An epidemiologic transition describes changing patterns of population age distributions, mortality, fertility, life expectancy, and causes of death, was first described by Abdel Omran in 1971. The world has had four transitions of which we are presently in the fourth.

- **The Age of Pestilence and Famine**: Mortality was high and fluctuant, precluding sustained population growth, with low and variable life expectancy vacillating between 20 and 40 years. It was characterised by an increase in infectious diseases, malnutrition and famine, common during the Neolithic age. Before the first transition, the hominid ancestors were hunter-gatherers and foragers, a lifestyle partly enabled by a small and dispersed population. However, unreliable and seasonal food sources put communities at risk for periods of malnutrition and nutritional deficiencies.

- **The Age of Receding Pandemics**: Mortality progressively declined, with the rate of decline accelerating as epidemic peaks decreased in frequency. Average life expectancy increased steadily from about 30 to 50 years. Population growth was sustained and begins to be exponential.

- **The Age of Degenerative and Man-Made Diseases**: Mortality continued to decline and eventually approached stability at a relatively low level. Mortality is increasingly related to degenerative diseases, cardiovascular disease (CVD), cancer, violence, accidents, and substance abuse, some of these due primarily to human behavioural patterns. The average life expectancy at birth rises gradually until it exceeds 50 years. It is during this stage that fertility becomes the crucial factor in population growth.

- **The Age of Delayed Degenerative Diseases, Aging and Emerging Diseases**: Declining age-specific mortality results in a gradual shift of non-communicable burden to older ages, with underlying causes of death showing little change overall. Technological advances in medicine stabilise mortality and the birth rate levels off. Emerging diseases become increasingly lethal due to antibiotic resistance, new pathogens like Ebola or Zika, and mutations that allow old pathogens to overwhelm human immunity. With more frequent travel, globalised trade and greater interconnectedness between countries, infectious disease outbreaks of international concern are becoming as inevitable as they remain unpredictable. In the final phase, disease is largely controlled for those with access to education and health care, but inequalities persist.

**SARS and MERS**: We are in the fourth epidemiologic transition from the turn of the COVID-19 Pandemic and Health System Preparedness: Pathways to Reform

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century. This was first exemplified by the SARS (Severe Acute Respiratory Syndrome) epidemic in 2003. SARS-CoV is an animal virus from an as-yet-uncertain animal reservoir, perhaps bats, that spread to other animals (civet cats) and first infected humans in the Guangdong province of southern China in 2002. The epidemic of SARS affected 26 countries and resulted in more than 8000 cases in 2003. Since then, a small number of cases have occurred as a result of laboratory accidents or, possibly, through animal-to-human transmission.

This was followed by the MERS (Middle East Respiratory Syndrome) in 2012, which was an illness caused by a coronavirus called Middle East Respiratory Syndrome Coronavirus (MERS-CoV). Most MERS patients developed severe respiratory illness with symptoms of fever, cough and shortness of breath. About 2794 people have been infected so far mainly in the Saudi Arabian peninsula and neighbouring areas with a spread to South Korea as well. The case fatality of MERS was 37 per cent.

SARS Co-V2 – COVID-19: Towards the fag end of 2019 a atypical pneumonia of unknown origin in a cluster of patients detected in Wuhan, China was reported to the WHO country office in China on the 31 of December 2019. Reportedly the first patient in the city of Wuhan who had symptoms related to a then unknown coronavirus was on the 8 of December from the seafood market there. The disease quickly spread across in the city of Wuhan and province of Hubei in China prompting authorities to enforce a total lockdown of the province. The disease has since spread to 205 countries and territories with significant mortality.

Spread of COVID-19 Virus: The transmission of SARS-Co-V2 worldwide is best exemplified by the case of Italy. The first case confirmed in Italy was on 31 of January 2020, when two Chinese tourists in Rome tested positive for the virus. One week later an Italian man repatriated back to Italy from the city of Wuhan, China, was hospitalised and confirmed as the third case in Italy. A cluster of cases was later detected, starting with 16 confirmed cases in Lombardy on 21 February and 60 additional cases and the first deaths on 2 February. By the beginning of March, the virus had spread to all regions of Italy. The Lombardy region of Italy was most severely affected partly because tens of thousands of Chinese migrants work in the Italian textile industry, producing fashion items, leather bags and shoes with the brand “Made in Italy”. They worked in conditions where they were cramped closely together, which would facilitate the spread of the virus. The spread was also facilitated by the availability of direct flights from Wuhan to the Lombardy region, given the fact that the virus is asymptomatic for a period of 5-6 days after infection.

Pathogens with a Pandemic Potential

Pathogens that are capable of causing a global catastrophic biological risk (GCBR), which are events in which biological agents - whether naturally emerging or re-emerging, deliberately created and released, or laboratory engineered and escaped - could lead to sudden, extraordinary, widespread disaster beyond the collective capability of national and international governments and the private sector to control. If unchecked, GCBRs would lead to great suffering, loss of life, and sustained damage to national, international relationships, economies, societal stability and global security. The SARS-Co-V2 pandemic has fulfilled all the above criteria of a GCBR and could be called one.

In May 2016 the WHO had listed seven diseases requiring urgent Research and Development, comprising (1) Crimean Congo haemorrhagic fever (2) Filovirus diseases (i.e. EVD & Marburg) (3) Highly pathogenic emerging Coronaviruses relevant to humans (MERS Co-V & SARS) (4) Lassa Fever (5) Nipah (6) Rift Valley Fever, and (7) R&D preparedness for a new disease. Also listed were three further diseases determined to be serious, necessitating further action as soon as possible: chikungunya, severe fever with thrombocytopenia syndrome, and zika.
What are the characteristics of a microbe that determine its GCBR potential?

- **Infectivity**: The capacity of an infectious disease to spread in a host population can be quantified in terms of its basic reproduction number, R0. R0 is defined as the average number of secondary cases generated by a single primary case in a large, previously unexposed host population, and its value tells us a great deal about the epidemiology of a pathogen. R0 = 0 indicates no spread in that population; this value would apply to zoonotic infections that do not spread between humans. R0 in the range 0<R0<1 indicates that chains of transmission are possible but that outbreaks will ultimately be self-limiting. R0>1 indicates that major epidemics can occur or that the disease may become endemic in that host population. A higher value of R0 also indicates that a greater reduction in transmission rates must be achieved to control an epidemic. R0 values have been estimated for more than 60 common human pathogens, including human influenza A virus (R0<2), measles virus (R0<18), and dengue virus (R0<22). For any given infectious disease, R0 can vary between host species and between host populations.

- **Modes of Transmission**: Microbes have varied routes of transmission, ranging from blood and body fluids to vector-borne to faecal-oral to respiratory (airborne and respiratory droplet). While each mode of transmission is capable of causing large outbreaks if sustained human-to-human transmission is possible and left unchecked, certain modes of transmission are more amenable than others to intervention. For example, the transmission of an infectious disease caused by blood and body fluid transmission can be halted with infection control measures such as gloves or gowns. Of the various modes of transmission, the respiratory route is the mechanism most likely to lead to pandemic spread. This is chiefly due to the fact that interventions to interrupt this method of spread are more difficult to implement when the simple and universal act of breathing can spread a pathogen. The prolific spread of influenza, pertussis, measles, and rhinoviruses is testament to this fact.

- **Timing of Transmission**: The onset and duration of the period when a person is contagious during an infection also play a major role in spread. Diseases that are contagious during a late stage of infection, when infected people are very sick and, therefore, have more limited opportunities for spread, may be limited in their spread. On the other hand, diseases that are contagious prior to symptom development, during the incubation period, or when only mild symptoms are present have greater opportunities for spread as infected individuals are able to conduct their activities of daily living with little or no interruption.

- **Host Population Factors and Intrinsic Microbial Pathogenicity Characteristics**: Microbial pathogenicity cannot, in reality, be separated from host characteristics. Disease is a complex interplay between a host immune system and a microbe. For a microbe to cause a GCBR-level pandemic, it will be necessary for a significant proportion of the human population to be immunologically naïve to the agent so that the microbe would have a high number of susceptible humans to infect. Additionally, large quantities of a sufficiently effective countermeasure (vaccine or antimicrobial agent) would not be available.

- **Pandemic potential of Microbes- viruses, bacteria, fungi, prions and protozoa**: Of them, **RNA viruses** are the class of microbes that are most likely to cause a GCBR, though other microbes could evolve or be engineered to cause the same. Given the right context, any microbial organism could evolve or be engineered to be a GCBR. However, the most likely cause of a GCBR presently is a virus, with RNA viruses being the most probable.

- **Historically**, **bacterial infections** like the bubonic plague have had incredible impacts on the human species. However, the development of antibacterial therapies, beginning with the sulfonamides in 1935 and then penicillin in 1942, has severely limited the ability of this class of microbes
to cause a GCBR-level pandemic. In addition, the relatively slower speed of replication and accumulation of mutations also disadvantages this class over viruses. For example, a human infected with the hepatitis C virus (an RNA virus) produces trillions of virions per day, whereas the doubling time of Yersinia pestis, the cause of plague, is 1.25 hours. Fungi are largely thermally restricted, and only limited members of this class of microbes can infect warm-blooded organisms such as mammals.

- The transmission characteristics of prion diseases are such that very extraordinary circumstances, on a par with human cannibalism or massive food contamination, must be present for a GCBR-level risk to be present for humans. Additionally, and almost by definition, such an event would be slow-moving.

- Human protozoal infections: It is hypothesised that half of all humans who have lived died of malaria, which still kills approximately half a million humans annually (World Health Organization 2017). However, the development of antimalarial compounds and vector avoidance strategies has proved successful when they are able to be employed appropriately, and they have relegated malaria to a pathogen whose impact is amenable to control.

Factors Contributing to Pandemic Risk of Viruses

Traditionally, viruses have been ranked at the highest level of pandemic risk, and dedicated preparedness efforts often focus solely on viruses. The high rate of replication of viruses coupled with the inherent potential for mutations in short generation times gives viruses an unrivalled plasticity, allowing for host adaptability, zoonotic spillover, and immune system evasion.

The lack of a broad-spectrum antiviral agent - like ones available for bacterial and even fungal organisms - also confers a special status on viruses. With no off-the-shelf treatment available to contain a viral outbreak, and likely no vaccine, containment efforts, at least in the early stages, will likely need to be made in the absence of a medical countermeasure.

There is a strong consensus that RNA viruses represent a higher pandemic threat than DNA viruses. This assessment is derived from the fact that the stability of RNA as a genomic material is less than that of DNA, giving more genomic pliability to the RNA viruses. The influenza A viruses were widely judged to pose the greatest pandemic risk based on historical outbreaks and viral characteristics. There are several viral groups other than the orthomyxoviruses (which include the H7N9 strain of influenza A) that are spread by respiratory routes, possess RNA genomes, and merit enhanced attention: paramyxoviruses (especially these three genera: respirovirus, henipavirus, and rubulavirus), pneumoviruses, coronaviruses, and picornaviruses (especially these two genera: enterovirus and rhinovirus) all with the innate capacity of a GCBR threat.

The Possible Measures to Prevent a GCBR

- Increasing Specific Diagnoses of Infectious Disease: Tests to identify the viral pathogens are not routinely done in case of viral fevers as the treatment is still symptomatic given the non availability on anti-viral drugs
- Improving Surveillance of human infections with respiratory borne RNA viruses should be a higher priority
- Developing broad spectrum anti-viral drugs
- Investigating the role of monoclonal antibodies and immune-modulators
- Vaccines against RNA respiratory viruses

Economic Loss Secondary to Previous Epidemics

The SARS outbreak in 2003 led to 8000 infections and 800 deaths with a loss to the economy estimated at USD54 billion. The EBOLA outbreak in 2015 led to a cumulative loss of USD 2.2 billion to the countries Guinea, Liberia and Sierra Leone. The global GDP loss due to people infected by COVID-19 currently stands at USD 47.67 billion.
Pandemic Preparedness
The Johns Hopkins Center for Health Security in partnership with the World Economic Forum and the Bill and Melinda Gates Foundation hosted Event 201, a high-level pandemic exercise on 18 October 2019 in New York, NY. The exercise illustrated areas where public/private partnerships will be necessary during the response to a severe pandemic in order to diminish large-scale economic and societal consequences. The participants simulated a model of a pandemic spread due to a coronavirus which they called CAPS.

- The participants from multiple countries made “decisions” based on the spread of a fake coronavirus called CAPS, which turned out to be similar to the SARS-CoV-2 virus causing the current COVID-19 pandemic.
- By the end, CAPS killed 65 million people worldwide as countries argued over scarce vaccines and treatments and dealt with disinformation campaigns amongst other problems.
- The global economy was wrecked as people refused to work or travel, leading to a shutdown of communications, basic sanitation and health care, not to mention the devastation of entire economies dependent on tourism.

The present COVID-19 pandemic will probably not lead to 65 million deaths but in most other aspects we are reliving the simulated model. As per the Global Health Security (GHS) index, that assesses countries’ health security and capabilities across six categories, suggests that ‘no country is fully prepared for epidemics or pandemics, and every country has important gaps to address.’

Containment Strategy in a Pandemic
The objectives of actions to mitigate the impact of the pandemic would need to:

- Protect populations at risk of disease.
- Identify and treat those with disease.
- Decrease the acute burden on healthcare services on other fronts.
- Reduce morbidity and mortality related to the disease.

The proposed strategy geographically divides the outbreak area into ‘containment zone’ and a surrounding ‘buffer zone’. The containment zone would constitute geographical area and population harbouring the ‘index cluster’, where widespread antiviral medications for treatment and prophylaxis, movement restrictions, and non-pharmaceutical interventions (NPIs) would be used to restrict the virus from spreading beyond the zone. NPIs would include: isolation of ill persons, voluntary quarantine of contacts, social distancing measures such as school closures and cancellation of mass gatherings, other measures to minimise person density (e.g. staggered work and market hours), and community wide practice of hand and respiratory hygiene, use of masks, etc. This would reduce the possibility of an uninfected person coming into contact with a person ‘infected by’ and ‘infectious with’ pandemic influenza. The buffer zone would be simultaneously subjected to an intensive active and complete surveillance for possible ‘break-through’ cases, to evaluate whether the containment operation is succeeding. In both zones, emphasis will be placed on containment communications to different stakeholders.

Assessment and Planning for Surge Capacity
Planning for a surge capacity for health care, food and other supplies is not going to be a simple question of low income and high income countries. Pandemic situation may act as a leveller. Even in the richest of economies, most patients needing ventilator would not have access to it. Health care providers would fall sick and die at similar rates, or even higher than those in general public. Immune survivors of initial wave among the health workers may be the only trained personnel left. Going by the experience with SARS, some health workers would not show up for duty.

India is particularly well placed for contact tracing of index cases with a well-oiled machinery of frontline health workers in place, namely ASHAs (Accredited Social Health Activists), JPHNs (Junior Public Health Nurses) and HIs...
(Health Inspectors). They are at the forefront of surveillance for other diseases including polio, tuberculosis and other notifiable diseases. The success of India in contact tracing has largely been through this mechanism which has worked very well for India so far. This is what is different between the surveillance systems of the developed economies like the US, West Germany or the UK where contact tracing has been fraught with difficulties due to the absence of frontline health workers. The developed economies work on a system of surveillance where diseases and outbreaks are notified, pattern of pharmacy prescriptions analysed and pattern of health symptom searches on various search engines like Google analysed. This system has unfortunately not worked for them in the present pandemic.

**Health System Preparedness in India**

Given the unavailability of a vaccine and anti-viral drugs against SARS-Co-V2, India adopted the next best possible strategy, a complete lockdown for a period of six weeks. This has helped curtail the spread of the virus as also community spread to a large extent. The collateral damage that the lockdown would do to the economy is huge but it has definitely helped save lives as of now.

The secondary fallout of the lockdown on the health system includes:

- Decrease in the number of emergencies at hospitals largely due to fear of COVID infection and also contributed to by difficulties in transport post-lockdown
- Elective surgeries and procedures being postponed for later
- Difficulty in procuring medicines from pharmacies as also from Public sector hospitals and Primary health centres (PHCs)
- Routine public health driven initiatives like reproductive care, immunisation, etc, tend to get affected with focus shifting to COVID containment.
- RNTCP- DOTS (daily observed treatment, short course) programme for TB being affected in the affected areas
- Cancer patients particularly affected given the lockdown measures both in not being able to access care and in the availability of drugs (this is so as relatively few centres have the facilities for cancer care and cancer drugs are not stocked in routine pharmacies being very expensive)
- Patients on maintenance hemodialysis, haemophiliacs and other blood diseases like sickle cell anemia and thalassemia, congenital enzyme deficiencies on maintenance doses on a weekly basis, etc. would be the ones whose treatment schedule was upturned by the lockdown.
- Psychological and mental health being affected in individuals prone for the same
- The other section of patients who would have been affected by the lockdown is ones on palliative care either at home or in institutions, who were on tube feeding, urinary catheters, etc. This subset of patients includes those with dementia, terminal cancers, strokes, etc.
- Rehabilitation of patients from a stroke, heart failure, surgical and orthopaedic procedures is also likely to have been hampered by the lockdown.
- Maintenance of hospital equipment is affected as service personnel were not available.
- BARC is the only supplier for radionuclide compounds used for medical purposes. Procurement of shipments of the same has been very erratic during the lockdown.
- Supply chains to be maintained for hospital essentials in daily use like oxygen, anesthetic agents, surgical gloves, masks and gowns, IV fluids and other fast moving items
- Blood banks to be kept functional in case of emergency for both blood and other blood products like platelets
- Disposal of hospital waste would also be greatly affected post-lockdown as both collection and disposal is affected.
Benefits to the Health Care System and Society Post-COVID-19

Health being a state subject is largely under the purview of individual states, the pandemic has led to the states working in tandem with the centre in a concerted way which has given the right results most places.

Most affected districts have a COVID 19 command centre under the District Collector’s charge manned by staff from the health and other ancillary departments.

Tracing of contacts has been done very successfully especially in states like Kerala, frontline health workers (ASHAs) along with JPHs have been at the forefront of this effort which has been key in containment in the southern states.

Societies by and large have abided by the decision of health authorities and have been conscientiously following instructions regarding both the lockdown and quarantine. The success of the containment has largely been due to society following instructions as also the strict measures taken by the police in cases of braking lockdown measures.

The country has largely been able to surge capacity with respect to manufacture of masks, disinfectants, PPEs, ventilators, diagnostic kits, PCR instruments, drugs like HCQs, ICU bed capacity, quarantine beds, etc.

Though COVID-19 may be having a devastating impact on health systems, social lives, and industry, it has also prompted an outpouring of creativity in many areas. Some of these innovations have been in the field of medical devices (e.g. low-cost ventilators), pandemic management during lockdown (Bhilwara model), data aggregation using crowd sourced data\(^1\), etc.

India has one of the lowest public health expenditures in the world (1.15 per cent of its GDP). The COVID-19 pandemic could be a wake-up call to the Central and State Governments to increase their budgetary allocations towards health, and other social sectors such as water and sanitation, women and children, elderly, disabled, and informal sector populations.

On a lighter note, the immediate benefit from the COVID19 would probably be in a decrease in number of acute gastroenteritis which is bound to decrease with all the hand hygiene and sanitation measures. Similarly a face mask will be the new norm which would help decrease tobacco chewing and spitting especially in public.

Recommendations

What health policy makers should take home as a message from the pandemic is that the health system can only be strengthened from the grass root upwards. The focus should be on the strengthening the public health system form the Primary Health centre level upwards. We have also learnt that the ASHAs and front line health workers were the key in the surveillance and containment measures and greater leverage of this system should be made in the future especially for surveillance and awareness programs. With the ubiquity of mobiles and hand held devices we also learnt that a m-health platform could be used to reach out to a majority of our population which could be used in the future too for tracking, creating awareness and maintaining care of individual patients. We are working on a comprehensive policy statement on health preparedness in disaster management which would go into the details and make recommendations for specific areas in health care.

Conclusions

Life on earth is not going to be the same again for all its inhabitants, humans included, post-COVID-19. The price that humanity has had to pay for her follies by way of human lives has been immense. We lived like only we are and there was no tomorrow. Pandemics and wars bring out the inequities in the system, between countries and societies, like nothing else. There are certain sectors that cannot but be addressed urgently like, climate change, environmental

\(^1\) www.covid19india.org
pollution and emission, immunisation, public health, nutrition, availability of essential drugs, health for all and an ever increasing number of other issues. We risk not confronting these issues at the cost of another pandemic. Another lesson learned is that in the coming ages, health would neither be a state nor national issue but an international issue. It is only through international cooperation and proper surveillance mechanisms in place that such pandemics can be prevented.

Health infrastructure has sprung up overnight and in a few states projects in a state of limbo have fructified and been converted to COVID hospitals.

It is also imperative for nations as large as India to develop the necessary infrastructure to be able to stand on her own on all fronts.

Just as the World War II brought about major changes in the world order including formation of the UN, WHO, etc. it would be in the interest of nations to set up a confederation against pandemics at the earliest. Surveillance is the best pre-emptive measure available given that very few viruses have effective vaccines. Surveillance, vaccines and anti-virals are the way forward.

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