A case of imported Monkeypox in Singapore

Increasing international travel from areas with infectious disease outbreaks poses continual risks for the global spread of emerging infectious diseases (EIDs). As reported by Adesola Yinka-Ogunleye and colleagues,[1] the re-emergence of monkeypox in Nigeria in 2017 resulted in disease exportation by two travellers to the UK and one to Israel. Singapore, a globally connected city-state with 5·6 million people and where 65·6 million air travellers were received in 2018, is not spared.[2,3] On May 7, 2019, a 38-year-old Nigerian man was admitted to the National Centre for Infectious Diseases with fever, muscle aches, chills, and nodular skin lesions since April 30, 2 days after arrival in Singapore.[4] As monkeypox was suspected on clinical presentation, the patient was isolated immediately in a negative-pressure room and notified, as legally required, to the Ministry of Health.

Diagnosis was confirmed on May 8, 2019, by the National Public Health Laboratory using electron microscopy, PCR, and genome sequencing of blister fluid. The Ministry of Health immediately initiated contact tracing of individuals at risk using traditional interviews and surveillance camera footage at venues the patient had visited. 22 close contacts were offered the vaccinia vaccine as prophylaxis and were placed under quarantine (home-based or in designated government quarantine facilities). Because all health-care workers managing the patient had used appropriate personal protective equipment, they could continue to work while monitoring their own potential symptoms. The Nigerian National International Health Regulations Focal Point were informed about the patient. No secondary cases were detected.

Various EID preparedness capabilities were in place owing to Singapore's previous experiences with EIDs (eg, severe acute respiratory syndrome, Nipah, and Zika). The Ministry of Health routinely assesses risk of EIDs and proactively communicates information to all medical practitioners about disease epidemiology, diagnostic criteria, notification guidelines, and referral platforms. In 2018, in response to the Nigerian monkeypox outbreak, the Ministry of Health had alerted medical practitioners, a factor which contributed to awareness and early diagnosis. To enable EID management within a single centre, the National Centre for Infectious Diseases was purpose built as a 330-bed facility with onsite capabilities including the National Public Health Laboratory, which develops certified testing protocols for EIDs. This laboratory enables rapid diagnostic confirmation and provision of appropriate patient management. Additionally, frequent simulations test the national infectious disease preparedness framework to ensure readiness and competency.

This case reinforces the need for constant global disease monitoring, preparedness training including regular simulations, and capacity building of health-care systems as important measures that could be adopted, especially in other areas at high risk of disease importation.

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Sustainable actions needed to mitigate dengue outbreak in Bangladesh

We read with interest the Review by Lydia Franklinos and colleagues[1] about the effect of global change on mosquito-borne disease, which was published around the same time there was an increasing death toll from, and hospitals full of patients with, dengue in Bangladesh. The country is facing its worst dengue outbreak since 2000, with fears of mortality running deep as the infection reaches all parts of the country, particularly affecting children, pregnant women, and older people.[2–4] In 2018, 10 148 dengue cases were reported,[2] and as of Aug 23, 2019, 59 592 people have been infected, with 47 confirmed deaths (the unofficial death toll is 111).[3]

Dengue infection in tropical and subtropical countries is not new, but the outbreak in Bangladesh requires further contemplation. Poor water, sanitation, and hygiene systems, alongside a dense population, are prolonging the outbreak in Bangladesh. To prevent outbreak progression, short-term nationwide actions by government officials, non-governmental organisations, policy makers, and institutions must be initiated. Key mosquito breeding areas should be destroyed and sprayed with insecticides. Measures to address waterlogging and cleaning of canals, water tanks, rainwater collection tanks, sump pits, downpipes, and gutters

should be put in place. Distribution of dengue detection kits to health centres and training of health facilitators would be beneficial in rural areas. Since personal clothing acts as a preventive measure, a special focus should be given to school children through the improvement of school uniform. Mass media could act by disseminating information about dengue phases, use of bednets and mosquito repellents, and wearing of clothing that light coloured, loose fitting, long sleeved, and breathable.

Long-term sustainable control of dengue virus is essential to manage future outbreaks. Actions that could be taken include nationwide event-based dengue surveillance with environmental management; research on ecological, environmental, and entomological indicators of infection; development of geospatial and risk mapping for scoping vulnerable zones;[1] involvement of researchers to capture data on the trend and virus evolution over the geographical time period, considering seasonal influences and the impact of climate change;[1] and the implementation of inexpensive and accessible bioassay systems for early detection of dengue, especially in rural areas. In addition, a dengue virus vaccine could be launched in the country as it has been shown to reduce severity and hospital admissions by 80–90% among children in Asia.[5]

In addition to existing national guidelines from the Directorate General of Health Services in Bangladesh, we suggest the development of a national dengue control programme for clinical management of the infection, alongside a widespread community awareness campaign for greater responses. Although the government of Bangladesh has initiated some short-term measures, mainly in Dhaka, countrywide comprehensive action measures have been inadequate. The government and relevant stakeholders should prioritise this dengue outbreak and adopt a holistic dengue control programme to prevent premature deaths and reduce the disease burden of this epidemic.

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Suboptimal dosing triggers artemisinin partner drug resistance

3-day artemisinin-based combination therapy regimens are the treatment of choice for most cases of uncomplicated malaria. Their efficacy relies on artemisinin to clear most of the parasite load. The mechanism of action of artemisinin requires activation by haem, resulting in promiscuous targeting of parasite proteins, ensuring both specificity and potency to deliver unrivalled antiparasitic activity.[1]

Artemisinins are cleared relatively rapidly from circulation (usually in a few hours, depending on the derivative and formulation), a property that presents a weakness to parasites. This relatively short-term exposure to the drug has resulted in a selection of parasites carrying mutations in the propeller domain of the *kelch13* genes that are associated with extended ring stages of development.[2] This global developmental adjustment in lifecycle allows parasites to outlast the short-lived artemisinin component of artemisinin-based combination therapies, rather than causing treatment failures because of selection for conventional resistance.

Because 3-day courses of artemisinin do not cure infections, even those with so-called artemisinin-sensitive parasites, 3-day artemisinin-based combination regimens depend on a partner drug to achieve a complete cure. When faced with parasites with altered lifecycles, partner drug-resistance associated with treatment failures is then attributed to so-called artemisinin resistance, as reported by Rob van der Pluijm and colleagues[3] in the Greater Mekong subregion. When dihydroartemisinin–piperaquine treatment did not cure infections, van der Pluijm and colleagues found that a new combination of dihydroartemisinin–piperaquine–mefloquine increased efficacy.[3] However, dihydroartemisinin might be relatively less stable than artesunate in drug formulations,[4] and adding a third partner drug that is itself selecting for resistance might not provide a sustained advantage if the artemisinin component is not dosed optimally.

More effective measures must be taken immediately. In the short term, several artemisinin-based combination therapies (eg, artesunate plus pyronaridine and artesunate plus mefloquine) that are effective in geographical areas with parasites that

For the **guidelines from the Directorate General of Health Services** see http://www.dghs.gov.bd/images/docs/Guideline/NationalGuidelinefor Dengue2018.pdf