“We are standing on the brink of global crisis in infectious diseases. No country is safe from them. No country can any longer afford to ignore their threat.”

- Dr Hiroshi Nakajima, former Director-General of WHO

Each species is a thread in the close-woven fabric of our ecosystem. Whenever we try to pick anything by itself, we find it latched to everything else in the environment. The balance between species occurs either from the coevolution of mutually supportive species or from what Richard Dawkins called the ‘biological arm-race’ between competitive species.

For most of history, humans knew nothing about 99.99 per cent of the organisms on the planet – namely, the microorganisms – bacteria, fungi, archaea, protists and virus. This was not because they were of no concern to us. Indeed, all of us have a microbiome of bacteria (and a much smaller number of viruses, yeasts, and amoebas) that outnumbers the cells of our bodies by a ratio of ten to one. They live and work synergistically to play the key roles including programming our immune system, providing nutrients to our cells and preventing colonization by harmful bacteria and viruses.
As best we know, microorganisms have no consciousness, no aims in life, and no ability to plan ahead. Yet, a microorganism belonging to one species can incorporate genetic codes from a completely different species into its cell and thereby gain new capabilities, such as resistance to antibiotics. Just as microbes keep arranging their old genomes to come up with new ways to overcome our defenses, we humans will have to draw upon everything we’ve inherited or learned – from pre-colonial jungle medicines to genetic engineering – if we are to stay ahead in the evolutionary arms race.

It was only in 1674 that a human eye first saw a microorganism when Anton van Leeuwenhoek took a peek through his homemade microscope and was startled to see an entire world of tiny creatures. During the subsequent 300 years, humans have made the acquaintance of a huge number of microscopic species have managed to defeat most of the deadliest contagious diseases they cause and have harnessed microorganism in the service of medicine and industry.

Louis Pasteur, the father of the science of microbiology and a key figure in the development of vaccines in the 1880s, suggested that humans had the power ‘to make parasitic maladies disappear from the face of the globe’. Yet, since then hundreds of millions of people have died of infectious diseases – TB, malaria, influenza, AIDS, dengue, smallpox, cholera, plague, and scores of others.

Throughout world history, a variety of viruses and bacteria have infected the human population, reaching catastrophic levels within only a short span of time in the form of epidemics and pandemics. As many as 20 major maladies have emerged in novel, more deadly, or drug-resistant forms in the past three decades. Cholera, bubonic plague, smallpox, and influenza pandemics are some of the most brutal killers in human history.

The smallpox pandemic thrived long before the Egyptian pharaohs and continued to kill between 300-500 million people – one-third of those it struck until, after a heroic international vaccination effort, the last human was affected in 1978 and the disease was eradicated in 1980. However, in terms of the number of deaths, the severity of infection, mortality rates and, most importantly, taking into their social, economic and political impacts at least four deadliest pandemics in history deserve mention.

**Influenza Pandemic (viral)**

Spanish Flu (Estimated death toll: 50 to 100 million; Origin: not in Spain but first reported therefrom; Period: 1918 and 1920). Believed to have been caused by H1N1 virus with genes of avian origin, it is the deadliest pandemic in history and triggered a cytokine storm in which younger adults faced higher mortality rates. World War 1, fought between 1914 and 1918, claimed 8.5 million casualties. By comparison, this pandemic killed around 14 million Indians alone.

**Plague Pandemic (bacterial)**

Three of the deadliest pandemics in recorded history were caused by a single bacterium, *Yersinia pestis*. The plague of Justinian arrived in Constantinople, the capital of the Byzantine Empire, in 541 CE. It decimated Constantinople and spread like wildfire across Europe, Asia, North Africa and Arabia killing an estimated 30 to 50 million people, perhaps half of the world’s population. It is known by various terms: Black Death, Black Plague, Great Plague or Great Bubonic Plague (Estimated death toll: around 200 million; Origin: Central Asia).
Since 1918, three influenza pandemics have occurred – in 1957 (Asian Flu, H2N2 Flu), 1968 (Hong Kong Flu, H3N2 Flu) and the most recent one occurred in 2009 (H1N1 Flu) which is estimated to have caused between one lakh and 4 lakh deaths globally in the first year alone. Influenza viruses are highly unpredictable. Considering the probability that another influenza pandemic is inevitable, WHO has released a Global Influenza Strategy for 2019-2030 outlining a framework to work together to prepare for, prevent and control influenza.

Cholera Pandemics (bacterial)
Six cholera pandemics have occurred in the period 1817-1923 (1817-1821, 1829-1832, 1852, 1863, 1881, 1899-1923) with the first pandemic originating in India in 1817. Deaths caused by these six pandemics were as many as 40 million. Cholera pandemic was the first disease for which modern public health surveillance and reporting was carried out in an organized way.

HIV/AIDS Pandemics
First identified in 1981 in Central Africa, the virus quickly progressed to pandemic levels as its spread has proven impossible to halt. Today, it is estimated that nearly 37.9 million people are currently living with the disease, with over 75 million individuals being infected globally by HIV since it was first identified in 1981. Out of 75 million cases, it is estimated by WHO that nearly 32 million people have died from HIV/AIDS since 1981. HIV/AIDS continues to be one of the most serious pandemics in human history as infection rates have remained relatively stable for several decades.

COVID-19 Pandemic (viral)
At present, the planet is under the tight grip of the coronavirus disease COVID-19 Pandemic. Globalization is punishing everybody for somebody else’s unpreparedness. The pandemic has exposed how fragile we are in the face of a globalized health emergency. As on 8 April 2020, confirmed coronavirus infection cases in 206 countries crossed more than 1.4 million as the pandemic spread at a ‘near-exponential’ rate, with a six-week-old baby becoming one of the youngest known victims.

Half of the planet is under some form of lockdown as governments struggle to tame the virus that has killed more than 46 thousand people worldwide. The virus is inflicting at a tremendous speed. Scientists still know too little about the virus and a vaccine is more resistive potential than SARS-CoV, was found to cause MERS (Middle-East Respiratory Syndrome) that spread in 27 countries.

COVID-19 is caused by novel Coronavirus-2019 (2019-nCov). While SARS-CoV primarily affected the lungs, 2019-nCov causes infection in the upper respiratory tract or throat as a result of which the spread of infection becomes easier. Every time a COVID-19 patient coughs or sneezes, the droplets containing the virus are released and the infection spreads.

Research reveals that novel Coronavirus-2019 that emerged in the city of Wuhan, China last year (2019) is the product of natural evolution. Researchers focused on two important features of the spike protein: (1) the Receptor-binding Domain (RBD), a kind of grappling hook that grips onto host cells, and (2) the cleavage site, a molecular can opener that allows the virus to crack open and enter the host cell. Moreover, it was found that the backbone of the virus differed substantially from those of the already known coronaviruses and mostly resembled related viruses found in bats and pangolins. There is no evidence that the virus was made in a laboratory or otherwise engineered.

The stunning discoveries in molecular biology including DNA cloning and the sequence of the human genome, new developments in techniques for human stem cell research, improved sanitation, mosquito control, global vaccination, and modern antibiotics made us believe that we had won the war against microbes. Flush with our early successes against them, we concluded that microbes were no competition for our big human brains. We are indeed wrong.

We still face the tragedy of preventable human illness, some ancient, others new, unpredicted, and even more virulent. Pandemics continue to be tremendous threats to human populations worldwide. As many as 30 new diseases have emerged in the last two decades and now together threaten the health of hundreds of millions of people. For many of these diseases, there is no treatment, cure or vaccine. COVID-19 that makes us helpless is a glaring example.

Largely unnoticed the world is changing. In developing nations, people are hacking their way into previously inaccessible areas, where a menacing menagerie of microbes, especially bacteria and viruses, skulked about, hungry for new warm-blooded hosts. Third world metropolises are growing increasingly crowded, overwhelming sewage and water systems and proving a microbial mixing bowl for the creation of new diseases. Virus transference is happening because of our dystopian relationship with nature.

We are making our food a potent source of disease by pushing every kind of chemicals and toxin into our food. Antibiotics are being shoveled into animals and even crops – not for disease control but to make them grow more, put on weight, so that business profits. As a result, resistance to drugs needed for human survival is on the rise.

After 10 years, in 2012 in Saudi Arabia, a new strain of CoV, Coronaviruses (CoVs) were discovered in 1960s. The common hosts of these viruses are specially camels, pigs and bats. In rare cases, they are zoonotic. However, the lethality of the virus drew our attention when SARS (Severe Acute Respiratory Syndrome) appeared in 2002 in China and spread worldwide within a few months. SARS was quickly contained.
We are growing our food in vertically integrated industrial farms, which is becoming the source of contagion. Origin of swine flu from industrial hog factories in Mexico teaches us that the breaking of boundaries between animal and human habitats will lead to more such outbreaks. Though we don’t know exactly when and where the next pandemic will surface, we know how it will surface. The next pandemic will be a zoonotic disease.

According to a study in Science by Princeton University researchers Andrew Dobson et al., global warming is causing the spread of bacteria, viruses and fungi that cause human diseases into areas that were hostile to them. Dobson opined, “Climate change is disrupting natural ecosystems in a way that is making life better for infectious diseases.”

Microbes that cause human diseases – and the species that carry them – seem to increase their range. The Union of Concerned Scientists wrote: “Climate change affects the occurrence and spread of disease by impacting the population size and range of hosts and pathogens, the length of the transmission season, and the timing and intensity of outbreaks.”

Though no direct link has been established between COVID-19 outbreak and climate change, studies say warming temperature and melting of ice are exposing new viruses to the ecosystem. For instance, researchers recently found 33 viruses trapped in the Tibetan glaciers. Out of these, 28 were completely new to science and all of them had the potential to cause an outbreak. As ice melts, viruses are being released in the air, which would travel through rivers and streams, infecting humans.

The most outstanding feature of life history is the constant domination of microbes as they are capable of developing new strategies every now and then for their own survival. Antimicrobial drugs were once effective weapons in our arsenal to fight microbes. But citing the ‘catastrophic threat’ AMR (Antimicrobial Resistance) microbes, the WHO has warned that it could lead to ‘a return to the pre-antibiotic era’, where curable infections prove to be fatal. Mere paper-cuts can kill and superbugs could easily wipe out humanity.

Indeed, in the continuing epic struggle, we are in the critical stage. Jim Hughes, Ex-Director of the National Center for Infectious Diseases at the Center for Disease Control and Prevention (CDC) in Atlanta aptly said, “The world definitely favours the bugs; microbes have the advantage. There are a lot of them than us. Their generation time is minutes instead of years. They evolve rapidly. And, of course, we aid and abet them in many ways – by travel, commerce, in foodstuffs, transportation of animals, and our abuse and overuse of antibiotics. We’re playing right into their hands.”

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