

## COVID - 19

**ORIGIN OF PANDEMICS****\*Gouri Rao Passi**

**Abstract:** *The incidence of infectious disease outbreaks is increasing over time. This article presents an overview of some major pandemics. The majority of them are zoonoses and the causes underlying spillovers to humans are analysed. Degradation of wild life habitats, intensive animal husbandry and changing land use are some important causes. The concept of "One Health" is highlighted.*

**Keywords:** *Pandemics, Wild life, One health.*

Currently, the world is in the throes of a pandemic of unprecedented magnitude. Looking back sometimes not only clarifies the future and also helps us to look forward with confidence into the future.

History books abound with tales of pandemics. A prominent story is that of the Black Death. In October 1340 AD, twelve trading ships from Central Asia, weighed anchor in the Sicilian port of Messina. Port authorities panicked when they found most of the sailors on board dead and the rest afflicted by a terrifying new disease. They had nodules breaking out using blood and pus. Though the ships were ordered to summarily leave, it was too late. The infection had set foot in Europe and in five years a third of Europe's population was wiped out.

This was the bubonic plague, caused by *Yersinia pestis*. Its natural reservoir is the rat but other animals like dogs, cats and camels can also be infected. The vector which transmits it from rat to rat is the flea. Poor sanitary conditions and congested surroundings set the stage for spillover to humans. On a positive note, the plague pandemics led to the birth of widespread public health measures and the first example of quarantine.<sup>1</sup>

An important question haunts mankind today. Are pandemics just random events or is the incidence of

novel infectious diseases burgeoning over time? Jones et al., analyzed a database of 335 infectious disease outbreaks between 1940 and 2004. They found that outbreaks have risen significantly over time after taking care of reporting bias. Importantly, 60.3% are zoonoses and the vast majority (71.8%) originated in wildlife. They also identified certain global 'hotspots' where they are most likely to begin.<sup>2</sup>

A careful analysis of the influenza epidemics sets the stage for a deeper understanding of why diseases sometimes go out of control. In the last 100 years there have been 4 major pandemics in humans - "Spanish" influenza, H1N1 (1918), "Asian" influenza, H2N2 (1957), "Hong Kong" influenza, H3N2 (1968) and Swine flu Mexico/USA, H1N1 (2009). The deadliest was the Spanish flu which killed 40 million people and infected a third of the world's population between 1918-1919.<sup>3</sup> Genetic testing and phylogenetic analysis of the influenza viruses from the fixed and frozen lung tissue of the 1918 epidemic victims have revealed that it originated from avian influenza viruses.

Repeated investigations have shown that the natural reservoir of influenza viruses are wild water fowls. But these viruses regularly undergo antigenic drift and shift. The drift is due to mutations in the single stranded RNA of the virus. Because the RNA polymerase of these viruses lacks proof reading capacity, all RNA viruses are prone to multiplicative errors. The antigenic drift helps the virus evade host immunity and is responsible for annual outbreaks. However, pandemics occur due to antigenic shifts. The influenza virus has two viral proteins, namely hemagglutinin (HA) and neuraminidase (NA) which get attached to the sialic acid on the human epithelial cells glycoprotein. They have alpha-2,6 residues while birds have alpha-2,3 residues. Interestingly, pigs have both. As influenza virus has a segmented genome, pigs act as reassortment vessels where genes of avian influenza viruses mix resulting in antigenic shifts and develop capability to infect humans by reassortment.<sup>4</sup>

The innovative influenza virus is relentlessly evolving new strategies to infect humans and the humans are fighting back. In 1997 a global web-based surveillance system called FluNet was established. Data of the various influenza

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subtypes isolated is continually entered here by various countries. According to data collected, vaccines effective against the predicted strains are annually manufactured just before the flu season. It also predicted pandemics such as the 2009 H1N1 outbreak which was rapidly evaluated and contained after just a few cases were detected in Mexico and USA.

In the mid 1990's, investigations into a mysterious illness which killed horses and their caretakers in Australia identified a new virus called the Hendra virus (HeV).<sup>5</sup> A serological study in horses failed to show any significant antibodies implying that they were not the primary reservoirs. A careful study of 46 animal species finally clarified that fruit bats were the reservoirs.<sup>6</sup>

When the virus spreads to horses, they not only acted as amplifying agents but further spread it to humans. Since then bats have been repeatedly identified as the reservoir for a series of zoonoses including the Nipah virus, Ebola, SARS-CoV-1 and now the SARS-CoV-2 (COVID-19).<sup>7,8</sup> The extraordinary characteristics of bats need detailing. Bats form the largest aggregation of mammals on the planet around up to a million members. They are greatly vilified in common folklore but vital to maintaining nature's balance. They control insect populations, reseed cut forests, pollinate plants and scatter nutritious guano to enrich the soil. Less known fact is that they act as reservoirs for more than 200 viruses.<sup>9</sup>

Their large breeding grounds, long life spans and ability to fly long distances all contribute to harbouring and spreading viruses. There is intense research into why bats are such rich reservoirs of viruses. Delay in recruitment of B and T lymphocytes suggests that the immune system in bats has evolved to favour incomplete viral clearance to evade immune mediated morbidity and mortality.<sup>10</sup>

Bats played a crucial role in the occurrence of the Nipah virus epidemic in Malaysia in September 1998. It began as an unexplained acute febrile encephalitis in pig farmers of Malaysia with a mortality rate of 40%. But a zoonosis was suspected in view of the preceding epidemic of barking cough and encephalitis in pigs in the same area. Virus isolation in the CSF of patients and fruit bats in nearby orchards and forests helped to piece together the parts of the puzzle.<sup>11</sup> It is edifying to note that the story started much earlier and natural climatic variations, human behaviour, diminishing forest cover, bats, pigs and our intensive animal husbandry practices by human all played a role.

In 1997, there was an unusually hot summer due to the El Nino Southern Oscillation effect. In Indonesia the

traditional slash and burn cultivation triggered huge fires. A severe haze enveloped the entire surrounding areas. Forest trees failed to flower and fruit. Unable to feed in the forests, fruit bats had to look towards greener pastures. They flocked to cultivated fruit orchards often adjacent to pig farms, a burgeoning industry in Malaysia. Pig feed was contaminated with bat excrements. The pigs passed it further to the pig farmers and were an intermediary amplifying host. Pigs exported to Singapore infected abattoir workers sparking risks of global spread.

The epidemic sent shock waves all over South East Asia. Abattoirs in Singapore and Malaysia were shut down. One million pigs were culled in Malaysia and the rest of the pigs were kept under close surveillance. An international team of virologists, epidemiologists and public health experts were instrumental in finally quelling the outbreak.<sup>11</sup>

Later, during outbreaks of Nipah in Bangladesh, by using infrared cameras, it was revealed that bats whose natural habitats had been disturbed had started frequenting forest fringes to eat date palm sap. The contamination of the date palm sap which was collected by the village people to make tari (fermented date palm juice) led to transmission of the virus to humans without any other animal intermediary.<sup>12</sup>

In 2018, prompt action by public health experts and the administration helped to halt the Nipah virus encephalitis in Kozhikode, Kerala after an outbreak involving 18 people with 88.8% mortality. The virus was again isolated in bats of neighbouring forests and transmission occurred probably during cleaning of an unused bat infested well or perhaps, visits to the forest by the locals.<sup>13</sup>

The first pandemic of the 21<sup>st</sup> century was due to SARS- CoV-1 in 2002. The severe acute respiratory syndrome (SARS) infected 8422 patients in 29 countries with 916 deaths.<sup>14</sup> Painstaking epidemiological tracing identified that the first patients were in Guangdong province of China. A single patient who travelled from there to Hong Kong and stayed in a hotel on February 22, 2003 managed to infect 10 more people living in the hotel by aerosols generated. This led to international spread when guests flew back home to Canada, Singapore, Hanoi, etc. The reservoir of the SARS CoV-1 virus was again traced to bats. There was probably an intermediary host, either the Himalayan Palm Civets or raccoon dogs linked to a live animal market in Shenzhen, China.

A closely related outbreak in April 2012 of severe acute respiratory infections in a hospital in Jordan needs

mention. Of the 11 people infected, 8 were health care workers and two of them died. In September 2012 the etiological agent was identified as a novel corona virus and the infection was named the Middle East Respiratory Syndrome (MERS).<sup>15</sup> Subsequently, there were several other small outbreaks in Saudi Arabia as well as certain countries in Europe. In view of the annual Haj pilgrimage attracting 2 million people from 182 countries, there was an urgent evaluation for any pandemic potential. Detailed epidemiological studies to find the animal host identified that 22.8% of dromedary camels tested in Saudi Arabia harboured the virus and camel shepherds were at high risk for infection. Mathematical modelling by Breban, et al showed that the  $R_0$  (the number of secondary cases) was below 1 and hence pandemic potential was low<sup>16</sup> and this has been borne out with time. Between 2012 and December 2019 about 2502 patients have been infected with MERS with a case fatality rate of 34.4%.<sup>17</sup>

The details of the current novel SARS-CoV-2 epidemic is still evolving. Chinese authorities announced a cluster of pneumonia of unknown etiology on 31<sup>st</sup> December 2019 in Wuhan province. Most had an association with a local sea food market which sold wild animals also. By 7<sup>th</sup> January 2020, the infectious agent had been identified as a novel corona virus (2019 nCoV). Human to human transmission was soon confirmed with a  $R_0$  of 2-3.5.<sup>18</sup> Wuhan's gargantuan population, widespread trade and travel connections and presence of asymptomatic carriers are some of the reasons for the consequent malignant global spread. The natural reservoir has again been traced to bats with the possible animal intermediary being the pangolin.<sup>8</sup>

Hidden behind each outbreak is an urgent lesson for mankind. The recurrent patterns are obvious. Most deadly emerging infectious disease outbreaks are zoonotic in origin. New outbreaks are inevitable because of the constant evolution of organisms. Excessive replicative errors in RNA viruses are the reason why they are the commonest novel infections to emerge.<sup>19</sup>

Animals in the wild coexist harmoniously with deadly viruses. The association probably goes back to millions of years. Nuclear gene analysis has dated bats to the Eocene period 50 million years ago. Viruses which evolved with them probably used key cellular receptors some of which have been conserved in later mammals like humans.<sup>20</sup> Hence, it is easy for viruses to cross infect man.

Finally, one needs to ask - why do spillovers occur and why are they increasing over time? There are two parts to the problem - 'the spark' where the spillover starts and the 'spread', determines how it transforms into a pandemic.

The natural habitats of wild animals are shrinking. They are being forced to migrate to newer areas often near human settlements. The reasons are protean with wanton destruction of forests, unprecedented changes in land use, intensified agricultural practices due to an explosive growth in human population and their need are just to name a few.<sup>21</sup> Intensive animal husbandry such as poultry farming and pig farming increase the risk of spillover of new viruses from animals.<sup>22</sup> Yet another hotspot for spillovers include wet markets where animals are slaughtered in unhygienic conditions. Certain diseases like Ebola are linked to hunting and eating of wild meat.<sup>23</sup>

The rapid spread across countries is linked to the large scale movements of people, livestock, food and goods as well as ubiquitous air travel due to tourism in today's world.<sup>24</sup> The human population is predicted to cross 10 billion by 2050. It has increased from 1 billion in the beginning of the 20<sup>th</sup> century to 6 billion by the turn of the century.<sup>2</sup> Urban spaces are overloaded and it takes just a spark to unleash a wildfire.

Cataloguing problems without contemplating solutions is a recipe for disaster. So, what must be done to reduce the risk of further inevitable outbreaks? We need to solve it at many different levels. Public health experts, ecologists, scientists, economists and sociologists and all mankind need to come together.

Short term solutions include monitoring emerging infectious diseases in both wild animals and livestock with systems such as the Global Early Warning System (GLEWS) developed by the Food and Agriculture Organization-World Organisation for Animal Health formerly the Office International des Epizooties (OIE) - World Health Organization (FAO-OIE-WHO), streamlining the animal husbandry industry and wet markets, strengthening core public health services, increasing pandemic preparedness and developing a surge capacity to scale up delivery of health interventions, if required.

Long term solutions include conservation of forests, wild life and other complex ecosystems. The solution lies in the concept of 'One Health'.<sup>25</sup> We need to understand that the health of humans is inextricably linked to that of all other animals, organisms, plants and the entire biosphere. The economy of unjustified overconsumption needs questioning. Each one of us has a role in nurturing the planet.

400 years ago, John Donne rightly said, "No man is an island. Every man is a piece of the continent. So never send to know for whom the bell tolls. It tolls for thee."



## Points to Remember

- *World had constantly faced pandemics, the most prominent being black death caused by bubonic plague in 1340, causing death of one third of European population in a span of five years, which led to the birth of widespread public health measures and the first example of quarantine.*
- *Bats have played a crucial role in the appearance of many virus epidemics involving, Nipah virus, Ebola, SARS-CoV-1 and now the SARS-CoV-2 (COVID-19).*
- *Bats not only play a vital role in maintaining nature's balance, but also act as reservoirs for more than 200 viruses.*
- *Hidden in each outbreak is an urgent lesson for mankind that the natural habitats of wild animals are shrinking. They are being forced to migrate to newer areas often near human settlements.*
- *Long term solutions include conservation of our forests, wild life and other complex ecosystems. The solution lies in the concept of "One Health". We need to understand that the health of humans is inextricably linked to that of all other animals, organisms, plants and the entire biosphere.*

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