



Coronavirus Disease 2019 Pandemic and 15 million Deaths: What went wrong

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A Colossal Calamity

World Health Organization scientists, in May 2022 reported that between 13.3 million and 16.6 million people had died worldwide from January 2020 to December 2021 because of Covid19 pandemic, more than 2.5 times the number of reported COVID-19 deaths (1). However according to estimates from other very reputed organizations, the total Covid death toll during first two years may be even higher. According to a Lancet study, the Covid death toll during the first two years of the pandemic was 18 million (2). The Economist weekly put the estimated death figure as high as 25.4 million (3). When on February 29, 2020, the first American Covid Death was reported (4), it was unimaginable to anyone even remotely concerned that by the end of two years, even the United States of the America, the most powerful nation state ever conceived on this planet will reach a grim milestone of 1 million official direct Covid19 death (5). Not only loss of lives, against the backdrop of Covid19, the global economy was projected to contract sharply by 3.2 per cent during the year 2020, according to the United Nations World Economic Situation and Prospects (WESP) mid-2020 report. The report goes on projecting that the global economy was expected to lose nearly \$8.5 trillion in output over the next two years due to the COVID-19 pandemic, wiping out nearly all gains of the previous four years (6).

So how did we come here? What went wrong?

By the end of 2019, on the verge of conquering long term foes like cancer, cardiovascular diseases and breathtaking inventions and developments in therapeutics and technology, our human civilization started feeling invincible. Well, until a small lifeless molecule of subatomic 100 nano Meter size (7) went to war with our civilization and brought us down to our knees.

We did see it coming

In early 2018, during a meeting at the World Health Organization in Geneva (8), a group of experts belonging to R&D Blueprint (9) coined the term “Disease X”; referring to the next pandemic, which would be caused by an unknown, novel pathogen that hadn’t yet entered the human population. Disease X, as said back then, would likely result from a virus originating in animals and would emerge somewhere on the planet; where economic development drives people and wildlife together. By the fag end of 2019, when Covid19 was already in circulation in parts of China, a major relevant conference was jointly organized by Duke/ National University of Singapore Medical School (Duke-NUS) and the Coalition for Epidemic Preparedness Innovations (CEPI). Although the conferences particularly rang the warning bell about NIPAH virus’s potential to cause a pandemic, a whole session of the conference was dedicated for discussing Disease X (10).

But we followed the wrong playbook

Former FDA chief Scott Gottlieb (11) and many other experts noted, Part of the problem was that our pandemic playbook always envisioned that a pandemic would be caused by influenza. So, when a Coronavirus pandemic hit us, we tried to engage following the rules of engagement instructed in the influenza pandemic playbook. Although there was a clear lapse in memory that the first pandemic of 21st Century, the SARS pandemic was indeed a coronavirus pandemic! Possibly because of Spanish flu memory and from experience of a few other outbreaks earlier in the century and a few near misses, the whole focus was on an Avian influenza pandemic.

Diagnostics Debacle

It's worth reminding that, in the setting of influenza, having a diagnostic test widely deployed isn't as important for one reason — because the incubation period for flu is shorter. Patients come into contact with flu and get sick in a much shorter period of time, and they're usually not contagious until they're infectious. So, diagnosing people when they're asymptomatic and carrying the infection isn't as important in the setting of controlling a flu as it is for a coronavirus. When Covid19 first started circulating, a German group led by Prof. Dr. Christian Drosten, Director of the Institute of Virology on Campus Charité Mitte, developed the world's first diagnostic test for the coronavirus (12) and made it's publicly available. WHO quickly coopted this technique and proposed it as the global standard test. However, while developing its own RT-PCR testing system, American Center for Disease Control and Prevention (CDC) fumbled (13). During the first several months, the pressure caused by covid pandemic in US healthcare system was significantly amplified by lack of testing kits. The testing kits developed by the CDC in the early weeks of the pandemic were not only contaminated but had a basic design flaw (14). CDC not only failed to produce, let alone mass produce effective RT-PCR kit in a timely manner, the US FDA was also slow (15) in authorizing private labs start developing their own test kits. By the time when test kit became more available, the virus has already spread uncontrollably inside continental USA.

Chicken Stockpile – Flu Playbook

As our administration has been fixated in flu as the next pandemic, USA government maintains a strategic stockpile of chickens. As flu vaccine is manufactured in chicken eggs and as a hedge against an avian flu that would either decimate the chicken flocks around the country or overwhelm our supply of eggs, this strategic stockpile of chickens was created and is being sequestered in carefully maintained facilities. This is mentioned here to show as an example that there was a lot of pandemic planning that went on. But it just focused around flu.

The Mask Controversy

Despite clear data coming out China and Italy of the disease's highly infectious nature, hanging onto flu pandemic mindset of fomite transmission dominance of influenza virus, US authorities kept discouraging healthy Americans from wearing Masks. On March 27, 2020, in an interview with Science magazine (16), George Gao, the head of the Chinese Center for Disease Control and Prevention warned that not wearing masks to protect against coronavirus is a big mistake. Yet a clear mask instruction and mandate wasn't forthcoming from the CDC or United States health Authorities. Finally on April 3, 2020, the Centers for Disease Control and Prevention made a formal recommendation (17) that people wear cloth or fabric face coverings, which can be made at home, when entering public spaces such as grocery stores and public transit stations. However, several well conducted studies by than demonstrated that clothe mask is not adequate to protect against SARS-CoV-2 transmission (18). And two years later, despite highly transmissible nature of B.2 sub lineage of SARS-CoV-2 Omicron and pressure from relevant experts, there has not yet been a clear instructions from CDC regarding N-95 mask.

Airborne vs Air-borne

On December 23, 2021, World Health Organization finally edited it's SARS-CoV-2 related scientific page to categorize SARS-CoV-2 as an airborne virus (19). This change marks the culmination of two years of research, pressure, debate, public campaign by a group of focused scientists and health analysts and journalists. Despite clear evidence otherwise, World Health Organization, Center for Disease Control and Prevention and other related healthcare authorities continued to categorize SARS-CoV-2 transmission as flu like droplet transmission and kept on emphasizing on handwashing instead of proper mask wearing of correct type of mask. The debate prior to this silent change of heart of WHO and CDC scientists were breathtaking, and occasionally spilled over from scientific journals to national daily OpEd pages (20, 21).

This one single change in transmission mechanism made all the Covid19 pandemic time preventive measures like Plexi glass barrier totally useless.

There was NO Treatment

As the disease devastated the main city of Hubei province, Wuhan – there was a great influx of epidemiological data. But although Chinese authorities did shock and awe campaigns like building a new hospital in 24 hours (22) etc., the initial Chinese experience could not guide the physician community with a solid and effective treatment data. Every single medication was being tried without any clear evidence for or against. However, to be fair to the Chinese physicians, they were totally caught off guard at the onset of the Wuhan outbreak, and they didn't have any direction to follow and experience to learn from. When Coronavirus waves hit Western Europe and USA a couple of months later, the epidemiological data from China were of immense help in modelling and planning.

Steroid and dogma

During the Wuhan phase of Covid19 pandemic, one retrospective study from China suggested that steroid might have some beneficial effect (23) and that data guided the physicians in Henry Ford Hospital in Detroit Michigan do a study on the use of steroid, which yielded positive results (24). Based on this data, one group of physicians started using steroid as people were dying and there was no other available effective treatment. Then slowly more and data in favor of steroid started trickling in. Based on a recent data of steroid's effectiveness in ARDS (25), the society of Critical Care Medicine, as early as March 2020, suggested use of steroid in patients with Covid19 pneumonitis (26).

However, despite all the developments, another group of physicians with strong anti-steroid dogma in infectious disease patients, kept on denying patients this life saving intervention. However, after the publication of large randomized multicenter RECOVERY trail data from UK, which confirmed the lifesaving role of steroid in patients with Covid pneumonitis, the anti-steroid dogma slowly waned (27).

'Viral' Antiviral

During the early months of the pandemic, Antiviral Remdesivir rapidly became the gold standard treatment for patients hospitalized with Covid19 without any convincing evidence in its support. The 'viral phenomenon' of this antiviral became so intense that governments and states had to ration its shipment and allocation (28). It would take nearly two more years to get the first effective antiviral (29) against Covid19 and later studies on Remdesivir will prove that to be effective Remdesivir would have to be used early (30) in the disease process during pre-hospital phase.

Convalescent Plasma Misadventure

With lack of a clear therapeutic option and mounting mortality, like a drowning man catching at a straw, physicians and general population alike resorted to century old therapeutic strategy of using convalescent plasma. It quickly became an overwhelmingly popular (31) therapeutic options, with blood banks getting overwhelmed collecting and distributing convalescent plasma from covid infected patients. However, the science and evidence behind this gold rush has never been solid and there are allegations that the US government overhyped the data to promote this potentially harmful therapeutic intervention (32). Thankfully convalescent plasma mania faded away after randomized control trials (33) kept failing to show its efficacy.

The Roller Coaster of Immunomodulators

Among the immunomodulators, the Il-6 agent Tocilizumab went through the wildest ride. As in convalescent plasma, Tocilizumab started being used widely and globally without much data and one early positive study gave it's usage a significant boost. However, five back-to-back negative data (34-38) put cold water on Tocilizumab excitement. But to add to the drama after five back-to-back negative trials, along came suddenly two strongly positive platform randomized clinical trial vouching for the effectiveness of Tocilizumab and steroid combination (39-40).

Early or Appropriately Timed Intubation

This is another part of the management where the pendulum of practice swung wildly without any conclusive evidence till date (41). Early in the pandemic, some physicians in Wuhan, China started practicing selective early intubation citing personal experience of poor outcome of prolonged noninvasive ventilation. By trying to follow the same practice, the physicians in Italy and New York city quickly exhausted the supply of available mechanical ventilators. This created serious strain on healthcare infrastructure at the peak of Pandemic in New York City (42).

The known and Unknown Unknowns

Not a litany of Mistakes

The above list of our mistakes is not a litany of complaints rather are bullet points of our learning. Every single misstep and fumble in managing Covid19 pandemic is a learning lesson for our scientific community. Let's look back at all these mistakes, analyze and find a solution that we don't repeat the mistake next time around.

European Epidemics and Sanitary Latrine Movement

The whole concept of closed sanitary latrine system was a lesson that came from several consecutive enteric microbial epidemic that devastated Europe during the 18th and 19th centuries. Let this pandemic be our turning point towards a smart and safe indoor air handling system.

Smart Next Generation Vaccine and Pan Variant vaccine

One can hardly find a flaw in the way effective Vaccines were developed in a lightning speed. If there was any problem, that was in vaccine nationalism and vaccine distribution inequity between rich and poor countries. We must learn to be better human to come over this flaw. There is other easy way in fixing this

problem. We also need to quickly work on next generation vaccines, pan-coronavirus, pan-influenza virus vaccines. These must be our highest priority sector.

1.67 million Viruses

There are 1.67 million (43) unknown viruses on this planet. Using our best estimates, anywhere between 631,000 and 827,000 of those have the ability to infect people. Scientists currently know of only 263 viruses that can infect people, which means that we know almost nothing about 99.96 percent of potential pandemic threats. We still could not find the bat or species where SARS-Cov-2 came to us from. This also means that 'if' is not the point, rather 'when' is the questions when we discuss about the next pandemic that will lash at us. And we have not talked about the unknown unknowns yet.

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