outbreak (Ladner et al., 2015).



Source: PLoS

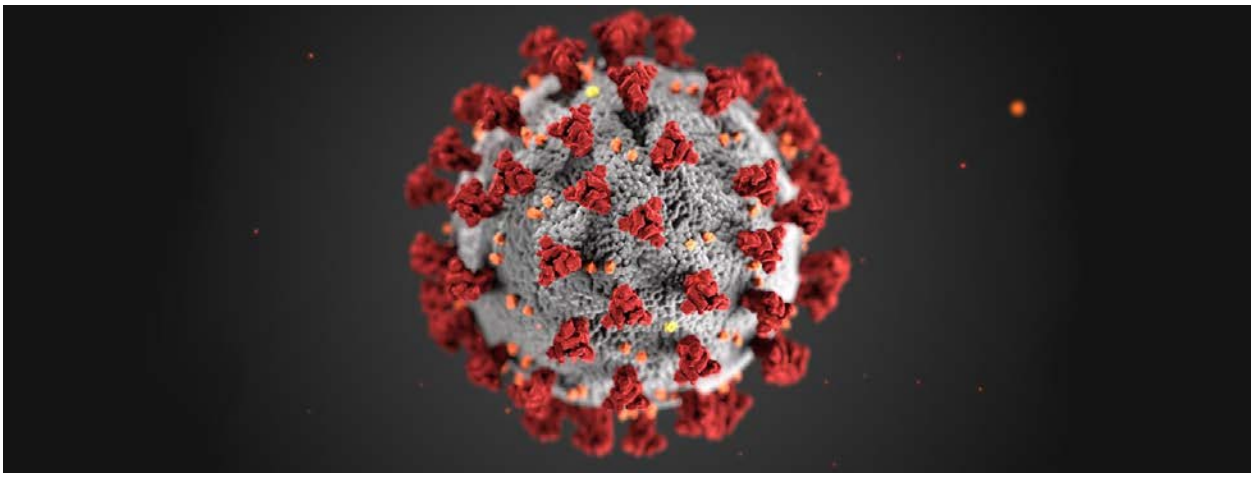
Prevention: A high fever and vomiting leads to dehydration of the body. Clean water should be consumed by the person, ideally bottled water. Rehydration salts can also be of help to replace fluids and minerals (Medical News Today, 2020).

Painkillers, for example Tylenol or paracetamol: These can be of help to lower fever and ease pain (Medical News Today, 2020)

Non-steroidal anti-inflammatory drugs (NSAIDs) for example aspirin or ibuprofen, can increase the risk of internal bleeding, so they are not advised (Medical News Today, 2020)

8. COVID-19(2019- Present)

COVID-19 is an infectious disease which is caused by the coronavirus. Respiratory illness is experienced by the infected person.When the person infected, coughs or sneezes, the virus spreads via droplets, saliva or discharge from his/her nose.(WHO Bulletin, 2020).



Picture Courtesy: https://www.knowablemagazine.org/article/health-disease/2020/closing-new-coronavirus

Total number of people affected worldwide is 17,853,488.The number of confirmed deaths is 684,765(As of 1 August, 2020) (Worldometer Bulletin, 2020). Coronavirus was first identified in Wuhan, China and has now spread across many countries namely China, Italy, United States of America, Spain, Germany, France, Republic of Korea, The United Kingdom, India, etc. (ArfaJavaid, 2020).

Nobodycan say for sure when it will be contained and what its long-term impact could be, the stress will be placed irregularly on the individual, society, and on the government. The structural risk is as economic as it is biological, which affects everyone(Nayar, L. and Sood, J., 2020).

Workforce has reduced across all economic sectors. Many jobs have been lost due to social-distancing, travel limitations,etc. The need for commodities and the production has decreased with educational institutions having been shut down when the lockdown was declared. The need for medical supplies has increased significantly. Due to panic-buying and stockpiling of food products the food sector also faced increased demand. COVID-19 has affected communities and organizations globally, affecting the world's economy. Italso had a large impact on sporting schedules (Nicola et al., 2020).

CONCLUSION

Currently,almost the entire world is suffering from one of the worst pandemics that have hit in the last 200 years. The past viral pandemics resulted in millions of deaths worldwide and have devastated regions socio-economically. With the advancement of science, vaccine and drug development have become easier. However, that doesn't reduce the magnanimity of destruction caused by different viruses. While some viral strains get mutated and impose severe threats, many viruses are yet to be discovered that can be potentially pathogenic and life-threatening. Necessary hygiene and sanitization conditions must be maintained and awareness must be created to deal with such pandemics effectively.

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The Start of The New Era: A Long Series of Scourges

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Abstract

The Pandemic has a long history, but the term of “pandemic” is still not been defined by many medical texts. There have been many significant pandemics recorded in human history, and the pandemic related crisis has caused enormous negative impacts on health, and even national security in the world. Despite the fact that most emerging diseases stem from the transmission of pathogenic agents from animals to humans, the factors that mediate this process are still ill defined. What is known, however, is that the interface between humans and animals is of paramount importance in the process. This article will explore the literature for the concept and history of pandemics; summarises the key features of pandemics, and discusses the negative impacts on health, economy, social and global security of pandemics and disease outbreaks. This Review Article talks about such outbreaks, known to be occurred in the recent times and explains them in a summarized way. The necessity to review this title is because the information is scattered and to source them and compile them into a single article could help the medical practitioners and healthcare workers to understand what this country has been through in the past and what reforms have to be made by them, the community and the government in preventing such outbreaks in the future.

Keywords: Pandemic, World, Negative Impacts and Crisis

1 Introduction

From the start of the 20th Century, till now, the world has been sharply reminded several times the degree to which people in all countries and on all continents, remain chronically vulnerable to infectious diseases, known and unknown.

In the 1970s, and for years afterwards, this remarkable progress, including the development of new vaccines, antibiotics, and other treatments and technologies, led to a proclamation of a victory of mankind over microbes, but they are constantly evolving so that they pose a threat to the mankind. For this, we have to evolve our understanding of microbes, and work accordingly. There have been a significant number of pandemics throughout history and in many instances; their control had been difficult because of the lack of a proper, working global surveillance system.

In order to try to see the road ahead more clearly, we frequently need to look over our shoulders - more, because the early years of the century have already been deeply scarred by so many major epidemics. **And they will help us to strengthen ourselves from the "so called enemies" that lead the life.**

The History's Worst Epidemics/Pandemics Ever Witnessed

We have witnessed several Epidemics/Pandemics, which are consisted of some known & unknown are present in our Nature.

1.1 Zika Virus

As we know, for some time, there is a disease, which is there in our nature, had been transmitted by *Aedes* mosquitoes during the day, and had circulated in many parts of the world affecting many people out there in **2015**. Yes, we are talking about the **Zika virus disease**.(WHO, 2018) This disease mainly does not show any symptoms, but it can show some like fever, rash, conjunctivitis, joint & muscle pain, headache and many more which typically last for 2 – 7 days, but this does not explain the incubation period (the time from exposure to the onset of symptoms) which is unknown to many of us, but some say, it is estimated to be between 3 – 14 days.("Zika Virus," 2018) But to many people, especially during pregnancy, it can cause

Microcephaly (A condition where the infant's head is smaller than those of other babies of the same age and sex) to newborn infants as well as other congenital malformations, which is known as congenital Zika syndrome.(WHO, 2018) With this, there are other complications like preterm birth, miscarriage of foetus, seizures etc. This mixture of symptoms along with in-term paralysis, is specifically known as the Guillain-Barré Syndrome (a rare condition in which a person's immune system attacks the peripheral nerves).(WHO, 2018) This virus has a tendency to transmit through sexual contact, blood transfusion and organ transplantation, so it is been advised/ensured that the people who had the disease, along with their partners receive information about the risks of the virus, tell them to use contraceptives, and have a knowledge about whether and when to become pregnant, in order to prevent possible adverse pregnancy and fatal outcomes.(WHO, 2018) Also vector control strategies should be implemented in the area, which should address all life stages of the Aedes mosquito by eliminating breeding sites of eggs/larvae/pupae in stranded waters, spraying of insecticides in the resting site of the mosquitoes. All these should be implemented in accordance with the **IHR** (2005) and Mosquito surveillance. Currently, there are no antiviral drugs or specific treatment for the people infected with Zika virus. Research is ongoing for potential therapies, for vaccines to prevent Zika virus infection or Congenital Zika Syndrome. (WHO, 2018)

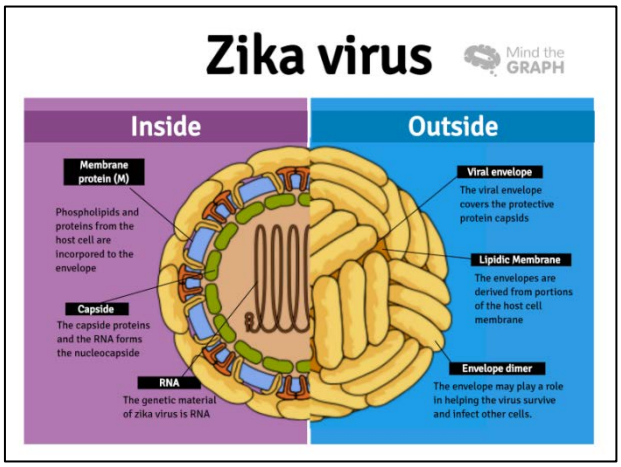

Figure 1: Structure of the Zika Virus

Picture Courtesy: https://medium.com/the-science-educator/zika-virus-the-awarded-study-that-brings-new-light-to-the-long-term-

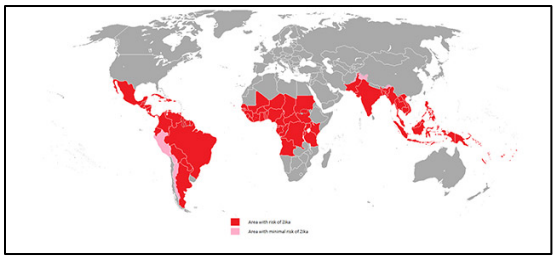

Figure 2: Affected Areas of the Zika Virus Disease

Picture Courtesy: https://healthywa.wa.gov.au/Articles/U_Z/Zika-virus

1.2 Ebola Virus

A disease, which was first appeared in **1976**, where two simultaneous outbreaks happened, one in what is now Nzara, South Sudan and the other in Yambuku, DRC, where, a river flows, known as the Ebola river. From there, this disease takes it's name. (WHO, 2018) Yes, we are talking about the **Ebola Virus Disease.** But from there, it has caused an epidemic in **2014-2016** in West Africa, which is the largest outbreak, since the virus was discovered and in the recent times of **2018-2019**, it had caused an outbreak in eastern DRC, is highly complex with insecurity adversely affecting public health response activities.(WHO, 2018) As we know, it was first introduced into the human population by close contact through blood, secretions etc of infected animals such as Fruit Bats, Chimpanzees, Gorillas & many more. From there it spreads through human-to-human transmission via direct contact.(WHO, 2018) The first symptoms of Ebola are common to many other diseases, as it can cause hemorrhage and like sudden onset of fever, fatigue, muscle pain, headache and sore throat. After that, the first symptoms are followed by vomiting, diarrhoea, symptoms of impaired kidney & liver function, and in some cases both internal & external bleeding. And the symptoms will start showing after 2 - 21 days. (WHO, 2018) Ebola virus is known to persist in immune-privileged sites in some people who have recovered from Ebola virus disease. These sites include the testicles, inside of the eye, and the central nervous system.(WHO, 2018) Mainly, the risk of being infected is high in Health care workers if **Infection Prevention and Control**

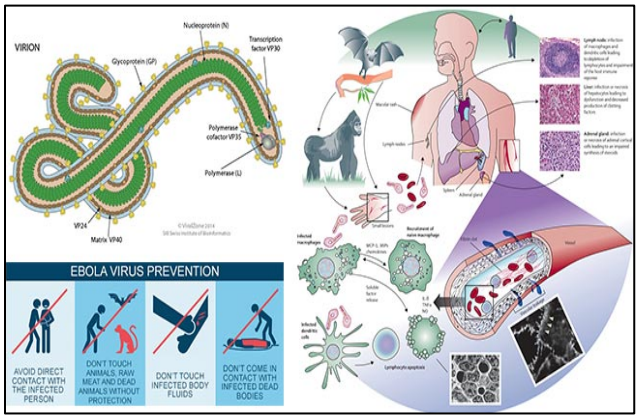

Figure 3: Structure & Transmission of Ebola Virus

Picture Courtesy: https://microbenotes.com/ebola-

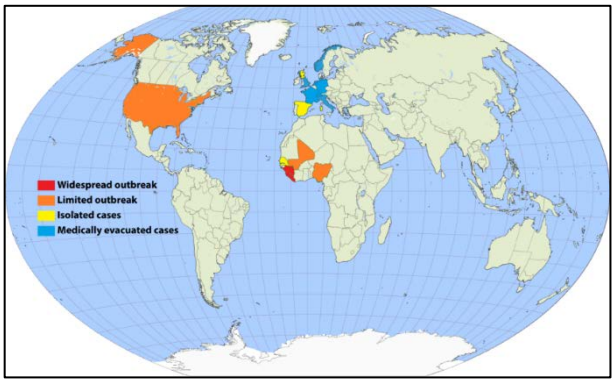

Figure 4: Affected Areas of the Ebola Virus Disease

PictureCourtesy
https://en.wikipedia.org/wiki/West_African_Ebola_virus_epidemic_timeline

(IPC) measures are not in place/not followed while caring patients, Mourners, as levels of Ebola virus remain high after death, and also in family members or others who are in close contact with infected people and caring for them and in contact with body fluids or contaminated items. People, who are survived from this deadly disease, may suffer from some physical like musculoskeletal, ocular, auditory, neurological & many more.(WHO, 2018) Research is ongoing to develop and evaluate vaccines, diagnostics tools and therapeutics. Currently, no vaccine or new therapeutic has been licensed. But an experimental Ebola vaccine named **rVSV – ZEBOV vaccine**, which was highly protective against this virus in a major trial in Guinea involving 11,841 people during **2015**, is 100% effective to eradicate this virus.(WHO, 2018)

1.3 Influenza Virus

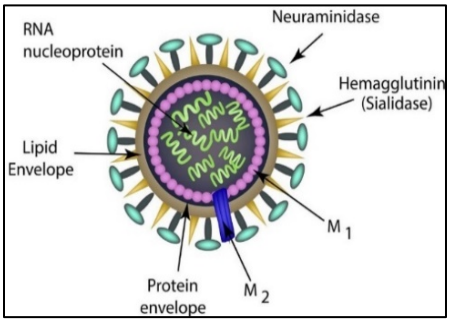

Figure 5: Structure of the Influenza Virus

Picture Courtesy:
https://medicalxpress.com/news/2018-10-flu-americans-year.html

Now, we want to talk about an epidemic/pandemic, which have it's widespread attention, occurs at an interval of 10 to 50-years, with varying severity and impact. Yes, we are talking about the disease **Influenza** (WHO, 2018). It has come in many names, like the Spanish Flu in **1918** (H1N1 strain of the Influenza A virus), the Asian Flu in **1957** (H2N2 strain), the Hong Kong Flu in **1968** (H3N2 strain), and the recent one in **2009**, the Swine Flu (H1N1/09 strain). Also, some epidemics & outbreaks, like the Avian Influenza (H5N1 strain of the A virus) and Seasonal Influenza.(Samal, 2014; WHO, 2018) There are four types of influenza viruses - types A, B, C and D - but only influenza A and

B cause epidemics.(WHO, 2018) As the person, who was in contact, may develop symptoms like sudden onset of fever, cough (usually dry), headache, fatigue & many more.(Samal, 2014) Also, some complications can be seen like pneumonia, sepsis & inflammation of the heart, brain or muscle, and the incubation period lasts for 1 - 5 days.(WHO, 2018) For this, Influenza is hard to differentiate clinically from other respiratory diseases. But, it is a belief that Pandemic influenza might be different from Seasonal influenza and symptoms might be more severe and complicated and more frequent (WHO, 2018).

Influenza viruses are in constant mutation. This is called antigenic drift and results in changes to the viruses which make people susceptible to catch flu every year, as they do not have immunity against the drifted viruses.(WHO, 2018) As there is no vaccine to protect against this disease and no antibiotics to treat secondary bacterial infections, that can be associated with it, Antiviral drugs like neuraminidase inhibitors (oseltamivir & zanamivir, peramivir & laninamivir) may reduce severe complications & death. Also non-pharmaceutical interventions (NPI), should be put in place, at an early stage, such as social distancing, good personal hygiene, use of disinfectants, having good hygiene (like cough etiquette, hand washing and cleaning of touched surfaces and objects) & many more, can slow down the rate of transmission of this deadly virus.(WHO, 2018)

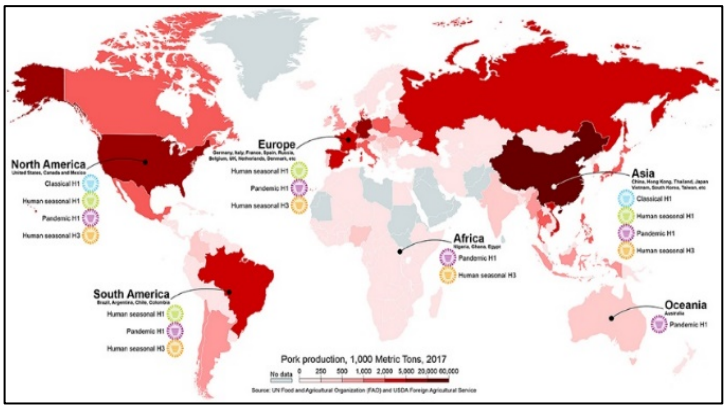

Figure 6: Affected Areas of the Influenza Disease

Picture Courtesy:
https://www.frontiersin.org/articles/10.3389/fvets.2018.00

Headlines of The Recent Times: Corona Virus Disease-19

Throughout history, infectious diseases have caused havoc among societies & communities, especially to the whole world. A new feather in the cap has been joined on **December 2019**, in Wuhan, China.(Rabaan et al., 2020; Petrosillo et al., 2020) **The COVID-19 disease**, caused by the SARS-CoV-2 virus,which primarily spreads by respiratory droplets, is easily transmissible by the asymptomatic or minimally symptomatic individuals.(Zheng, 2020) It's

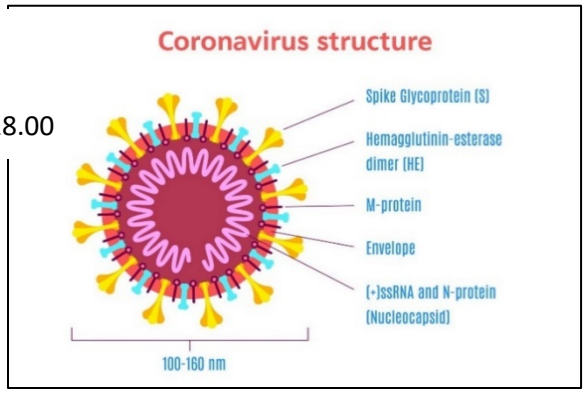

Figure 7: Structure of The Corona Virus in General

Picture Courtesy:

main highlight is the varying degree of severity, ranging from a mild upper respiratory tract illness to severe interstitial pneumonia & acute respiratory distress syndrome (ARDS). As of now, more than 10 Million people are affected worldwide. (Balkhair, 2020)

This, virus belongs to a family known as Coronaviruses infecting Humans (HCoVs), in which SARS-CoV virus, causing the **Severe Acute Respiratory Syndrome,** happened in **2002**& the MERS-CoV virus, causing the **Middle East Respiratory Syndrome**, happened in **2012** are also it's members, which are zoonotic in nature.(Rabaan et al., 2020) These three are (+)-sense, single stranded enveloped RNA viruses.(Wu et al., 2020) Genome sequence analysis has shown that SARS-CoV-2 belongs to the "Betacoronavirus" genus of the "Nidovirales" order, which includes SARS-CoV, and MERS-CoV (Petrosillo et al., 2020; Rabaan et al., 2020) & accumulating evidence based on genomic analysis suggests that SARS-CoV-2 shares with SARS-CoV the same human cell receptor, the angiotensin-converting enzyme 2 (ACE2), while MERS-CoV uses dipeptidyl peptidase 4 (DPP4) to enter host cells. (Petrosillo et al., 2020)

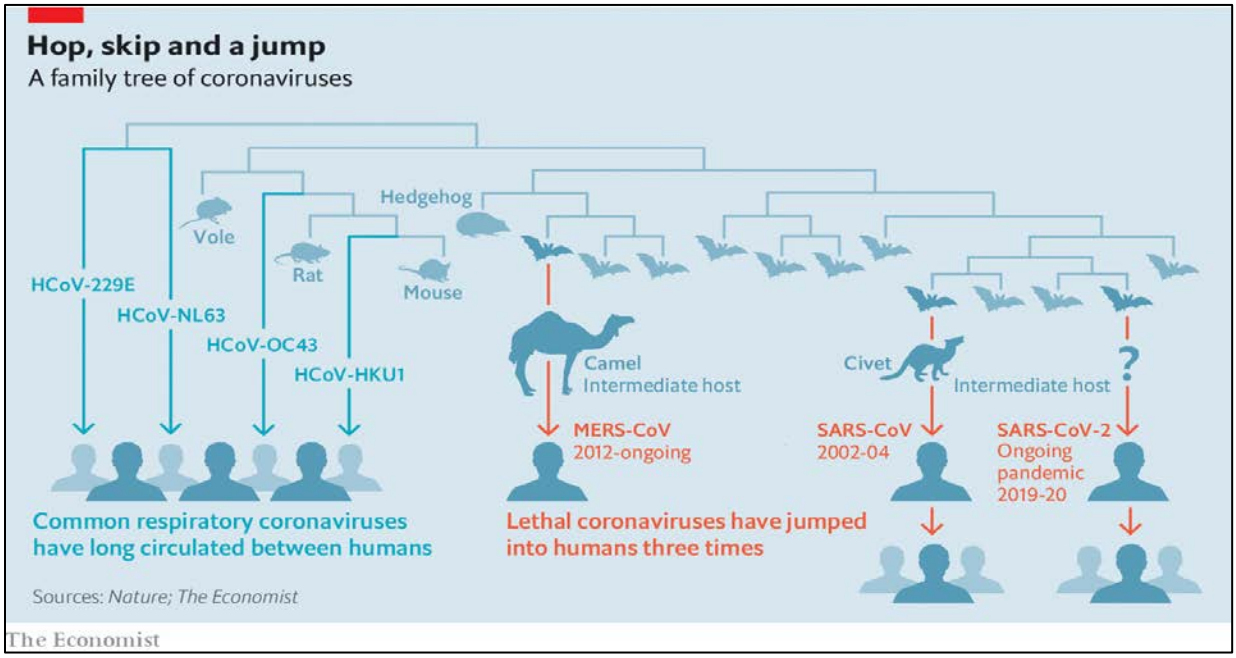

Figure 8: The Family Tree/Lineage of the Corona Viruses which Infect Humans

Picture Courtesy: https://www.economist.com/science-and-technology/2020/05/02/the-pieces-of-the-puzzle-of-covid-19s-origin-are-coming-to-light

All the three viruses have been mainly originated from bats, intermediate hosting by camels &civet cats, that changed their characteristics, and then spread via direct and indirect transmission in humans.(Wu et al., 2020; Zheng, 2020) The reproductive number (R_0) of COVID-19 is estimated by the **World Health Organization** (WHO) to range between 2 and 2.5, which is higher than that for SARS (1.7-1.9) and MERS (<1), suggesting that SARS-CoV-2 has a higher pandemic potential. But, some studies show that the R_0 of COVID-19 can be as high as 3.(Wu et al., 2020; Petrosillo et al., 2020; Balkhair, 2020) The major clinical manifestations, for this family are cited to be fever, chills, cough, shortness of breath, generalized myalgia, malaise, drowsiness, diarrhoea, confusion, dyspnea and pneumonia.(Zheng, 2020; Wu et al., 2020) As we know, research & development for possible vaccines, therapeutics and treatment are on their full swing for this family, but work in progress in going on slowly and steadily.(Balkhair, 2020) So, for the time being, non-pharmaceutical interventions (NPI), such as social distancing, good personal hygiene, use of disinfectants & many more, can slow down the rate of transmission.(Balkhair, 2020; Wu et al., 2020)

Figure 9: Safety Measures Against COVID-19 Picture Courtesy: https://myrepublica.nagariknetwork.com/

COVID-19 seems not to be very different from SARS & MERS. As it generally has a less severe clinical picture, and thus it can spread in the community more easily than MERS and SARS, which have frequently been reported in the nosocomial setting. The lessons learned from SARS and MERS might have contributed to the emergence of more efficient preventive measures in healthcare settings.

Conclusion

So, we are at the end of our Article. At last, we all want to keep in mind that, Viral infections are the most frequent infectious diseases, which can trigger biological, clinical and socio-economic problems worldwide. It can be established that throughout time, many infectious diseases have become widespread due to the mere lack of sanitation and crowded environment. Thus, they have the power to escalate to a stage of outbreak/epidemic/pandemic and thus, shook the world to their senses. For this, Global health authorities should take immediate measures to prevent such emerging & re-emerging diseases across the globe to minimize the burden locally & globally.

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MICROSCOPIC MONSTERS THAT STALKED THE ENTIRE WORLD

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Abstract

When a disease occurs in colossal numbers than expected in a community, region or season, it is considered a pandemic. There are many significant pandemics recorded in human history. Pandemic related crisis causes huge negative impacts on health, economy and even national security in the world. The way a pandemic can change the socio-economic pattern of a country is surprisingly depressing. At present, the world is dealing with the COVID-19 pandemic which has already affected millions of people across the globe. Through all these years, various communities have made progress to mitigate the impacts of pandemics. Despite these improvements, significant gaps and challenges exist in global pandemic preparedness. While we cannot foresee when or how the next pandemic will occur or how much destruction it will cause, we can explore ways to sustain it and learn from it. In this article, we explore in detail regarding the impacts of a pandemic on world health and how it has been a major issue of concern since time immemorial. This article also summarises some intricate and detailed information about the Coronavirus and discusses the key features of its causal agent (virus).

Key Words: Global pandemic, Disease, novel Corona virus, RNA, strain

1. *An Introduction to Viral Pandemics*

A pandemic, by definition is regarded as the widespread occurrence of disease caused either by a virus or bacteria, whose outbreak is so colossal that it affects lives globally. Cholera, bubonic plague, small pox and influenza are some examples of pandemics that have taken lives brutally throughout the world. Two major pandemics which have been caused by viral infections are the infamous 1918-1919 “Spanish flu” that killed 20 to 40 million people and HIV/AIDS that killed an estimated 1.5 million people in 2013 alone. Also, the small pox and it’s outbreak across international borders has killed 300-500 million people throughout the history. Hence, from all these we now have a clear idea as how gruesome a pandemic can be. However, many scientists have understood and discussed the difference between a pandemic and an epidemic. According to the WHO, a pandemic refers to the worldwide spread of a disease, i.e. something that affects lives throughout the globe. On the other hand, an epidemic remains restricted to one city, region or country. A pandemic can be more lethal than an epidemic as it affects a higher number of people than the latter. It can also lead to more social disruption, loss of economy, and general hardship on a wider scale. If due to rapid transmission, an infection becomes widespread in several countries simultaneously, it may turn into a pandemic. (*Felman, A. et. al., 2020*) Viral pandemic mainly occurs when a new virus strain or

subtype easily transmits between humans, thus spreading rapidly. For example, seasonal flu is a kind of disease that would generally occur as a result of subtypes of a virus that is already circulating among people. Novel subtypes, on the other hand, generally cause pandemics. These subtypes would not have circulated previously among humans.

Speaking of novel subtypes or strains, we are all aware of the ongoing COVID-19 pandemic. It first appeared among the people of Wuhan, China in the month of December, 2019. Since then, it has continued spreading its brutality all over the globe. It is called Covid-19 because it is the shortened form of "Corona virus disease of 2019." The WHO declared this disease a pandemic in March, 2020 and by the end of that month, the world saw more than a half million people infected and nearly 30,000 deaths due to this terrible disease called Corona. Because of the newness of this virus, no one is immune to Covid-19 because no one had Covid-19 until 2019. It's transmission from one person to another started occurring so rapidly that governments had to put populations under strict lockdown and this situation is still ongoing in many of the countries across the world. This pandemic, like any other pandemics, started spreading like a wildfire. As a bitter yet obvious consequence to that, people in many countries have lost their employment and even if they are not dying because of corona, they are dying due to poverty. A pandemic can also lead to an increment to the pressure on healthcare systems as these kinds of situations require raising the demand for certain treatments. Such is the case for Covid-19 as well. People with severe Covid-19 symptoms are kept in quarantine under strict vigilance and under intensive care and they require more ventilators, beds and other equipments. As a result, resources may be in short supply for others who need it. (*WHO, 2020*)

2. Some of the most horrifying pandemics

2.1 The Influenza Pandemic of 1918-1919

This pandemic killed 20 to 40 million people. While an influenza pandemic is quite seasonal, it occurs periodically and this one was devastating. 2009 H1N1 influenza was a more recent global pandemic. The causative virus was called novel Influenza A (H1N1). That is because it contained a unique combination of influenza genes not previously identified in animals or people. This pandemic was really severe. (Frost WH Statistics of Influenza morbidity).

2.2 H1N1 Swine Flu Pandemic of 2009-2010

The Swine Flu pandemic that was caused by a new strain of H1N1, originated in Mexico in 2009 before spreading to the rest of the world. Unlike other strains of flu viruses, this strain affected the children and younger people immensely. The virus infected as many as 1.4 billion people across the globe in one year.

2.3 AIDS Pandemic: 1981-Present Day

AIDS became a pandemic in the late 20th century. It has claimed an estimated 35 million lives since the time it was first identified. For a really long time, the disease had no cure but fortunately medication developed in the 1990s and it now allows people to experience a normal life span.

2.4 The Ongoing COVID-19 Pandemic

Ever since the first outbreak of the disease in Wuhan, China on December, 2019, it has spread to every continent except Antarctica. It was declared a pandemic by WHO on 11th March, 2020. More than 12.5 million cases of Covid-19 have been reported till now, resulting

in more than 560,000 deaths; also, more than 6.89 million people have recovered. Some detailed information regarding this particular pandemic is given below-

The ongoing global pandemic of corona virus disease is caused by severe acute respiratory syndromes coronavirus 2 (SARS-CoV-2). It is a positive sense single stranded RNA virus. It is highly contagious in humans. From a taxonomic point of view, SARS- CoV-2 is a strain of severe acute respiratory syndrome related coronavirus. It was found to have close genetic similarity to bat coronavirus, suggesting it emerged from a bat-borne virus. This SARS-CoV-2 infection mainly exhibits respiratory illness ranging from mild disease to severe one and finally death. Some people infected with the virus never develop any symptoms although they are affected. SARS- CoV-2 infected persons who have symptoms can infect others mainly through droplets and close contact. As the disease is highly contagious, SARS-CoV-2 infected persons without symptoms, can also infect others; these persons can be asymptomatic or pre-symptomatic. This virus spreads very easily and rapidly because of its nature. It all comes down to the microscopic structure of the virus, presence of key proteins on its surface and other such factors that can explain as to why it is so much contagious. Spike proteins are present on the surface of the virus with which they bind to the membrane of the human cells that they infect. SARS-CoV-2 has some sort of specific structure that allows it to bind extremely tightly with the receptor cells. Partly, this is due to the fact that the spike protein contains a site that recognizes and becomes activated by an enzyme called furin protease. (which is a host cell enzyme present in human organs). Apart from that, the human cell also contains elements that make it vulnerable to the corona virus. (*Sandoiu, A. et. al., 2020*)

Due to the corona virus pandemic, a major part of the population went on total lockdown as commanded by the higher authorities of the government. The world literally came to a standstill and although countries are collaborating on sourcing medical equipment and developing a vaccine, it may take several months or even years. People are taking precautions and getting more aware about the “best practices during a pandemic”, starting from proper hand washing to social distancing. The guidelines as to how one can protect themselves from the attack of Covid-19 are released in graphic details by WHO and other organizations. They mostly include washing hands with soap and water for at least 20seconds, using alcohol based hand sanitizer which must have at least 60% alcohol. Other than this, one mustn’t touch eyes, mouth and nose with unwashed hands and tissues must be used while coughing or sneezing. Also, one must avoid close contact with sick people and stay at home themselves if they are sick, that is infected.

3. Conclusion

As we all are miserably dealing with the present corona pandemic, hence this discussion mainly centered around it. But, the effect of all viral pandemics is more or less equally destructive in all aspects. For instance, the way a pandemic affects the socio-economic structure around the world is terrible and long lasting. Every day, people are losing jobs and income, with no way of knowing when normality will return. Moreover, it will increase poverty by a large scale and pave its way to create inequality around the globe. The best everyone can do in these circumstances is to protect themselves and hope that the government works for the betterment of the condition. The push for the human race to survive is the main concern of everyone during all pandemics, and so it is right now, as the whole world is dealing with the deadly trap of coronavirus.

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Viral pandemics: A bane for mankind.

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Abstract:

Infectious diseases remain a significant cause of human and animal morbidity and mortality, leading to exponential expenditure on healthcare in India and the rest of the world. The Viral pathogens are known to cause outbreaks foreshadowing a global epidemic or pandemic. Currently, the novel Coronavirus is one of the viral pathogens that is currently causing the global pandemic, “COVID-19”. Inevitably new human viruses will continue to emerge, mainly from other mammals and bird reservoirs, for the foreseeable future. Diversity in biological, socio-cultural and ecological factors, together with novel aspects of human-animal interphase, in ever changing synced coaction, only enhances the challenges analogous with the emergence of infectious diseases. The important challenges faced in the control and prevention of emerging and re-emerging of infectious diseases, range from understanding the impact of factors that are necessary for the emergence, to development of strengthened surveillance systems that can somewhat alleviate human sufferings and deaths.

Keywords: Viral pathogens, global pandemics, Novel Coronavirus, RNA viruses, Zoonotic transmission.

1. Introduction:

There are about 10 million individual viruses that inhabit our planet, infiltrating every aspect of our natural world. These infectious pathogens can indistinguishably blend into our surroundings, from simmering in seawater, drifting through the atmosphere, to lurking in miniscule motes of soil. For them replication is largely possible with the help of a living host, and are capable of hijacking organisms from every branch of the tree of life, also seizing a multitude of human cells along the way (WU, 2020). Amongst the colossal number of virus species, there are about 250 species that are known to be able to infect humans. The first of these to be discovered was yellow fever virus in 1901, while an average of three to four new species are found every year (Woolhouse et al., 2012). Receptors, the host molecules that viruses glom on to, tend to be highly wavering from one species to the next. For a virus that can accomplish "zoonosis"- a transmissible disease that infects people through an animal, the key property is that, it can, with a trifling number of significant evolutionary steps, acclimatize itself to use the human version of that receptor.

2. Transmission of the infectious viral agents:

Emerging infections that loom in foreseeable future, at the elemental level can be defined as diseases, whose prevalence has been found to either increase within the recent decades or which threatens to increase in the future. Such emergences often escalate and disperse pathogens in newer, priorly unaffected areas, and bring about unique patterns of distribution of viral diseases (Mourya et al., 2019). Mammals and birds individually host about 1.7 million undiscovered types of viruses—a number that has largely influenced scientists around the world for surveying Earth's wildlife to envision the next pandemic humans are going to encounter and take necessary steps (WU, 2020). The current pandemic caused by the novel coronavirus has also been transmitted by zoonosis (Madhav et al., 2017). Gaining entry to a new host's cells, which houses the molecular machinery that these viral pathogens need to replicate, is supposedly one of the most challenging aspects of transmission for a virus. This process typically involves a virus latching on to a molecule located at the exterior of a human cell—in more basic terms, a bit like a key clicking into a lock. The better the fit, the more likely the pathogen can access the cell's interior.

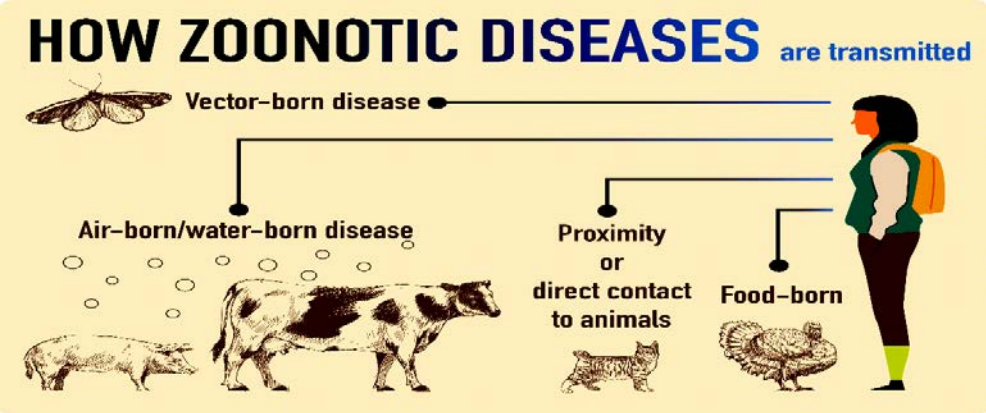

FIG1: Zoonotic diseases and their mechanisms of transmission (picture courtesy: https://blogs.egu.eu/divisions/cl/2020/03/16/corona/).

For any given host, there's a very insignificant number of pathogens that can break into its cells this way. Most of the viruses we encounter, ricochet off our cells, eventually exiting our bodies as harmless visitors. Human viruses can be broadly classified into two categories-RNA and DNA viruses. Viruses that has RNA genomes rather than DNA, along with substantial genetic flexibility are well-suited to cross the species divide. Compared to viruses and cells that rely on DNA; RNA viruses tend to be sloppy when copying over their genetic code, causing rewriting and introducing mutations at a high rate. This error-prone process creates an immense amount of diversity into populations of RNA viruses, accustoming them to new environments—including new host species—at a rapid pace. Of the pathogens that have infected the human population in recent decades, majority have been RNA viruses, including but not limited to Ebola, SARS, MERS, Zika, several influenza viruses, and SARS-CoV-2 (Madhav et al., 2017).

Some viruses use a second method, a bit like primitive sexual reproduction, that can change their genetic code. When two genetically dissimilar viruses infect the same cell, they may swap segments of their genomes with each other as they replicate, yielding hybrid viruses that differ from both their "parents." Flu viruses, which rely on RNA, are among those that both, mutate independently and frequently mingle their genomes—traits that largely formed a contributing factor in helping influenza shuttle back and forth between an entire menagerie of wild and domestic species, including pigs, whales, horses, seals, several types of birds, and, of course, humans. This largely is the underlying cause for the new strains of the influenza virus to be produced, with the epidemic/pandemic striking back after every few years.

3. Pandemics – Types, causes and impacts:

Evidence suggests increased global travel and integration, urbanization, changes in land use, and greater exploitation of the natural environment increased the likelihood of pandemics over the past century. Pandemic risk is driven by the combination of effects consisting of spark risk (where a pandemic is likely to arise) and spread risk (how likely it is to diffuse broadly through human populations). Probabilistic modelling and analytical tools such as exceedance probability (EP) curves are valuable for assessing pandemic risk and estimating the potential burden of pandemics (Madhav et al., 2017). These severe pandemics can cause economic damage through multiple channels, beginning with short-term fiscal shocks continuing till long-term negative shocks to economic growth. Individual behavioural changes, such as fear-induced aversion to workplaces and other public gathering places, are a primary cause of negative shocks to economic growth during pandemics. Some pandemic mitigation measures can cause significant social and economic disruption, bringing life to a standstill.

One must distinguish between several broad categories of pandemic threats. At one extreme are pathogens that have high potential to cause truly global, severe pandemics. This group includes pandemic influenza viruses and COVID-19. These pathogens efficiently transmit between humans, facilitate the undetected movement of infected persons due to long asymptomatic infectious periods, and have symptomatic/asymptomatic profiles that present challenges for differential diagnosis (particularly in the early periods of infection). A second group of pathogens presents a milder global threat. These agents (for example, Nipah virus, H5N1 and H7N9 influenzas) have not demonstrated sustained human-to-human transmission but exhibits risks of being transmitted more efficiently as a result of mutations and adaptation. A third group of pathogens (for example, Ebola, Marburg, Lassa) has the potential to cause regional or interregional epidemics, but the risk of a truly global pandemic is limited because of the slow pace of transmission and/or high probability of detection and containment.

4. Functioning and threats of the novel Coronavirus:

Presently, the world is facing a confrontation with COVID-19 that has become one of the most severe pandemics to hit the world in the last hundred years. The Coronavirus can be categorized as a medium-sized, enveloped, positive-stranded RNA virus. Its large viral RNA genome encodes for necessary structural proteins that aid in its growth. The characteristic spikes that surround the coronavirus is formed by the spike (S) protein that projects through the viral envelope and promotes receptor binding and fusion with the host cell membrane. The membrane (M) protein on the outer surface of the envelope performs an essential role in viral

assembly. RNA synthesis is regulated by nucleocapsid (N) protein that binds with the RNA genome to form the nucleocapsid. The coronavirus undergoes viral RNA replication in the cytoplasm of its host cell using an RNA polymerase to start gene transcription. The coronavirus is subclassified further into 4 genera (alpha, beta, delta, and gamma) with the alpha and beta genera types identified to cause disease in humans. It enters the host cell through the (S) protein binding to the ACE2 that is found in the lungs and heart, with a high affinity to invade alveolar epithelial cells. Thus, SARS-COV primarily targets epithelial cells of the alveoli (Sanyaolu et al., 2020).

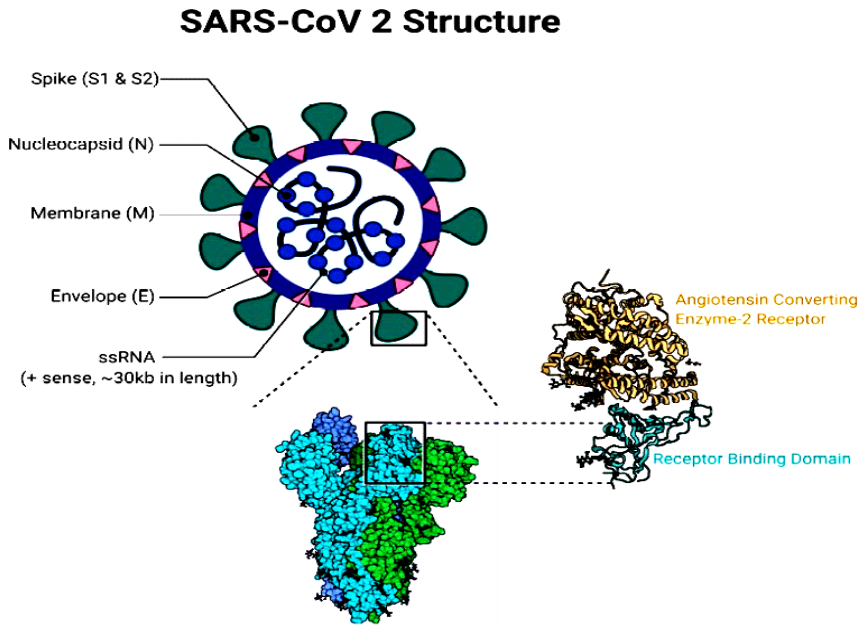

FIG 2: Structure of SARS-CoV 2, (picture courtesy:

https://www.ncbi.nlm.nih.gov/books/NBK554776/figure/article-52171.image.f3/)

Current data demonstrates that coronavirus transmission can spread from both an asymptomatic or symptomatic person, to another person through respiratory droplets that remain in the air, deposits on surfaces, and possible fecal-oral route of transmission. The viability and potent infectious effect can last in aerosols for hours and on surfaces for few days; while it has been detected on plastic and stainless-steel surfaces more than 72-hours later (Sanyaolu et al., 2020). The spread of COVID-19 can be characterized by 3 distinct phases: An initial phase of slow accumulation of new infections that are often undetectable, the second phase of the rapid growth of infection that could lead to death, and eventually a slowdown of transmission due to the gradual depletion of susceptible individuals which leads to the termination of the first epidemic wave of transmissibility.

A 14-day period of monitoring and self-quarantine is the current recommendation after any potential exposure, while predictions cite that 101 out of every 10,000 cases (99th percentile) gradually develops symptoms after the initial 14-days (Sanyaolu et al., 2020). Chances of having critical cases majorly increases with underlying medical conditions such as hypertension, diabetes mellitus, and respiratory illnesses. As the pandemic rages on without any astute medical intervention, a global lockdown has been issued along with quarantine orders and social distancing restrictions to prevent further transmission. The transmission and control effort of COVID-19 is based on available information since the disease outbreak.

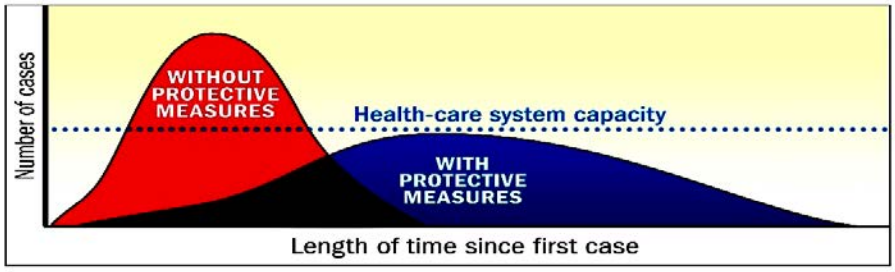

FIG 3: Indicating the positive effects of social distancing. (Picture courtesy: https://www.timeforkids.com/g56/flattening-the-curve-2/).

5. Reduction of pandemic spread:

Once a pandemic has begun in earnest, public health efforts largely focus on minimizing its spread. Reduction in the number of total people who are infected, thus mitigating the indirect health and economic effects can be achieved by limiting the spread of a pandemic. Strategies to minimize pandemic spread includes the following:

- Curtailing interactions between infected and uninfected populations: largely through patient isolation, quarantine, social distancing practices etc.
- Reduction in the potency of infectiousness of symptomatic patients: through antiviral and antibiotic treatment and infection control practices.
- Reducing susceptibility of uninfected individuals: for example, through vaccines.

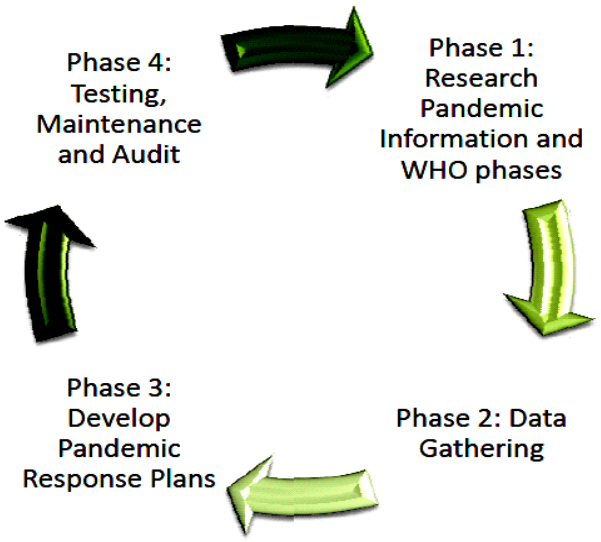

FIG 4: Key elements of the Pandemic preparedness planning cycle. (Picture courtesy: https://www.business-continuity-plan.com/Pandemic_Disaster_Plan.php)

The pandemic period should be preceded by plans for implementing the measures and should be developed and tested through simulation exercises. Patient isolation, quarantine, social distancing practices, educational institution closures, use of personal protective equipment and travel restrictions forms the crux of measures for curtailing interactions between infected and uninfected populations (Madhav et al., 2017). During a pandemic, health authorities work to reduce the severity of illness through patient care and treatment, can help decrease the likelihood of severe outcomes such as hospitalizations and deaths. Treatments may range from nonspecific, supportive care to disease specific drugs. A strong supportive care during an epidemic or pandemic can cause mortality rates to descend by alleviating the symptoms of disease.

6. Conclusion:

The world has become a global village, interconnecting lives and remote places from all around. The boon of emerging technologies and easier mobilities, simultaneously comes with the bane of significant acceleration in large scale spreading of the pandemics, giving rise to a need for strengthening disease surveillance in the world, focusing on the epidemiology and disease burden. There is also a pressing need to gain detailed insights into disease biomics, including vector biology and environmental factors influencing the diseases. Strengthening of emergency preparedness and response for these diseases by focusing on 'one health' approach is need of the hour.

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The Crown-like tiny particles and the Pandemic

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Abstract:

A crown-like tiny particle about 20nm in diameter called a pandemic. Starting from our ancestors until today's generation "Pandemic" is found to be a very familiar word to us. How can such a small particle bring such a huge pandemic? How today's civilization and technology is failing in front of it? And why Viral Pandemic is being a serious concern even in today's generation?

Keywords: *Zoonosis, Fomite, T-cells*

1. Introduction to Pandemic:

Pandemic, it is an epidemic of infectious diseases that have spread across a large region or worldwide affecting an enormous number of people throughout human history. There have been several pandemics such as Black Death, influenza, tuberculosis.

1.1. History of Pandemics:

In our history, the earliest pandemics known to be the 430 BC Athens. In 1350, Black Death is known to be the most devastating pandemic inhuman history. The Black Death was responsible for killing one-third of the world population. This one was the second large outbreak of the bubonic plague.

The great plague of London caused the death of 20% of London's population in 1665. The first Cholera pandemic originated in Russia in 1817. Pandemic flu is called the most significant civil emergency risk on the national risk register of civil emergencies in 2013. COVID-19, on March 11th, 2020, the World Health Organization announced that the COVID-19 officially a Pandemic, which has caused misbalance in everyone's life even in this advanced field of medicine and technology (History Pandemics that changed history, 2020).

1.2. Pandemic Situations:

No one is safe until everyone is safe. A pandemic situation arises when the infectious disease does have the ability to spread at a high rate, it is unstoppable, and it transmits through the contaminated air, water, fomite or even little contact to the infectious person.

The main cause for this unstoppable infection is maybe because of the silent spreaders. There are silent spreaders which spread the disease unknowingly and increase the infection in a wide range within a few minutes.

These silent spreaders can be divided into three categories:

1. Asymptomatic

2. Pre-symptomatic

3. Mildly symptomatic

An asymptomatic person carries the active virus in their body but never develop any symptoms. Several research publications have demonstrated like ‘annals of internal medicine’ have said that after infection, symptoms might not develop for even weeks and the time between catching the virus and showing symptoms is called the pre-symptomatic. And mildly symptomatic people feel a little unwell from a viral infection like COVID-19 infection but continued to come in close contact with others. These three kinds of vectors do the viral transmission unknowingly between humans and then cause the viral epidemic which leads to the pandemic.

These infected people may go to different places, during an even small conversation can spread the disease from an infected to a healthy person. Sneeze or cough of an infected person may contain 200 millions of droplets and a single droplet may contain about 3500 viruses and these droplets somehow come in contact to the healthy person via shaking hands, holding any contaminated object or any fomite. Then the pathogenic virus somehow enters into another healthy host and hijacks the host (npr What we know about the silent spreaders of COVID-19, 2020).

2. Viral Pandemic is a Concern:

Proper medicine for the treatment of an infectious viral disease is still on the waiting list even in today’s generation with high technology.

“Science is not developing is a wrong thought”- Peter C. Doherty, Australian scientist.

The virus acts upon our T-cells which is the main producer of antibodies in our body. These antibodies help to identify foreign particles. Some viruses are also known to us already. But still, the medicines are not developed yet.

Viruses replicate inside a human cell, they cannot live outside the human body. The virus inserts its genome and the human machinery starts to code the viral genes instead of the human gene

and eventually numerous viral progenies produced within a few minutes. There are many viruses whose strains are new and no medicines are developed yet and it is new to our immune system as well. Failure in recognition by our immune system may cause the virus fatal and increases its ability to produce progeny by simple replication or via reverse transcription in some viruses.

3. But, still why Pandemic is so dangerous?

There are many antiviral drugs and, in case of scheduled vaccine production, it takes 4 phases to complete: preclinical, phase-I(applied to one individual), phase-II(applied to more than one individual) Phase-III(applied to a group of individuals)and then the last approval phase.Passing all these phases and to come out with a perfect result takes a longer period and it is a very slow process.

The mutation is also another factor which occurs at a high rate in viruses so even if we try to identify the virus genome (to produce the drugs and vaccines) we may take a lot of time because of its high mutation rate.

Due to all these factors, the production of proper vaccine or drugs takes a long time, sometimes more than a year. And during the absence of the medicines and proper nursing, spreading of the disease at a high rate leads to an epidemic which may further lead to a Pandemic which is a threat to our human race. And that is why it is considered to be dangerous (Drugs.com Why don't antibiotics kill viruses, 2019).

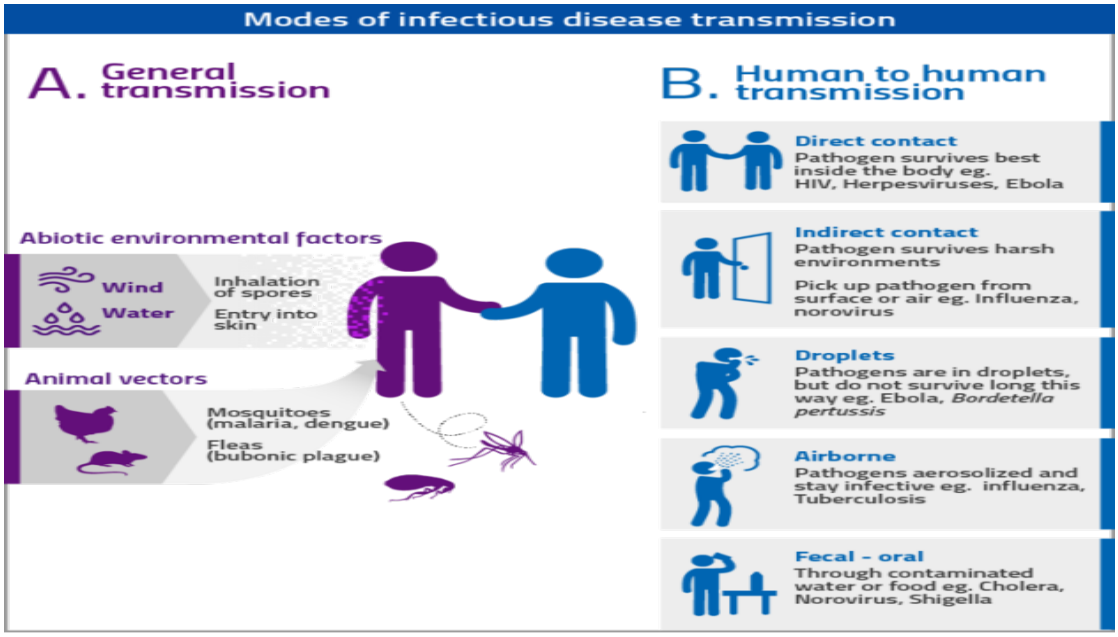

Fig: Mode of infectious disease transmission. Picture Courtesy: www.i.pinimg.com

4. Source of Infectious Viruses:

Most researchers said that viral diseases are mostly zoonotic.This process is called “zoonosis”. Other sources are like contaminated air, water, food, body contact or contact with any contaminated surface or fomite. Infectious organism like bacteria or viruses cannot be seen using your naked eye so it is easier for them to get transmitted easily (Healthline Zoonosis, 2017).

5. Preventions of Pandemics:

The first step we can take to prevent such deadly pandemics is to break the transmission chain. This can be done in very easy steps like wearing masks in any public places, reducing the contact between individuals, maintaining social distance, being hygienic, sanitizing the outside objects when brought inside like vegetables, grocery items, other items. Touching a fomite contaminated with the virus and then touching their mouth, nose or eyes, according to the Centers for Disease Control and Prevention can spread the disease easily.

Maintaining social distance with each other is vital and mainly staying at home is crucial.The crowded places are most affecting places which cause the spreading of the disease more suddenly. If we can somehow disconnect this chain of transmission then the whole pandemic can be stopped.

6. Effects of Pandemic:

Due to this Pandemic, the whole world is now under lockdown. Pandemic affects mostly those people badly whose everyday meal depends on their daily work. The government should take care of these people and we must do what we can as an individual.

Pandemic has imbalanced everybody's daily life. All the institutes are been closed, restaurants and every public place are closed. The streets are empty. A pandemic may have stopped the socialization, may have called a lockdown but on the other hand, it also gives us self-development time, time for ourselves out of the busy life. Due to this Pandemic, world pollution record has also dropped down. Pandemic might be stressing at some point but on the other hand, it has also provided some good effects as well.

According to the Theory of Charles Darwin “Survival of the fittest”, we must change along with the changes in the situation.

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Tracing the ‘enemy unknown’ – a walk through the pages of TIME

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Abstract

Throughout history,the microorganisms have played an important role in the biosphere of the Earth. Despite their origin being quite unknown, microorganisms had a wide impact in every era of history. The chief among them were the Viruses,which caused a lot of destruction in the life of all living creatures,especially humankind.

Its very hard to believethatsomething so tiny, can destroy so manybut evidently, it’s all true. Still, for a long time,scientists couldn’t figure out what led to the outbreaks of these so called ‘pandemics’ and the cause of their widespread.

In the medieval ages, when people didn’t know much about scientific thinking and deductive reasoning, ‘pandemics’ were thought to be the scourges by heaven to punish the ill acts of humankind, but with the evolution of ‘way of thinking’ and the discoveries of scientific tools like microscopes and vaccines, these superstitions started to fade away and gave people a new concept about the ‘Microverse’, where at an extremely small scale, a large number of different microorganisms reside.

For ease of reading, this article is divided into several sections which briefly describe almost all effects of viral pandemics throughout timeline. A small part of detailed recorded history is also provided here along with a brief note on the possible future events that may occur due to the recent re- emergence of viral pandemics.

Keywords: *influenza, history, immunity, pandemic, virus.*

1. WHAT IS A PANDEMIC and WHY THE TERM IS SO IMPORTANT?

A pandemic is a disease that can spread from person to person affecting many individuals, all at the same time, while the location of the disease is not permanently prevalent. Its quite like an epidemic but much larger in scale.**(WHO Bulletin,2020)**

Although, pandemics can be caused by any microorganisms but the ones which are caused due to viral infections, are known as viral pandemics. Till now, among all the pandemics, the viral pandemics are thought to be the most lethal and deadliest of all that there is.

2. An outbreak which started the whole concept – The First cases

In light of, the recent catastrophic events caused by the new virus: SARS -COV-2, the search for the first cases for something like this type of viral outbreak has been amongst Google's top searches. However, this type of outbreak is not as recent as it seems. Tracking back to the 430 BCE, the first cases of this kind of pandemic was found to be recorded in the library of Athens. They called it'The plague of Athens' **(WatchMojo.com, 2015).** During the Peloponnesian war this plague took out lives of one hundred thousand people - the 25 percent of the entire Athenian population. It is so ancient, that it was very hard to track down. Luckily, the Athenian general and historian – Thucydides, recorded with his own eye and witnessed the plague and its symptoms. It is believed that the plague of Athens was caused by not only one but by viruses of multiple infectious diseases like influenza, typhoid, bubonic plague (Black Death), smallpox, and measles. Before that event, which continued for almost 3 years, there were epidemics but not something such devastating as this one.

3. A brief look, through History's Pages - Viral pandemic outbreaks throughout the ages

After that dark phase in the timeline, throughout the ages, the world has seen various viral pandemics, several times. Some has affected less, while others have wiped out a wide percentage of population of the whole world.

After the first pandemic occurrence in Athens, the Antonine plague or the plague of Galen (165-180 CE) ravaged the Roman Empire, killing 60 million people including Lucius Verus, a Roman emperor. The empire was again hit with another massive plague called Plague of Cyprian which possibly containeda strain of the Ebola virus (in 249 CE).

The Plague of Justinian and the Russian plague, though occurring in separate eras, killed almost one third of the total population of the affected area.

In the ancient ages, Smallpox, a disease caused by the Variola virus is believed to have decimated the Aztec and Inka civilizations. **(Weird History, 2020)**

The pandemic known as the Spanish flu started in 1918 and infected one third of the entire world's population. It was later identified that a typical H1N1 (Influenza A) virus caused the disease. However the name itself is a hoax, as the disease was not originated in Spain.

The Swine flu pandemic lasted from 2009 - 2010 and has killed two hundred thousand people worldwide. **(WHO Bulletin, 2009)**

The 2014 Ebola outbreak, originating in westAfrica killed nearly eleven thousand peoplebefore vanishing off in March 2016.

Now, in 2019 – 2020 we are facing another major viral pandemic which is decimating people worldwide at an immense rate on a daily basis.

All this makes it clear how incredibly vulnerable we humans are to typical virus strains.

4. SORTING PROCESS OF A PANDEMIC - by World Health Organization

The WHO, calls an outbreak as a pandemic only after being certain of several steps.

First, it is seen, the wide spread of the area of the affected population. Then the nature of the virus is characterized. Thirdly, after all this the way of spread is seen. At last, the mortality and the morbidity of the virus is seen before announcing it as a pandemic.**(The Telegraph, 2020)**

5. WHY VIRAL PANDEMICS ARE CONSIDERED TO BE THE DEADLIEST

In layman's terms – you can kill something living, but what about something that resides in the state between the Living and the Non-living? Viruses aren't truly alive. They are just bags containing genetic materials, and this is not the only reason behind its lethality and morbidity. **(BBC Contagion, 2018)**

Also, despite of the recent Antiviral therapies (eg – plasma therapy), the frequent mutations in the Genetic material of the viruses (also known as Antigenic Shift & Antigenic Drift) makes it more and more difficult to design a drug to neutralize these viruses. If the virus is airborne or waterborne, a new type of lethality and risks of infection goes high (like the cases of Flu, Ebola and Covid - 19).

Among all this, the only thing that can really help in stopping the spread at first hand, is the natural immunity of every human being. The more strong the immune system (especially the Macrophages), the lesser are the chances of the 'host' getting infected.

The only thing that can boost the immunity is maintaining a balanced diet - rich in minerals, proteins and vitamins, along with a little bit of exercise on a regular basis.

Now, coming to the point of using technology to prevent the widespread of the potential pandemic, scientists and microbiologists are using mathematical stimulations and potential progressions in order to know the paths of how a virus actually spreads. The main objective to them is tracking 'Patient Zero'. Apart from this using of modern computer algorithms, we can also differentiate between normal infected persons and 'Super spreaders' and can inoculate them at first hand. This will avert a huge loss of life and stop the spread of the Contagion. **(BBC Contagion, 2018)**

6. Impact of the pandemic on Socio Cultures of the SOCIETY and its effects on Mental Health

Firstly, the fact that 'It's very lethal and deadly 'creates a mixture of pandemonium, panic and disorder, building confusion and monstrosity amongst a population **(Unseen Enemy, 2017)**. If the pandemic creates a genocide like situation, the social health declines and the results becomes catastrophic. One such example of deadly impact of the pandemic was the Athen's plague of 430 BCE. There was a widespread belief, that 'the plague cannot be survived'made people to start behaving like criminals and mobs. The catastrophe was so overwhelming that men not knowing what will happen next to them became indifferent to every rule of religion or law .Also, in several pandemic movies like World War Z, Contagion 2011, etc. which depicted the reel show of the real life events during the major virus outbreaks, we see, people are looting shops, beating one another and doing whatever they want, outside the law. Even the law wears out as the ones guarding the law, themselves become agents of chaos.

This is the very reason, during this recent viral pandemic, why psychologists are suggesting to keep everyone's minds straight along with maintaining the immunity. Mental immunity is also a part of the immunity of a human system. After all,mind is the key to all the activities of a human body.

So, practicing yoga, watching good movies, reading motivational quotes, spending a quality time with family, keeps the minds sane in this pandemonium.

Since time immemorial, the viruses, in the form of pandemics has wiped out human populations, but the world is changing and its in order to survive the upcoming pandemics we have to change a part of our own. Many important personnel like Bill Gates, from time to time, has warned us about these tiny micro organisms –as the most lethal enemy to human beings. Although, as per as the recent news suggests, theHoly Grail or the Universal flu vaccineis almost ready but still we need to be very careful. It's high time that we stop underestimating these 'tiny enemies' or else when the whole human race will be busy fighting wars with their missiles, 'the tinies' will slowly sneak into the body of each and every human being. Survival is the key to ensure the

continuation of our species. Sure‘Life’ has many flaws but its has its own goodness too. So finally, when it all comes down to ‘whatever it takes’, we must remember the great words of Da Vinci - ‘Knowing is not enough, we must apply. Being willing is not enough, we must do”. By following this simple yet noteworthy line we can ensure us – A better future, a new tomorrow.

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