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Yellow Fever – What It Means for Singapore

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Yellow fever (YF) is an arthropod-borne viral haemorrhagic disease transmitted by *Aedes aegypti* and *Hemagogus* mosquitoes, belonging to the flavivirus family which includes dengue, Zika and West Nile virus. Infected persons may have symptoms that range from subclinical infection to multi-organ failure and death. In contrast to dengue which has a low mortality rate of approximately 1%, case-fatality ratio of YF is 20%-50% among the approximately 15% of infected persons who develop severe disease.¹ Fortunately, YF can be prevented using a live vaccine which confers lifelong protection 10 days after the vaccine is administered. The international certificate of vaccination or prophylaxis is issued by the World Health Organization (WHO) to a person who has been vaccinated. It is valid for life, and may be a requirement for entry to certain countries under International Health Regulations (IHR).²

YF is endemic in the tropical regions of South America and sub-Saharan Africa, and is estimated to cause up to 60,000 deaths worldwide every year.³ A succession of recent outbreaks has highlighted the propensity for YF to spread to urban areas and other geographic regions. In December 2015, a large urban outbreak of YF occurred in Angola with subsequent spread to Democratic Republic of Congo (DRC), resulting in 962 confirmed cases (884 in Angola and 78 in DRC) and emergency vaccination of over 30 million persons.⁴ The shortage of emergency vaccine stockpile prompted health authorities to immunise inhabitants with one-fifth of the standard dose to extend the vaccine supply. This outbreak spread to other countries including Kenya and resulted in the first ever cases of YF in Asia.⁵ In March 2016, 11 imported YF cases were reported in travellers returning to China from Angola, despite the requirement by China for proof of vaccination under IHR. Although no local transmission subsequently occurred, this represented a potentially catastrophic event of YF introduction into a large unvaccinated population.

Soon after the WHO announcement in February 2017 declaring the end of the year-long YF epidemic in Africa, Brazil reported the worst epidemic of YF seen in decades.

The earliest cases were first reported from the State of Minas Gerais as early as December 2016,⁶ followed by continued expansion towards the Atlantic coast of the country and closer to more densely populated areas of Rio de Janeiro. As of July 2017, there have been 3240 suspected cases reported with an overall case fatality rate of 35% among confirmed cases.⁷ In response to the ongoing outbreak, health authorities and the Brazilian Ministry of Health have conducted mass vaccination campaigns among residents in affected areas. In order to do so, Brazil requested 3.5 million doses of YF vaccine from global emergency stockpile managed by the International Coordinating Group (ICG) on Vaccine Provision for YF.⁸

Efforts to curb the spread of YF were hampered by the shortage of vaccines. Globally, YF vaccines continue to be in short supply due to pharmaceutical manufacturing problems, and the world's emergency vaccine stockpile faces impending depletion in the face of the Brazil outbreak. In the United States (US), there are ongoing efforts to import and use an alternative YF vaccine from an external source⁹ and the US Centers for Disease Control and Prevention (CDC) has issued a Level 2 travel alert recommending enhanced precautions to be taken prior to travel to affected areas.¹⁰

This current outbreak of YF in Brazil is disturbingly reminiscent of the Zika virus epidemic that spread across the Americas.¹¹ Singapore reported the first laboratory-confirmed Zika virus infection in April 2016 in a business traveller who returned from Brazil. National preparedness plans were in place, and initial efforts at containment included intensive vector control and mandatory hospital quarantine. However, subsequent clusters of Zika were detected, and Zika has now become a sporadic viral infection in Singapore.

The ongoing outbreak of YF in Brazil presents a serious public health risk for Singapore. Singapore receives over 50,000 travellers from the Americas every year, far higher than the 8000 travellers who arrive from Africa.¹² YF infection results in viraemia, which may persist for up to 5 days. The prospect of a viraemic patient being bitten by a competent vector, and causing onward autochthonous spread into an almost completely unvaccinated population

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is the scenario being contemplated. Local ecology, high volume of international travel, low vaccine coverage and an overlapping clinical syndrome with other endemic infections are prime conditions for a potentially devastating outbreak in Asia.¹³

Healthcare facilities in Singapore are expected to be fully capable of assessing a returning traveller with transmissible infections. Building on experience preparing for Ebola and Zika, YF preparedness measures have been put in place at national and hospital levels. These include enhancing laboratory diagnostic capability, clinical protocols, surveillance systems, ‘One Health’ collaborations with environmental agencies involved in vector control and plans to make YF vaccines available. The challenge lies in the broad range of differential diagnoses, including other viral haemorrhagic fevers, in an ill returning traveller from South America or sub-Saharan Africa. This increases the risk that an actual case of YF would go undiagnosed or mistaken for another non-specific febrile illness. Such an individual would be capable of spreading YF to local mosquitoes during the period of viraemia.

If local urban transmission of YF occurs in Singapore, and serological evidence subsequently demonstrates circulation in primate populations, Singapore could conceivably join the list of countries with documented YF transmission. Despite the availability of effective vaccination, persons in whom the YF vaccination is contraindicated or to be used with caution—such as immunocompromised persons, pregnant women, and infants under 9 months—could remain susceptible to YF infections acquired locally. Such a development, which is possible although currently improbable, would have far-reaching clinical, public health and economic repercussions. This would also adversely impact Singapore’s hard-earned status as a major international hub for trade and travel, for increased restrictions would be enforced upon persons travelling to and from the country under the IHR.

Singapore requires YF vaccination of all travellers entering Singapore from countries with documented YF transmission, and isolation of suspected cases can be mandated under the Infectious Disease Act. Aggressive vector control, ring vaccination protocols, quarantine and personal protective measures would be important strategies to activate if the first case of YF is detected in Singapore.

Despite all the factors that make the transmission of YF conducive in Asia, a possible explanation for its absence thus far is the hypothesis that cross-reactive dengue antibodies confer partial protective immunity to YF, in a region where dengue is endemic.¹⁴

In a health survey to understand health-seeking behaviour of Singaporeans attending a travel health clinic, it was found that less than 20% of them had consulted a doctor

before prior travel experience, and less than 70% of those who consulted a doctor before travel received pretravel or vaccination advice.¹⁵ The low rates of pretravel consultation is an area that may be focused on in improving destination-related vaccination uptake and travel precautions to mitigate the risks of infectious disease importation into Singapore.

With increased globalisation, Singapore will always be potentially vulnerable to the threat of infectious diseases that are imported as a result of international travel. Ongoing vigilance, strict adherence to international guidelines and investments in preparedness strategies are our safeguards against the risk of a YF outbreak in Singapore.

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