

# Pandemics

## Reviewed by

### **David Heymann**

Head and Senior Fellow, Centre on Global Health Security, Chatham House, Professor of Infectious Disease Epidemiology, London School of Hygiene & Tropical Medicine

### **Swee Kheng Khor**

Malaysian physician specialising in health systems & policies and global health

The COVID-19 pandemic has brought a genuine global catastrophic risk from merely theoretical and conceptual discussions into stark reality, with far-reaching public policy and global governance implications. Governments are now shifting their strategies to controlling SARS-CoV-2 as an endemic infection, and populations are learning to live with the virus in this third year of the pandemic.

It appears to most public health experts that SARS-CoV-2 is becoming endemic like the four other endemic human coronaviruses. These four endemic coronaviruses, like SARS-CoV-2, have their origin in the animal kingdom and have at some time in the past breached the species barrier and entered human populations. Human beings have learned to live with them as their epidemiology has evolved.

Although SARS-CoV-2 is presently more virulent than the other four human coronaviruses, there is an astounding array of vaccines, diagnostic tests and medicines that will help control and prevent infection. This is thanks to the unprecedented speed with which these tools have been developed, studied, licensed and deployed. However, there are new public policy issues to manage from the success of these tools, notably maintaining vaccine confidence while managing multiple rounds of boosters and maintaining healthy behaviours in populations that may become psychologically reliant on medical interventions.

On the scientific and virological front, a continuing major concern is whether the tools we have will continue to be effective because SARS-CoV-2, like other RNA viruses, is unstable and will mutate as it replicates in humans. Some mutations of SARS-CoV-2 have been shown to increase its ability to spread from person to person if the opportunity for transmission is created. The question remains as to whether the mutated variants of SARS-CoV-2 will escape the protective effect of the vaccines we have today, whether the many diagnostic tests will continue to identify infection



and whether SARS-CoV-2 will become more virulent. In response, scientists continue working on multi-valent COVID-19 vaccines as a step towards the ideal goal of a pan-coronavirus vaccine.

*“The question remains as to whether the mutated variants of SARS-CoV-2 will escape the protective effect of the vaccines we have today...”*

The world has learned much about pandemics during COVID-19. Countries that reacted more rapidly when the World Health Organization provided initial information on 5 January 2020 have been able to maintain low levels of hospital burden and mortality, and many were countries that had previous outbreaks of SARS and MERS coronaviruses that emerged in 2003 and 2012 respectively.

These countries also had strong public health and healthcare systems that permitted them to control outbreaks and accommodate the surge of patients in their health facilities, while ensuring healthcare for others who had non-COVID related illness. The rest of the world has also learned that robust and resilient health facilities are required to respond to the surge of patients caused by a pandemic, and all countries have seen that healthy populations are best able to resist serious illness when infected with newly emerged viruses. We can call this the three inter-locking functions of global health security: strong public health, resilient healthcare and healthy populations.

We have also seen the cost to economies of a pandemic, increased by the response actions by governments that have taken on the function of risk assessment and responded in a manner that required populations to protect themselves and others by being confined to their homes. The challenge now for many governments is to transfer these tasks to the population so that they are able to do their own risk assessment and management – protecting themselves and protecting others as they do for other infectious diseases.

However, early success may not always last; as exemplified by Hong Kong that, at the time of writing, has been unable to fully vaccinate and protect its populations at greatest risk of serious illness after infection. This makes it important that countries build the capabilities to change strategies and policies as the epidemiological situation changes. As the virus evolves, countries must also build systems and infrastructure for the evolution of their scientific, public health and public policy responses.

### **What is at stake?**

In the fifth and fourteenth centuries, plague epidemics spread internationally and were thought to have killed approximately 15% of the global population over the course of a few decades. Since then, systematic vaccination campaigns have allowed us to eradicate two diseases that had affected humanity for centuries, Smallpox in humans and Rinderpest in animals, and two more diseases – Guinea Worm and Polio – are close to being eradicated. Progress in vaccine development has permitted us to control other infectious diseases such as diphtheria, tetanus, whooping cough and polio; public health and sanitation have reduced the prevalence and impact of yet other infectious diseases such as Typhus and Cholera; and antimicrobial medicines have helped cure or control infections such tuberculosis, AIDS and malaria.



*“The best means to mitigate such an event is to ensure healthy populations and develop public health and healthcare systems”*

But there is a serious risk that the emergence of yet another new infectious disease in humans will cause a major outbreak or pandemic, with high mortality and rapid spread in our densely populated, urbanised and highly interconnected world. And there is also a major risk that the antibiotics and other antimicrobial drugs on which we depend will become ineffective because of misuse, causing outbreaks of resistant infections that spread first in communities and then within countries and across international borders.

The best means to mitigate such an event is to ensure healthy populations and develop public health and healthcare systems that have the capacity to deal with events such as the COVID-19 pandemic that we are witnessing today. The political will, economic investment and human capital development for these health systems will make the difference between life and death for millions of people, while safeguarding economic growth and national progress.

#### **How much do we know?**

Catastrophic pandemics – diseases with high lethality that spread globally such as COVID-19 – are extremely disruptive, and fortunately have been infrequent in the recent past. Outbreaks of lethal diseases that remain locally contained or pandemics with less acute effects on human health are more common, but they can also have significant disruptive effects.

Outbreaks occur when a microorganism – virus, bacteria or parasite – is able to spread across the population. At times and under certain conditions, such as failure of water or sanitation systems, an outbreak is caused by a micro-organism known to be circulating at low levels in human populations.

At other times, an outbreak is caused by a micro-organism that has crossed the animal/human species barrier to infect humans, and spreads to new and more densely populated areas. Those micro-organisms that replicate in the respiratory system, especially the passages of the nose, are easiest to transmit from person to person directly and can cause explosive outbreaks. If mutation occurs in a micro-organism as it replicates, or when it combines with genetic material from another microorganism, virulence can increase or decrease. Mutation can also cause a micro-organism to transmit more or less easily from human to human.

#### **What are key factors affecting risk levels?**

New micro-organisms affecting humans are more likely to arise when environments with high levels of biodiversity are disrupted, and when humans or domesticated animals come into close contact with other animal species that serve as reservoirs for micro-organisms not present in human populations. Experts now consider this is likely to be the way that the HIV/AIDS epidemic started – HIV/AIDS is now endemic in human populations, and its origin is thought to have been a single event when a retrovirus in non-human primates infected a human somewhere on the African continent. Chains of transmission of HIV began from this person, and they were eventually amplified into the HIV/AIDS pandemic when conditions were right.



Infections are easier to contain when they occur among small populations with limited external contact. Conversely, dense urbanisation and global interconnection strongly increase the risk of an infectious disease spreading internationally.

*“...dense urbanisation and global interconnection strongly increase the risk...”*

The broad adoption of hygiene and infection control practices in health facilities can have a significant effect in reducing the local and crossborder spread of an infection. This is especially true in health facilities where infection prevention and control through handwashing and other infection control measures can prevent transmission from amplifying into an outbreak. The capacity to monitor a disease and deploy very rapid containment early in the process can have a large impact on the final number of deaths as well.

Many of the key factors that affect risk levels are scientific in nature, dealing with the epidemiology, statistics, virological and laboratory aspects of pandemics. But there are other key factors that are non-scientific in nature, such as the political will to deliver strong pandemic responses, a resilient public healthcare system that can absorb a surge of healthcare needs, sociological factors of the health literacy and health-seeking behaviours of populations, and even economic factors of investment into health systems and population health.

### **Risk scenarios**

In February 2003, an elderly woman infected by the SARS virus travelled from Hong Kong to Toronto. SARS is a highly infectious and often fatal pulmonary disease that emerged in the Pearl River Delta, in China. The infected woman died soon afterwards in Toronto, after inadvertently infecting over forty people, resulting in a localised outbreak. One of those persons infected in Canada went on a plane to the Philippines, where another outbreak occurred. Meanwhile, from Hong Kong, the virus had also spread to Singapore, where it likewise caused an outbreak.

The outbreaks that occurred around the world were eventually contained, after infecting over 8,000 people, of whom 774 died, through concerted public health action coordinated by the WHO. Severe social and economic disruption occurred, despite a relatively small number of cases and deaths. A similar scenario with only minor variations – a few more international contacts, a slightly longer incubation period for the virus, or a few more days of delay in deploying strict containment measures – could have even more serious outcomes. In other words, while health systems can prepare carefully and thoughtfully, the unpredictable elements of luck and timing are also factors that determine the effectiveness of pandemic responses.

*“...the unpredictable elements of luck and timings are also factors that determine the effectiveness of pandemic responses...”*

In late 2013, in the Republic of Guinea in West Africa, an initial infection with the Ebola virus is thought to have occurred, possibly directly from a bat to a Guinean child. Small chains of transmission are thought to have occurred from this infected person, and transmission is thought to have been amplified in healthcare settings where patients admitted without Ebola infection became infected because of weak infection prevention and control measures. Health workers became infected as well, and they served as the entry point of the virus into their families and their



communities from where it spread across international borders to neighbouring countries. Over 28,000 persons were reported to have been infected during this outbreak in Guinea, Liberia and Sierra Leone, with over 11,000 deaths.

Infected persons from West Africa travelled to countries in Europe and North America for care, and rigorous infection prevention and control practices in health facilities in these countries prevented spread within health facilities and into communities. It is estimated that in addition to tragic loss of life from Ebola in West Africa, there was a reported increase in death from common infections such as malaria and measles because of the failure of health systems to accommodate needs of those with endemic infections.

These two examples show that there are some similarities in risk scenarios resulting in a global pandemic: animal-to-human transmission, globalized travel causing cross-border infections, and the strength of national-level healthcare systems predicting the quality of pandemic response.

### **Risk factors**

Three main factors determine the potential danger of an outbreak:

1. **Virulence:** the ability of a micro-organism to damage human tissues and cause illness and death.
2. **Infection risk:** the probability that a microorganism will spread in a population. One key factor is the means of transmission – whether by blood, bodily fluids, direct contact with a lesion such as a skin ulcer, or by aerosol in the air; another is the level of immunity in the population; and a third is whether population behaviour creates a risk of transmission.
3. **Incubation period:** the time between infection and appearance of the first symptom(s). A longer incubation period could result in a micro-organism spreading unwittingly, as in the case of HIV.

Conversely, a shorter incubation period, if the infection is highly lethal, is less likely to be transmitted unwittingly, and can cause considerable disruption of social, economic and medical systems in a very short period of time.

Ebola is a highly lethal infection with a short incubation period but a relatively low infection rate, which explains why most Ebola outbreaks to date have been localised.

New developments in synthetic biology, however, raise concern among certain scientists that an engineered micro-organism both highly virulent and with a high infection rate could be released in the population – whether by malice or accident – and cause an unprecedented outbreak, possibly leading to the international spread of a highly lethal infectious disease.



### **Antibiotics and Bacteria**

Antibiotics have saved millions of lives and dramatically increased life spans since they were introduced in the 1940s, allowing us to contain most bacterial infections and diseases. However, more recently, as a result of random mutations due to improper use of antibiotics among humans and animals in agriculture, some strains of bacteria have become resistant to traditional antibiotics. These ‘superbugs’ require alternative medications with more damaging side effects or, in the worst cases, can no longer be treated effectively. Antibiotic-resistant bacteria currently kill an estimated 700,000 people every year. That number is predicted to reach 10 million by 2050 if efforts are not made to curtail resistance or develop new antibiotics.

*“Antibiotic-resistant bacteria currently kill an estimated 700,000 people every year.”*

There is growing awareness that anti-microbial resistance (AMR) is a species-wide problem. The World Health Organization (WHO) lists AMR as a top ten threat to global health, and there is a growing body of public policy, economic incentives and laws to address AMR.

Two recent examples are the Combating Antibiotic-Resistant Bacteria Biopharmaceutical Accelerator (CARB-X, a global non-profit partnership to find new antibiotics, vaccines and diagnostics) and the PASTEUR Act (a bipartisan bill in the United States that would create advanced market commitments to incentivize pharmaceutical companies to conduct research in anti-microbial agents).