

## EMERGING INFECTIOUS DISEASES AND THE ROLE OF FRONTLINE PHYSICIANS

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### ABSTRACT

**There is currently greater awareness of emerging infections occurring around the world. Increasing human-animal interface over the past decades may explain the origin of such zoonotic agents, and its spread is further perpetuated by climatic changes, vector migration, and international travel and trade in our global village. It is paramount that frontline physicians stay vigilant, as the threat of importation of such diseases via returning travellers as agents with outbreak potential will challenge our healthcare systems and socioeconomic structures, just like how COVID-19 did. It is not sufficient to rely on global public health measures. Individual frontline physicians have a role to play in preventive measures such as pre-travel advice, ensuring vaccinations are up to date, and advocating antimicrobial stewardship. Steps to take during an outbreak include mobilising a response team, ensuring infrastructure is in place, ensuring good communication amongst healthcare workers and patients, and lastly, investing in the training, safety, and welfare of frontline staff.**

**Keywords:** Emerging infections, Outbreak, Pandemic preparedness, Frontline physicians

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### INTRODUCTION

The concept of emerging infections had been underappreciated until the end of the last century.<sup>1</sup> The emergence of the Nipah virus, Severe Acute Respiratory Syndrome (SARS) coronavirus in 2003, and avian influenza highlighted gaps in public health response to emerging infections globally. There is now greater awareness and emphasis on strengthening our healthcare systems to manage novel infections, including establishment of reporting and surveillance platforms and advancement in diagnostics, vaccinology, and therapeutics. Since 2007, WHO has declared several Public Health Emergencies of International Concern (PHIEC): the H1N1 influenza A pandemic in 2009, Ebola (West Africa 2013-2015, Democratic Republic

of Congo 2018-2020), poliomyelitis (2014 to present), Zika (2016), COVID-19 (2020 to present), and Monkeypox (2022).<sup>2</sup> These infections pose a constant threat to healthcare systems, economies and our psychological well-being.

### EMERGING INFECTIONS AND ZOOONOTIC ORIGINS: THE ANIMAL-HUMAN INTERFACE

More than 60 percent of human-emerging infectious diseases are zoonotic viruses.<sup>3</sup> Novel coronaviruses such as SARS, Middle East Respiratory Syndrome (MERS), and COVID-19 have emerged over the past two decades. SARS coronavirus was introduced into humans from bats via civet cats sold for consumption in the local Chinese markets, MERS coronavirus likely also from bats via contact with camels in the Middle East, and SARS-CoV-2 probably from bats, all of which demonstrated the ability to cause human-to-human transmission to varying degrees. Another zoonotic virus of outbreak potential is the Nipah virus, which originated from bats, spilled over into domestic animals such as pigs, and ultimately to humans in the outbreak that occurred in 1998-1999 in Malaysia and Singapore. This was postulated to be due to the movement of bats to pig-rearing areas in Malaysia due to changes in agriculture practices. The subsequent outbreaks of the Nipah virus in South India and Bangladesh since the early 2000s and most recently in 2021 were also linked to contact with fruit bats, with reports demonstrating human-to-human transmission and devastating mortality rates of 40-75 percent.<sup>4</sup> With increasing proximity in which humans coexist with animals such as poultry and pigs (which are natural hosts of the influenza virus), strains of influenza such as Avian H5N1 influenza, the 2009 H1N1 influenza (otherwise known as swine flu), and the H7N9 influenza in 2013 had evolved due to reassortment of genetic information between viruses affecting humans and animals or mutations in animals.<sup>5</sup>

### CLIMATE CHANGE AND MIGRATION OF VECTORS

Climatic changes and migration of vectors have also expanded the geographical area in which diseases occur. Since 2014, chikungunya infections have been reported in Europe and the Americas, including parts of the United States such as Florida and Texas. In 2022, locally acquired cases of Japanese Encephalitis have also been increasingly reported in various states in Australia, postulated to be introduction of the mosquito vectors through changes in wind and climate, transportation by planes and vessels, or the introduction of Japanese Encephalitis-infected migratory birds.<sup>6</sup>

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## EMERGING INFECTIONS IN OUR GLOBAL VILLAGE

As we live in a global village, we are not protected from emerging infections from other parts of the world. The first case of SARS in Singapore was linked to a Singaporean who acquired the infection during travel to a North Asian city<sup>7</sup>; the first reported Zika case in Singapore in April 2016 was a returning traveller from Brazil<sup>8</sup>; and the first case of Monkeypox in Singapore was a business traveller from Nigeria, who was diagnosed in 2019, ahead of the current monkeypox pandemic in 2022.<sup>9</sup> Even cases of “airport malaria” are known to occur outside malaria-endemic regions.<sup>10</sup> A recent cluster of non-travel associated cases of melioidosis in United States was linked to an imported aromatherapy spray product originating from a melioidosis-endemic area,<sup>11</sup> highlighting that importation of emerging infections occurs on all fronts. Notwithstanding stringent food product and safety measures, foodborne outbreaks can also cross international borders as illustrated by the 2018 listeria outbreak associated with consumption of rock melons imported from Australia,<sup>12</sup> as well as the Group B Streptococcal (Sequence Type 283) outbreak linked to consumption of ready-to-eat raw Asian bighead carp and snakehead fish in Singapore in 2015.<sup>13</sup>

Living in a global city, we are also facing a silent pandemic of our time – antimicrobial resistance. There has been an emergence of difficult-to-treat sexually transmitted diseases such as azithromycin- and moxifloxacin-resistant *Mycoplasma genitalium*<sup>14</sup> and ceftriaxone-resistant *Neisseria gonorrhea* (FC428 clone) infections,<sup>15</sup> as well as dissemination of multidrug resistant organisms such as carbapenem-resistant gram-negative organisms, *Candida auris*, and multidrug-resistant tuberculosis throughout the world, leading to great therapeutic and infection control challenges. International travel and social networks across the globe play a large role in the perpetuation of these infections.

## SOCIAL DETERMINANTS OF EMERGING INFECTIONS

Poverty and social inequality are also underlying drivers of emerging infections.<sup>16</sup> Consumption of bushmeat in the poorer communities in Africa may have contributed to their increased exposure to Ebola and Monkeypox. Overcrowded living conditions with greater transmissibility of diseases, poor access to healthcare facilities, higher rates of chronic medical conditions, lack of trust in healthcare professionals, and reliance on traditional medicine, which may sometimes be contaminated, are common amongst people worldwide of a lower socio-economic status and may fuel the emergence and spread of infections.

Finally, a breakdown of effective immunisation programmes and public health measures can spark the re-emergence of infections once thought to be kept at bay. The resurgence of diphtheria in Rohingya refugee campsites in Bangladesh in 2018, the sharp increase in measles cases in Brazil since 2020, and the occurrence of vaccine-derived poliomyelitis

in an unvaccinated man in New York are just a few vaccine-preventable diseases that continue to re-emerge<sup>17</sup> – marginalised populations in Singapore have not been spared.<sup>18</sup>

## THE ROLE OF FRONTLINE PHYSICIANS

### 1. Resources to Help Us Keep Up-To-Date

The challenge with frontline workers is staying abreast of information on emerging infections, particularly those with outbreak potential. Valuable resources that will provide such information include:

- ProMED supported by International Society for Infectious Diseases
- MMWR (Morbidity and Mortality Weekly Report) from the Centre of Disease Control and Prevention
- European Centre for Disease Prevention and Control: <https://www.ecdc.europa.eu/en>
- Shoreland Travax provides useful pretravel advice although it is a subscription-based service
- NCID website: <https://www.ncid.sg> contains Joint MOH-NCID guidance on prevailing outbreaks
- Journals such as *Emerging Infectious Diseases*, *Journal of Infectious Diseases and Vaccine*, *PLoS Pathogens*. The *Singapore Medical Journal* also frequently carries information about cases and case clusters of emerging infectious diseases<sup>19</sup>

### 2. Surveillance and Patient Care

Coupled with the knowledge of emerging infections reported across the globe, a heightened alert is required especially with travellers, migrant workers, and persons working with animals who present with fever or infective symptoms. A meticulous history including a thorough exposure and travel history as well as recognising and reporting unusual trends will be key to identifying these emerging infections. This is exemplified by how a group of clinically astute primary healthcare physicians pursued the diagnosis of the first Zika case in Singapore in 2016 in the face of a Zika outbreak worldwide upon obtaining negative diagnostic tests for dengue, and other common viruses in migrant workers presenting with a viral-like illness.<sup>20</sup>

Singapore houses a large migrant worker and domestic helper population, and this poses specific challenges in diagnosing infections that may have been acquired from their home country or as part of a transmission chain in their congregate living quarters. Arthropod-borne diseases such as chikungunya, Zika infections, or malaria, communicable diseases such as tuberculosis, and foodborne diseases such as cholera or typhoid are just a few of many.<sup>21</sup> In fact, the multidrug resistant tuberculosis outbreak that occurred in 2012 in five young men who frequented two LAN-gaming centres in Singapore was found to be linked via whole-

genome sequencing to a migrant lounge hostess who had multidrug resistant pulmonary tuberculosis in 2008.<sup>22</sup> It was discovered through epidemiological investigations that one of the 2012 cases had worked in the same karaoke as the lounge hostess. Some of these migrant workers may be afraid of deportation and thus reluctant to give detailed travel histories or may downplay their symptoms. This is a major challenge for the frontline physician doing routine examinations or treating a febrile patient in a busy clinic.

### 3. Deliver Holistic Care While Not Neglecting Prevention

It is common to have travellers presenting to primary healthcare for pretravel advice. Providing good travel health and vaccination advice to these patients will be paramount in preventing the acquisition of potential diseases. For example, appropriate vaccines and advice to avoid raw camel milk or contact with camels during trips to the Middle East will reduce the risk of getting infected with MERS or even Brucellosis. Preventive measures to avoid arthropod-borne infections such as using mosquito nets and effective insect repellents will reduce the risk of acquiring arthropod-borne infections such as chikungunya, Zika, Japanese Encephalitis, and malaria. Ensuring that travellers are up to date with their vaccinations such as measles and polio is important, especially for those travelling to countries where these infections are still widespread.

A detailed post-travel consultation and having a high index of suspicion of an imported infection is crucial. In 2016, China reported imported yellow fever in 11 migrant workers returning from Angola.<sup>23</sup> This could easily be imported into Singapore to cause autochthonous spread, especially when Singapore has a high population density and is largely unvaccinated against yellow fever, given that the *Aedes* vector is widespread in Singapore.

Curbing the silent pandemic of multidrug resistant infections is the responsibility of all. Antimicrobial overuse in animal and human health has contributed to the emergence of drug-resistant bacterial and fungal infections. Singapore's National Strategic Action Plan on Antimicrobial Resistance aims to issue guidelines on antimicrobial stewardship in community hospital and primary care clinics to improve prescribing practices and guide antimicrobial use. Frontline physicians can play their part through provision of careful antibiotic stewardship and patient education.

### 4. Pandemic Preparedness

We have experienced multiple pandemics such as SARS, H1N1, and COVID-19, as well as some localised outbreaks in the past two decades. There is an escalating need to strengthen emergency preparedness and gear up our response capacities. While such measures may be limited to a handful of disciplines such as infectious diseases, critical care medicine, and emergency medicine, we recognise the need to extend this skillset to primary healthcare and fill knowledge gaps, especially in the area surrounding that of infection prevention and control. In the past, simulation

exercises such as Exercise Sparrowhawk in 2006 and from 2014 to 2015 have been held to test the robustness and preparedness of our healthcare providers as well as to refine operational plans in the case of an influenza pandemic or ebola outbreak respectively.<sup>24,25</sup>

### 5. Response During an Outbreak

Despite the extraordinary progress we have made to prepare ourselves for a pandemic, it is never possible to predict the nature of Disease X. All frontline physicians need to be adaptable and prepared to manoeuvre through uncharted territories with agility, updating themselves with new knowledge gleaned from an evolving situation. Below are some general principles in response to an outbreak:

- **Rapid mobilisation of a response team or a taskforce:** A concerted effort to establish protocols, workflows, and guidelines, and to implement measures will require coordination between the medical team, operations team, infection control team, contact tracing team, and other relevant stakeholders such as radiology, diagnostic laboratory, pharmacy, and environmental services. While these are usually done at the national level, frontline physicians can ensure that they are in regular contact with their primary care networks and partner primary care providers so that supplies are procured and up-to-date protocols can be implemented at the local clinic level.
- **Ensure essential infrastructure are in place:** screening centres, isolation rooms, availability of personal protective equipment, safe patient transfer, specimen testing, and environmental cleaning. Arrangements have to be made to transport specimens to the appropriate laboratories as well as patients who require evaluation at tertiary care centres including the NCID.
- **Communication:** Decisions and information should be communicated and disseminated to all staff and patients efficiently. Frontline physicians are probably the most important sources of information for lay people during an emerging infectious disease outbreak. Thus, it is crucial for accurate information to be first garnered from official sources and then disseminated to patients and their families.
- **Frontline staff should be trained and regularly updated in the following areas:**
  - a. Early recognition and testing according to case definitions; enhanced surveillance if required
  - b. Early notification and reporting
  - c. Early identification of contacts and linkages with MOH and other official contact tracing teams
  - d. Rapidly updating themselves perhaps through the College or other professional bodies together with the MOH and NCID on evidence-based practice on the emerging infection



- i. Incubation period
  - ii. Infectious period
  - iii. Route of transmission and infection control measures including use of personal protective equipment and transmission-based precautions
  - iv. Clinical features including phases of disease course and signs of severity or those at risk of severe disease and escalation of care
  - v. Diagnostics and its limitations
  - vi. Countermeasures such as therapeutics, prophylaxis, vaccines
- Human Resource management, occupational health, and staff welfare:
    - a. Allocation of manpower to sustain routine medical care while expanding capacity to manage mild cases of emerging infections when care is decentralised to primary health centres. For example, Public Health Preparedness Clinics (PHPCs) were instrumental during COVID-19 surge when public hospitals reached maximum capacity. The use of innovative methods of sustaining healthcare such as teleconsultation took off during COVID-19 pandemic
    - b. Contingency planning for absenteeism/staff on medical leave
    - c. Post-exposure prophylaxis for staff – ensuring tracking of staff and ensuring that they have access to tertiary centres where post-exposure treatment can be provided rapidly
    - d. Staff welfare and support of frontline staff who experience psychological stress while experiencing long work hours, protracted isolation from families, or witnessing infection or bereavement of loved ones

## CONCLUSION

Emerging infections have been increasingly recognised in global public health in the past three decades and will continue to challenge healthcare and our socio-economic structure for years to come. The World Health Organisation has published a priority list of pathogens that are likely to cause major epidemics in the future, including Filoviruses (Ebola, Marburg), Lassa, Rift Valley, Crimean-Congo, Nipah, Henipaviral diseases, Zika, highly pathogenic coronaviruses (MERS-CoV, SARS-CoV, SARS-CoV-2), and Disease X.<sup>26</sup> Over the past three years, we experienced the devastating effects of COVID-19 and we are only just emerging from its effects now. Facing the threat of a future novel and highly pathogenic emerging infection or even a re-emerging one, beyond enhancing pandemic response and preparedness in our healthcare units, we need to arm ourselves with continued vigilance, agility, and resilience in these uncertain times. This is especially so for the frontline healthcare workers who are in daily contact with patients

and their families and thus likely to be the first to encounter these emerging infections in Singapore. As a society, we also need to adopt a One Health approach in creating sustainable collaborations between human, animal, and environmental health sectors to stem the emergence of future novel infections. As with most things in medicine, communication is key. Communication between scientists, clinicians, public health authorities, and the frontline workers and patients ensures optimal outcomes and minimal disruptions to our daily lives.

## REFERENCES

1. Institute of Medicine (US) Committee on Emerging Microbial Threats to Health. *Emerging Infections: Microbial Threats to Health in the United States*. Lederberg J, Shope RE, Oaks SC Jr, editors. Washington (DC): National Academies Press (US); 1992. PMID: 25121245.
2. Wilder-Smith A, Osman, S. Public health emergencies of international concern: a historic review. *J Travel Med*. 2020 Dec 23;27(8):taaa227. doi: 10.1093/jtm/taaa227. PMID: 33284964; PMCID: PMC7798963.
3. Chan EH, Brewer TF, Madoff LC, Pollack MP, Sonrick AL, Keller M, et al. Global capacity for emerging infectious disease detection. *Proc Natl Acad Sci U S A*. 2010 Dec 14;107(50):21701-6. doi: 10.1073/pnas.1006219107. Epub 2010 Nov 29. PMID: 21115835; PMCID: PMC3003006.
4. World Health Organization. Nipah Virus [Internet]. [Place unknown], [publisher unknown]. 2018 [2018 May 30; cited date]. Available from: <https://www.who.int/news-room/fact-sheets/detail/nipah-virus>
5. Rambaut A, Pybus OG, Nelson MI, Viboud C, Taubenberger JK, Holmes EC. The genomic and epidemiological dynamics of human influenza A virus. *Nature*. 2008 May 29;453(7195):615-9. doi: 10.1038/nature06945. Epub 2008 Apr 16. PMID: 18418375; PMCID: PMC2441973.
6. Waller C, Tiemensma M, Currie BJ, Williams DT, Baird RW, Krause VL. Japanese Encephalitis in Australia - A Sentinel Case. *N Engl J Med*. 2022 Aug 18;387(7):661-662. doi: 10.1056/NEJMc2207004. PMID: 36070717.
7. National Library Board, Singapore. SARS outbreak occurs in Singapore. Available at: <http://eresources.nlb.gov.sg/history/events/187adc0f-841a49cb-86e8-86734b65691a>.
8. The Straits Times. First case of Zika virus in Singapore; 48-year-old man who travelled to Sao Paulo. Available at: <https://www.straitstimes.com/singapore/health/first-case-of-zika-virus-in-singapore-48-year-old-malepr-who-travelled-to-sao>.
9. Koh XQ, Chio MTW, Tan M, Leo YS, Chan RKW. Global monkeypox outbreak 2022: First case series in Singapore. *Ann Acad Med Singap*. 2022 Aug;51(8):462-472. doi: 10.47102/annals-acadmedsg.2022269. PMID: 36047521.
10. Huang Z, Tatem AJ. Global malaria connectivity through air travel. *Malar J*. 2013 Aug 2;12:269. doi: 10.1186/1475-2875-12-269. PMID: 23914776; PMCID: PMC3766274.
11. Gee JE, Bower WA, Kunkel A, Petras J, Gettings J, Bye M, et al. Multistate Outbreak of Melioidosis Associated with Imported Aromatherapy Spray. *N Engl J Med*. 2022 Mar 3;386(9):861-868. doi: 10.1056/NEJMoa2116130. PMID: 35235727.
12. World Health Organization. 2018 [Internet]. [Place unknown], [publisher unknown]. 2018 [2018 April 09; cited date]. Available from: <https://www.who.int/emergencies/disease-outbreak-news/item/09-april-2018-listeriosis-australia-en>
13. Tan S, Lin Y, Foo K, Koh HF, Tow C, Zhang Y, et al. Group B Streptococcus Serotype III Sequence Type 283 Bacteremia Associated with Consumption of Raw Fish, Singapore. *Emerg Infect Dis*. 2016 Nov;22(11):1970-1973. doi: 10.3201/eid2211.160210. PMID: 27767904; PMCID: PMC5088028.
14. Durukan D, Read TRH, Murray G, Doyle M, Chow EPF, Vodstrcil LA, et al. Resistance-Guided Antimicrobial Therapy Using

- Doxycycline-Moxifloxacin and Doxycycline-2.5 g Azithromycin for the Treatment of Mycoplasma genitalium Infection: Efficacy and Tolerability. Clin Infect Dis. 2020 Sep 12;71(6):1461-1468. doi: 10.1093/cid/ciz1031. PMID: 31629365.
15. Eyre DW, Town K, Street T, Barker L, Sanderson N, Cole MJ, et al. Detection in the United Kingdom of the *Neisseria gonorrhoeae* FC428 clone, with ceftriaxone resistance and intermediate resistance to azithromycin, October to December 2018. Euro Surveill. 2019 Mar;24(10):1900147. doi: 10.2807/1560-7917.ES.2019.24.10.1900147. PMID: 30862336; PMCID: PMC6415501.
  16. Houéto D. The social determinants of emerging infectious diseases in Africa. MOJ Public Health 2019 Mar;8:57-63.
  17. Russo GB, Goyal T, Tyler K, Thakur KT. Re-Emergence of Poliovirus in the United States: Considerations and Implications. Ann Neurol. 2022 Nov;92(5):725-728. doi: 10.1002/ana.26504. Epub 2022 Oct 6. PMID: 36120838.
  18. Lai Y, Purnima P, Ho M, Ang M, Deepak RN, Chew KL, et al. Fatal Case of Diphtheria and Risk for Reemergence, Singapore. Emerg Infect Dis. 2018 Nov;24(11):2084-2086. doi: 10.3201/eid2411.180198. PMID: 30334727; PMCID: PMC619979.
  19. Lum LHW, Tambyah PA. Outbreak of COVID-19 - an urgent need for good science to silence our fears? Singapore Med J. 2020 Mar;61(3):169. doi: 10.11622/smedj.2020034. Erratum for: Singapore Med J. 2020 Feb;61(2):55-57. PMID: 32488270; PMCID: PMC7905108.
  20. Leo YS, Chow A. Zika virus has arrived in Singapore. Lancet Infect Dis. 2016 Dec;16(12):1317-1319. doi: 10.1016/S1473-3099(16)30448-0. Epub 2016 Nov 15. PMID: 27998580.
  21. Sadaragani SP, Lim PL, Vasoo S. Infectious diseases and migrant worker health in Singapore: a receiving country's perspective. J Travel Med. 2017 Jul 1;24(4). doi: 10.1093/jtm/tax014. PMID: 28426114.
  22. Chee CB, Hsu LY, Sng LH, Leo YS, Cutter J, Wang YT. MDR TB transmission, Singapore. Emerg Infect Dis. 2013 Jul;19(7):1151-2. doi: 10.3201/eid1907.120372. PMID: 23763791; PMCID: PMC3713962.
  23. Wasserman S, Tambyah PA, Lim PL. Yellow fever cases in Asia: primed for an epidemic. Int J Infect Dis. 2016 Jul;48:98-103. doi: 10.1016/j.ijid.2016.04.025. Epub 2016 May 6. PMID: 27156836.
  24. Cutter J. Preparing for an influenza pandemic in Singapore. Ann Acad Med Singap. 2008 Jun;37(6):497-503. PMID: 18618062.
  25. Lum LHW, Badaruddin H, Salmon S, Cutter J, Lim AYT, Fisher D. Pandemic Preparedness: Nationally-Led Simulation to Test Hospital Systems. Ann Acad Med Singap. 2016 Aug;45(8):332-7. PMID: 27683737.
  26. <https://www.who.int/activities/prioritizing-diseases-for-research-and-development-in-emergency-contexts>

## LEARNING POINTS

- **Emerging infections have been increasingly recognised in global public health over the past three decades. It is not a question of IF but WHEN the next emerging infection will once again result in another pandemic that will test the robustness of our healthcare and socioeconomic structure as well the agility and resilience of mankind.**
- **Emerging infections can take the form of a novel or unrecognised infection (many of which are zoonotic viruses), previously known infections that may have spread to new geographical areas or populations due to climatic changes, migration of vectors and international travel, or re-emerging infections due to antimicrobial resistance or breakdown of immunisation programmes or public health measures.**
- **Frontline physicians should be vigilant and aware of reported emerging infections through surveillance platforms and online resources, have a high index of suspicion of importation of emerging infections in travellers or migrants whilst routinely providing holistic care including preventive measures such as pre-travel advice, ensure vaccinations are up to date, and advocate antimicrobial stewardship. Essential components of an outbreak response include mobilising a response team, ensuring infrastructure is in place, good communication amongst healthcare workers as well as with patients, and lastly training, safety, and welfare of frontline staff.**