Global Health & Medicine. 2025; 7(2):167-171.
COMMENTARY
DOI: 10.35772/ghm.2025.01028

Clinical considerations for the next pandemic: Japan's current challenges and strategic preparedness

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Abstract: This commentary aims to reflect on the clinical implications of past pandemics and discuss Japan's preparedness for future pandemics, with a specific focus on enhancing national countermeasures through clinical, infrastructural, and systemic reforms. By analyzing pandemics including the Spanish flu (1918), Asian flu (1957), Hong Kong flu (1968), H1N1 influenza (2009), and COVID-19 (2019-), the article discusses their clinical features, societal impacts, and the factors that drive the spread of infectious diseases. With Japan's clinical context as a case study, this commentary emphasizes the importance of enhancing healthcare systems to accommodate sudden surges in cases, with a focus on expanding infrastructure and ensuring rapid access to diagnostics, treatments, and vaccines. The commentary also advocates for improved early detection systems, effective global sharing of information, and the training of healthcare professionals to respond to emerging threats. This article argue that pandemic preparedness should go beyond lessons from COVID-19, promoting a comprehensive and flexible approach that can be adapted to a range of potential future scenarios. Such measures will help ensure that healthcare systems remain resilient and capable of mitigating the impact of future pandemics.

***Keywords*:** pandemic preparedness, Japan, clinical infrastructure, infectious diseases, healthcare policy

Introduction

Multiple global pandemics over the past century, including the Spanish flu (1918), Asian flu (1957), Hong Kong flu (1968), H1N1 influenza (2009), and COVID-19 (2019-) (*1-5*), have increasingly revealed that global healthcare systems must be robust, responsive, and forward-looking. Influenza and coronaviruses remain the primary threats, with emerging pathogens such as the Nipah virus, Ebola virus, and engineered bioweapons posing additional risks. Factors that accelerate pandemics include globalization, urbanization, climate change, and misinformation. Rapid international travel enables the rapid spread of diseases, whereas urban density exacerbates transmission. Climate-related changes increase the risk of mosquito-borne diseases and zoonotic spillovers.

The next pandemic could overwhelm healthcare systems, causing shortages in beds, intensive care units (ICUs), ventilators, and medical staff. High mortality rates can destabilize societies, whereas prolonged lockdowns can damage mental health, education, and economies. Supply chain disruptions can limit access to vaccines and medicines and exacerbate global inequality.

This commentary sought to clarify the clinical aspects of pandemics and discuss measures needed to prepare for the next one. Specifically, it: *i*) summarized past pandemics and outlined their clinical features, *ii*) discussed characteristics of infectious diseases caused by potential pandemic pathogens, *iii*) raised issues regarding Japan's clinical response to the current pandemic, and *iv*) discussed what measures Japan will need to take in the event of a future pandemic.

Lessons from historical pandemics

Spanish flu (1918)

This pandemic was caused by an influenza outbreak during World War I. Various theories have been proposed to explain the origin of this outbreak. Approximately one-third of the world's population was estimated to be infected, with 20-50 million deaths. The fatality rate was extremely high (> 2%), with many victims being mature adults in their 20s-40s. In Japan, approximately 23.8 million people were infected, and approximately 390,000 died (*6*). No vaccines or antivirals were available at the time, and non-drug measures against infection were implemented in many areas, including quarantines, masks, and bans on gatherings.

Asian influenza (1957)

The influenza A (H2N2) pandemic began in 1957. It is known as the "Asian flu." This new strain of influenza was first identified in Hong Kong and Singapore in the spring, and it spread worldwide to Europe and the United States in approximately 6 months. Although the fatality rate was low at approximately 0.2% (*7*), there were a vast number of infected people, resulting in many deaths. Vaccine development progressed in many countries, and the epidemic was controlled over a relatively short period.

Hong Kong influenza (1968)

This pandemic, also known as the Hong Kong flu, was caused by influenza A(H3N2) and occurred in 1968. A new strain, confirmed in Hong Kong, spread from Asia to Europe and the United States, and the global death toll was estimated to be at least 1 million (*8*). The symptoms were relatively mild and the fatality rate was low, but the death toll increased in the second wave through the winter of 1969. The H3N2 virus subsequently became a seasonal influenza virus and it has been circulating yearly.

H1N1 influenza (2009)

This pandemic, caused by influenza A(H1N1)pdm09, emerged in the spring of 2009. A new strain of influenza A(H1N1)pdm09 was identified in Mexico, and it spread worldwide in a short period of time. The highest alert level was declared during Phase 6 in June. Although young people were primarily infected, a few cases of infection among older adults were reported. The estimated global mortality was 201,200 (range 105,700-395,600) (*4*). In Japan, an estimated 20 million people were infected in over a year, with 203 deaths reported; therefore, the death rate per population was lower than that in other countries (*9*). The epidemic subsided within a few months, and the H1N1pdm strain was subsequently incorporated into seasonal influenza strains.

COVID-19 (2019-)

COVID-19 was first identified in Wuhan, China at the end of 2019 and eventually became a global pandemic. The virus responsible, SARS-CoV-2, is transmitted mainly by infectious particles containing the pathogen, through their mouth or nose and can spread asymptomatically; the World Health Organization (WHO) declared COVID-19 a pandemic in March 2020, and there were multiple waves of outbreaks worldwide. Countries implemented strict countermeasures such as urban blockades and border closures but were unable to completely prevent the spread of the virus. A vaccine was developed and administered after late 2020, and severe infections were suppressed, but the pandemic was prolonged by continued reemergence due to mutations of Delta, Omicron, and other strains. Preliminary estimates suggest that the total number of global deaths attributable to the COVID-19 pandemic was at least three million on May 20, 2021, representing 1.2 million more deaths than officially reported (*10*).

Assumptions regarding the next pandemic

Pathogens likely to cause the next pandemic

Diseases that have been identified as pandemics thus far include acute respiratory infections. However, other infectious diseases can lead to pandemics. Based on past cases, the next pandemic is likely to be caused by an emerging virus. The most typical pandemic occurs when an animal influenza virus, such as avian influenza, mutates and becomes persistently transmissible from person to person. In the past, all pandemics have been caused by influenza viruses, and currently, there are warning signs of the potential emergence of zoonotic viruses, such as the highly pathogenic H5N1 avian influenza virus.

Based on the examples of severe acute respiratory syndrome, Middle East respiratory syndrome, and COVID-19, coronaviruses are pathogens with a high potential for causing pandemics. An unknown coronavirus in nature could spread to humans; if a new virus emerges that is as lethal as severe acute respiratory syndrome or Middle East respiratory syndrome virus and that is as infectious as the virus that caused COVID-19, it could cause a serious situation.

Other potential viruses include enteroviruses, paramyxoviruses like the Nipah virus, and filoviruses like the Ebola virus. All of these viruses have thus far only caused local epidemics, but they could cause global pandemics if they mutate and become more infectious. In addition, the use of artificially modified pathogens and bioweapons poses a potential threat. Moreover, the emergence of unknown viruses is possible.

Factors contributing to the spread of infection

Factors unique to modern society will be responsible for the emergence and spread of the next pandemic. The global situation is rapidly changing, and the probability of a pandemic is increasing. In addition, the speed at which infectious diseases spread and their impact on human health and society is greater than ever before. Below are some of the specific factors:

With the development of transportation and logistics, people and goods move around the globe by air, and infectious diseases spread rapidly worldwide. In the modern era, the time from the first case to a pandemic is extremely short.

Economic growth is accompanied by large cities,

which are the centers of the economy; those cities are densely populated and a virus can, once introduced, spread rapidly. Moreover, public health measures may be inadequate in areas with rapid population growth. Such environments have poor sanitation and can serve as breeding grounds for the spread of infection.

Global warming will expand the habitats of mosquitoes and other vectors and increase the period of their annual activity, which may lead to the spread of mosquito-borne infectious diseases, such as dengue fever and malaria. Deforestation increases the risk of wildlife–human encounters. This means that humans will be increasingly exposed to zoonotic pathogens, and, as a result, so-called viral spillovers from animals to humans are more likely to occur. Climate change leads to disasters such as floods, which are more likely to trigger outbreaks of infectious diseases. Several post-disaster cholera outbreaks have occurred worldwide in recent years.

In areas with poverty or conflict, containing infectious diseases is difficult because of weak healthcare systems. Supply chain disruptions can lead to shortages in medical supplies. One can see an example in the recent worldwide outbreak of cholera, much of which occurred in conflict zones.

Information disseminated during a pandemic can have an impact on the spread of infection because it has a significant effect on people's behavior. Misinformation and disinformation are serious issues. If misinformation or disinformation causes panic and people avoid taking measures to prevent infection, preventing infection becomes more difficult.

Potential public health impacts

The next pandemic is expected to have the following severe impacts on public health:

i) A rapid increase in the number of patients over a short period of time will lead to a shortage of hospital beds, ICUs, and ventilators and exhaust medical personnel. The lack of appropriate treatment in a timely manner can result in the loss of life.

ii) The nature of the pandemic will change depending on the populations susceptible to this infectious disease. In the case of COVID-19, many older people have been affected, with significant morbidity and mortality, whereas many children became ill during the 2009 H1N1 influenza pandemic. The influenza epidemic that swept through the early 19th century, known as the Spanish flu, infected and killed many young people.

iii) If the fatality rate of an infectious disease is high, a sudden increase in the number of deaths can shock society and cause social chaos. Conversely, a low fatality rate but a high rate of infection would result in an increase in deaths, with long-term, significant losses due to health problems caused by aftereffects and loss of labor.

iv) Lockdowns, school closures, and suspensions to control the pandemic will severely restrict people's lives and cause the stagnation of economic activity. If prolonged, the measures could have serious impact, such as worsening mental health, loss of educational opportunities, and widening of social divisions. These problems became apparent during the COVID-19 pandemic.

v) Production may be unable to keep up with the sudden increase in demand for diagnostics, therapeutics, and vaccines, and the limited supply may flow only to countries with large economies. This can lead to international conflict. If vaccines and medicines do not reach low-income countries, the virus will persist in those regions. If the virus persists in some parts of the world, containing it globally may be difficult.

What preparations should be made?

Countermeasures have been developed based on lessons learned from the preceding pandemic. If, however, only the immediate preceding pandemic is the point of reference, then the countermeasures will be biased and insufficient to respond to the next pandemic. Therefore, a wide range of scenarios must be considered, and a flexible system that can be deployed to respond to various situations must be developed. In preparation for the next pandemic, the following measures should be taken from a medical perspective:

Enhancing research and development for diagnostics, pharmaceuticals, and vaccine production systems

Investment in research and development and manufacturing infrastructure during normal times is imperative; as a result, diagnostics, pharmaceuticals, and vaccines can be promptly supplied in the early stages of a pandemic. In Japan, the Strategic Center for Biomedical Advanced Vaccine Research and Development for Preparedness and Response was established to facilitate the development of promising vaccine technologies and new modalities (*11*). A similar system needs to be established for diagnostic approaches and therapeutics. Domestic production systems for raw materials and containers should be established within Japan, and public–private partnerships should be promoted to obtain the necessary quantities in the event of an emergency.

Healthcare infrastructure

A flexible healthcare system that can withstand the rapid increase in the number of patients, including the planned expansion of beds for patients with infectious diseases, ICUs, and ventilators; the formulation of a plan to set up temporary medical facilities on short notice; and the establishment of a network to dispatch support medical personnel is needed. Therefore, a mechanism

of coordination that can flexibly allocate staff and inpatient beds at medical facilities to treat patients with infectious diseases during a pandemic is needed. Striking a balance with non-infectious disease care is crucial. Such coordination is not easy, and administrative agencies must be closely involved. Japan's new National Action Plan for Pandemic Influenza and New Infectious Diseases includes training and enhancing cooperation during normal times; local governments must work with relevant organizations to promptly set up medical and inspection systems in the event of an outbreak (*12*).

Human resource development

Government officials, researchers, and healthcare professionals involved in public health response, treatment, and research and development of infectious diseases should be trained effectively. This objective has not yet been achieved. A major problem is the lack of jobs and positions for these individuals. Industry, academia, and the government must take this issue seriously and build an ecosystem in which the pool of talent can evolve and grow.

Planned stockpiling and ensuring production lines for supplies

Planned stockpiling and ensuring production lines for supplies such as masks and protective equipment, test reagents, therapeutics, ventilators, and daily necessities, which are in short supply during a pandemic, are necessary. Starting in normal times, national and local governments should cooperate to maintain appropriate inventories and diversify supply networks. This strategy reduces the dependence on imports of raw materials for pharmaceuticals and vaccines and ensures domestic production and alternative sources of procurement.

Establishment of early detection/warning systems and rapid sharing of information

A system for the early detection of and the rapid sharing of information on emerging infectious diseases must be established. In Japan, the government is currently enhancing the surveillance of acute respiratory infections to detect respiratory infections of unknown etiologies in a timely fashion. In Japan, there is a system of "suspected case surveillance." This surveillance system is designed to monitor patients exhibiting severe symptoms of unknown origin to detect and prevent potential infectious disease outbreaks. Designated medical facilities must promptly report such suspected cases to public health authorities. This proactive approach facilitates a rapid response, thereby safeguarding public health. Health surveillance, which integrates animal and human health information, is extremely important from the perspective of monitoring spillovers from animals to humans. To make these surveillance activities effective, a genome analysis network should be operational staring in normal times to speed up the detection of pathogens and the surveillance of mutant strains of emerging and re-emerging infectious diseases. The Japan Institute for Health Security (JIHS) (*13,14*) operates the Infectious Disease Clinical Research Network with a national repository. Funded by the Ministry of Health, Labor, and Welfare, this is a project for a clinical research network to act as a platform for rapid tallying of cases in an emergency. Moreover, Japan should comply with the obligation to report information to the WHO and develop a platform for the real-time sharing of data with other countries. Departments of the JIHS should function as hubs for infectious disease information, provide scientific advice to governments, and disseminate information to the public and international community.

Conclusion

This commentary examined past pandemics and discussed the measures that Japan will need to adopt in the future. What are required are measures, systems, and policies that are not biased from experience with COVID-19; these efforts need to be comprehensively developed to respond to future emergencies. However, responding flexibly and quickly is easier said than done. To ensure that actual operations are as smooth as possible, the processes of planning, checking progress, and confirming proficiency through training and revision of countermeasures should be repeated. These measures should be incorporated into daily healthcare and implemented regularly. These steps will enable us to respond flexibly to various emerging infectious diseases and build sustainable healthcare systems.

Funding: None.

Conflict of Interest: The author has no conflicts of interest to disclose.

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Received March 19, 2025; Revied April 24, 2025; Accepted April 27, 2025.

Released online in J-STAGE as advance publication April 29, 2025.

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