

Of migration, macaques, mice and men

Jun-Yang Tay^{1,2}, MBBS, MRCP, Shawn Vasoo^{1,2,3}, MBBS, MRCP, Yee-Sin Leo^{1,2,3,4}, MBBS, FRCP

Monkeypox was first isolated by a group of Danish scientists in macaques imported from Singapore in 1958,⁽¹⁾ with the first case of human disease being recorded in 1970 in the Democratic Republic of Congo. For Singapore, things came full circle on 7 May 2019, when a Nigerian man who had travelled to Singapore for a conference was admitted to the National Centre for Infectious Diseases and diagnosed with monkeypox, with confirmatory testing performed within 24 hours of his arrival.⁽²⁾

Singapore received 18 million visitors in 2018.⁽³⁾ This high flow of human traffic from different countries exposes it to the attendant risks of importation of various emerging infectious diseases. Over the years, importation of novel pathogens included Nipah (1999), SARS (2003), chikungunya (2008), pandemic influenza H1N1 (2009), Zika (2016) and monkeypox in 2019. Monkeypox is a zoonosis transmitted via contact with the monkeypox virus (e.g. from infected lesions or in large respiratory droplets). This may result from contact with animal reservoirs (e.g. rodents or primates) or via human-to-human transmission, although the latter is thought to be limited and unable to sustain the chain of transmission in the human population. Monkeypox continues to be persistent in regions in Central and West Africa, primarily via zoonotic spread. This is likely attributable to multiple reasons, including the cessation of smallpox vaccination, which afforded cross-protection against monkeypox,⁽⁴⁾ increasing interaction of humans with animal reservoirs, and as yet undetermined ecologic and environmental factors. The presence of a zoonotic reservoir also makes monkeypox impossible to eradicate, unlike smallpox.

Monkeypox has an incubation period of 5–21 days, with a prodrome lasting 1–5 days that consists of fever, malaise and lymphadenopathy, followed by a characteristic pustular rash that can cover the entire body.⁽⁴⁾ Persons are thought to be infective during the symptomatic period until scabbing and desquamation is complete; fortunately, in this case, the patient with monkeypox fell ill only after his arrival in Singapore. Public health measures were also rapidly instituted, centring on contact tracing, vaccination (with smallpox vaccine) and quarantine of close contacts.

Outside of Central and West Africa, monkeypox was exported to the United States in 2003 through exotic pet imports from Ghana, leading to 37 confirmed human infections in six Midwest states. In 2018, monkeypox was exported to the United Kingdom (two separate cases in unrelated travellers who had returned from Nigeria, with one transmission to a healthcare worker from one of these cases) and Israel (in a returned traveller from Nigeria).⁽⁴⁾ A further case of monkeypox was exported to England in December 2019.⁽⁵⁾ The Singapore case marked the first exportation of this disease to Asia.

The fact that the patient received a timely diagnosis and appropriate care, including the institution of isolation precautions, and that public health measures were rapidly instituted was not serendipitous. Since our experience with SARS in 2003, Singapore has built robust surveillance and response systems to face the challenge of emerging infectious diseases. This patient was triaged at the emergency department for further evaluation for a potential imported emerging infectious disease, given his symptoms and travel history. Our National Public Health Laboratory, which provides specialised testing as part of outbreak response, was then able to confirm the diagnosis of monkeypox via two separate polymerase chain reaction assays and electron microscopy on lesion material within 24 hours of the patient's admission. Nonetheless, systems are as strong as their 'weakest link' and, as Louis Pasteur notes, 'Chance favours the prepared mind' – the importance of the astute physicians who considered the diagnosis of monkeypox and acted on it cannot be overstated.

The exact reasons leading to the 2017 resurgence of monkeypox in Nigeria, which had not seen a case since 1978, remain to be elucidated.⁽⁶⁾ Monkeypox is but one of a myriad of zoonoses that have emerged over the years that pose a threat to human health. Besides strengthening health-infrastructure and surveillance networks, the global community needs to invest in the 'One Health' approach to understand and modify the factors associated with the emergence of various zoonotic diseases and, where appropriate, encourage the development of novel therapeutics, including vaccines. The arrival of monkeypox on our shores serves as a timely reminder that Singapore needs to remain vigilant in the surveillance and detection of emerging and re-emerging infectious diseases, and to continue to work closely with the greater international community to deal with these challenges that confront us.

REFERENCES

1. von Magnus P, Anderson EK, Petersen KB, Birch-Anderson A. A pox-like disease in cynomolgus monkeys. *Acta Pathol Microbiol Scand* 1959; 46:156-76.
2. Singapore confirms first case of monkeypox, patient's close contacts quarantined. In: Channel NewsAsia [online]. Available at: <https://www.channelnewsasia.com/news/singapore/monkeypox-case-imported-singapore-moh-11518664>. Accessed June 16, 2019.
3. Singapore Tourism Board. International visitor arrivals. Available at: <https://www.stb.gov.sg/content/stb/en/statistics-and-market-insights/tourism-statistics/international-visitorarrivals.html>. Accessed June 16, 2019.
4. Petersen E, Kantele A, Koopmans M, et al. Human monkeypox: epidemiologic and clinical characteristics, diagnosis, and prevention. *Infect Dis Clin North Am* 2019; 33:1027-43.
5. BBC News. UK patient diagnosed with monkeypox. December 4, 2019. Available at: <https://www.bbc.com/news/uk-england-50659118>. Accessed December 12, 2019.
6. Yinka-Ogunleye A, Aruna O, Dalhat M, et al. Outbreak of human monkeypox in Nigeria in 2017-18: a clinical and epidemiological report. *Lancet Infect Dis* 2019; 19:872-9.

¹National Centre for Infectious Diseases, ²Department of Infectious Diseases, Tan Tock Seng Hospital, ³Lee Kong Chian School of Medicine, Nanyang Technological University, ⁴Saw Swee Hock School of Public Health, National University of Singapore, Singapore

Correspondence: Dr Shawn Vasoo, Clinical Director, National Centre for Infectious Diseases, Tan Tock Seng Hospital, 11 Jalan Tan Tock Seng, Singapore 308433. shawn_vasoo@ncid.sg