

# Monkeypox – A danger approaching Asia

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**SUMMARY** Since the end of June 2022, there has been a dramatic increase in the number of monkeypox cases worldwide. Given the potential spread of this epidemic, WHO has declared the monkeypox epidemic a global public health emergency. In the face of the changing epidemiology during this monkeypox outbreak, vaccines and preventive measures are being researched around the world in response to this emerging disease. Recently, confirmed cases were reported in South Korea and Japan; as connections between countries around the world resume, imported cases may be inevitable. China is also concerned and prepared for the danger approaching Asia. In response to this risk, China issued the "Monkeypox Diagnosis and Treatment Guidelines" and the General Administration of Customs of China announced that travelers from countries reporting monkeypox cases and with suspected symptoms should be identified to customs upon entry. Chinese researchers have recently generated two pseudovirus reference materials for the monkeypox viral wild-type *B6R* gene and mutant *F3L* gene. Moreover, monkeypox as a communicable disease can be added to the current COVID-19 tracking system for better surveillance and management.

**Keywords** monkeypox, Asia, vaccine, preventive measures

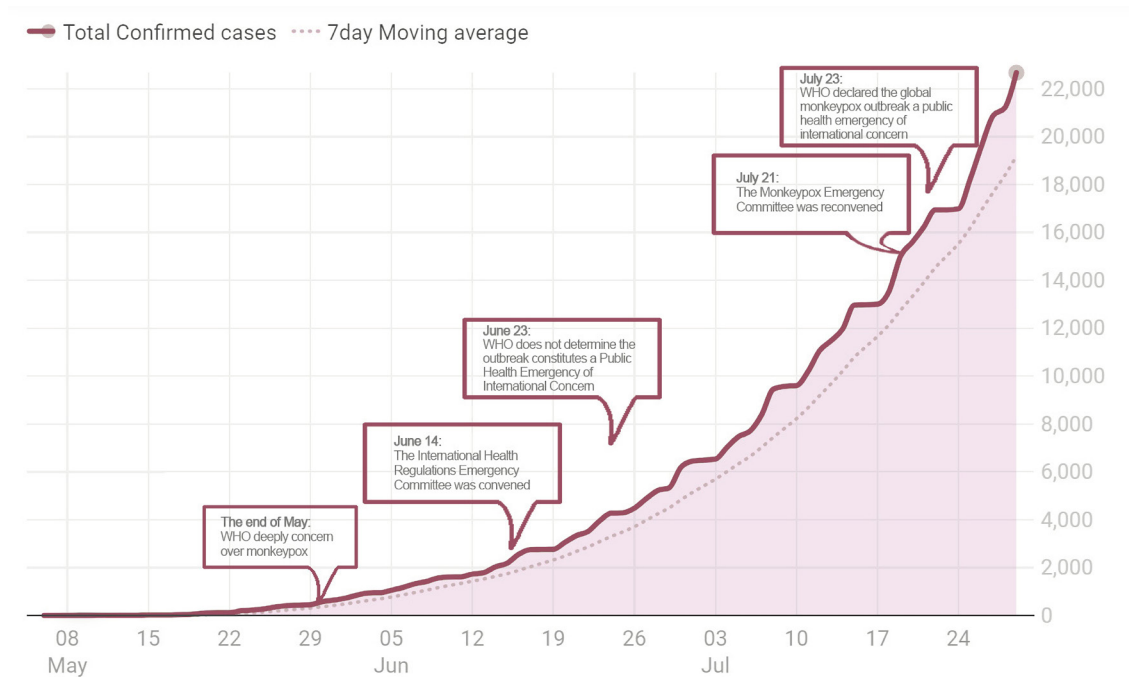
Monkeypox, a zoonotic disease, was first identified in humans in the Democratic Republic of the Congo in 1970. In the 50 years since its inception, the monkeypox endemic was concentrated in Central and West Africa. Sporadic cases reported in Europe and North America were linked to imported cases (1). On May 7, 2022, a confirmed case of monkeypox was first reported in the United Kingdom, and several countries subsequently reported cases of monkeypox, spanning the globe from Europe to North America, Africa, and Asia. Since the end of June 2022, cases have tended to sharply increase globally (2). Given the risk of this epidemic spreading, the WHO declared the monkeypox epidemic a global public health emergency, which is the WHO's highest level of public health alert (Figure 1).

## The changing epidemiology of monkeypox

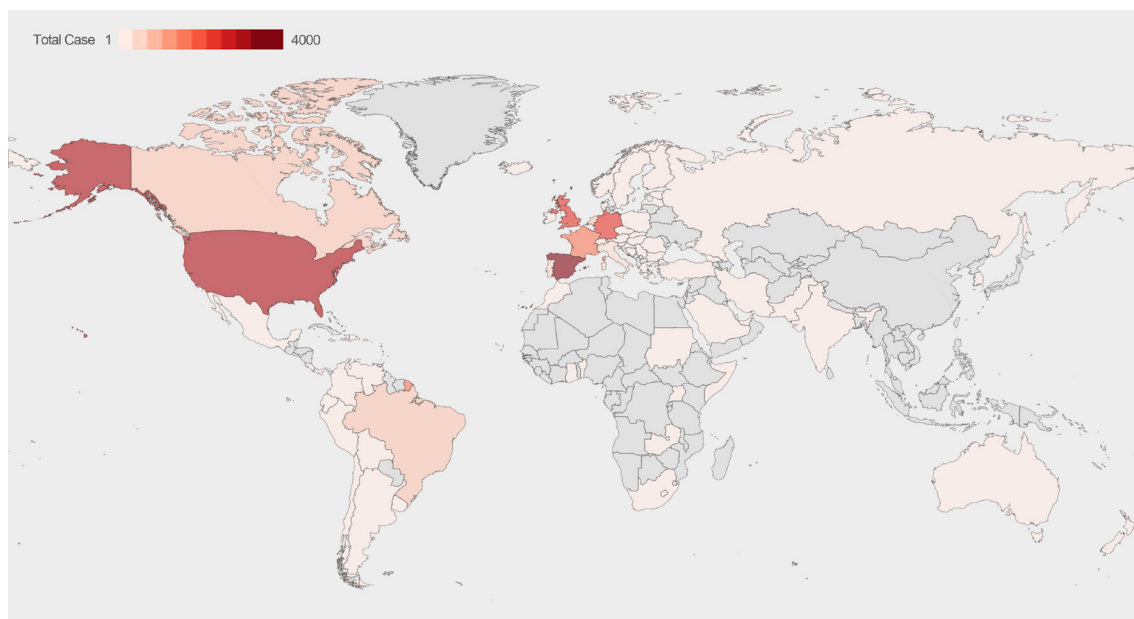
During the 2022 monkeypox outbreak, cases were reported from all five continents in less than three months. More than 90% of the known cases were in men who have sex with men (MSM). More importantly, none of the patients had a clear history of travel to the site of the epidemic. This aspect is very different from before

and has attracted the attention of researchers globally. An etiologic and epidemiologic study (3) published in the New England Journal of Medicine (NEJM) reported that 95% of the patients reported in the current monkeypox outbreak were infected via sexual contact and that monkeypox virus DNA was detected in the semen of 95% of patients. However, more clinical evidence needs to be gathered to corroborate whether monkeypox can be transmitted sexually.

A systematic review (4) reported that confirmed and suspected cases of monkeypox have clearly tended to increase since the 21st century. Over 19,000 cases were reported from 2000-2019. However, the current outbreak is spreading even more rapidly, with 80 countries worldwide reporting monkeypox infections since May 2022 and more than 17,000 cases have been confirmed as of July 23, 2022 (Figure 2). The number of confirmed cases in less than 3 months is comparable to the number over the last 20 years. A key reason for the rapid increase is the lack of protection from smallpox. Studies have indicated that the vaccine used for smallpox provides about 85% protection against monkeypox due to cross-immunization, which can prevent the occurrence of monkeypox or reduce the severity of symptoms (5).



**Figure 1. Timeline of WHO's responses to monkeypox outbreak.** Data source: <https://ourworldindata.org/monkeypox>; <https://www.who.int/news-room/fact-sheets/detail/monkeypox>



**Figure 2. Global distribution of monkeypox cases.** Data source: <https://ourworldindata.org/monkeypox>

Since the WHO declared the eradication of smallpox in 1980, smallpox vaccination has been discontinued worldwide (6). According to Thornhill *et al.* (3), the median age of patients during this outbreak was 38 years, so one can reasonably infer that most of this population lacks protection from smallpox. In addition, the relaxation of preventive and control measures for COVID-19 in many European countries has led to more frequent movement and travel of people. This is also one of the possible reasons for the rapid spread of the

epidemic.

Genetic mutation of the monkeypox virus is also a concern. The general understanding is that monkeypox viruses are unlikely to undergo sudden mutations that would cause a substantial increase in human-to-human transmission because they are DNA viruses and are better at detecting and repairing mutations than RNA viruses. However, a study (7) found that MPXV B.1, a post-April strain of the monkeypox virus, has an APOBEC3 escape mutation. This strain has mutated more, making the virus

more adaptable to the human environment compared to a closely related virus (MPVX A.1.1) identified in 2018-2019.

### Vaccine stockpile and vaccination

To date, there is no specific vaccine for monkeypox virus. The vaccines that exist for the prevention of monkeypox in high-risk groups or post-exposure prophylaxis are still smallpox-specific vaccines. Thus far, the third generation of smallpox vaccines has been developed. The effectiveness of the second-generation vaccine ACAM2000 and the third-generation vaccine IMVAMUNE at preventing monkeypox infection and for post-exposure vaccination has been partially corroborated by the results of preclinical and clinical studies (8,9).

Currently, the use of smallpox vaccine for monkeypox prevention is still mainly restricted to high-risk groups or health personnel who treat the disease. Given the risk of an outbreak, the United Kingdom has begun offering the smallpox vaccine to some medical personnel or people at risk of exposure to the monkeypox virus. On July 22, the European Medicines Agency recommended that the European Union approve an expanded indication for smallpox vaccines to prevent monkeypox and interrupt transmission of the virus. However, mass vaccination against monkeypox is not required or recommended at this time.

Immunodeficiency may lead to worse clinical outcomes of a monkeypox infection (10). Liu *et al.* (11) suggested that an advanced or poorly virally controlled HIV infection may lead to more severe outcomes after monkeypox infection. According to Thornhill *et al.* (3), there were no differences in clinical manifestation or outcomes between patients infected or not infected with HIV, but that study only included (people living with HIV) PLWH whose viral load was well-controlled. Therefore, awareness of the potentially serious outcomes of monkeypox infection is crucial for people with advanced or poorly virally controlled HIV. Mass vaccination of MSM, the main at-risk population, is not recommended at this time but enhanced monitoring of their HIV infection status is strongly recommended.

### Risk of monkeypox outbreaks in mainland China

Confirmed cases of monkeypox in countries neighboring China such as South Korea and Japan have been reported. Although most cases during this outbreak involve MSM, they also include a small number of children with no known epidemiological link to those cases. This indicates that close contact, droplets, and aerosols can still pose a considerable risk of transmission. Non-sexual close contact transmission still needs to be considered seriously to prevent and control the epidemic.

With the gradual restoration of connections between countries around the world, imported cases may be

inevitable in China (12). In response to this risk, China issued the "Monkeypox Diagnosis and Treatment Guidelines" (13) in June; on July 24, the General Administration of Customs of China announced that travelers from countries reporting monkeypox cases or with suspected symptoms should be reported to customs upon entry. In fact, monkeypox as a communicable disease can be added to the current COVID-19 tracking system for better surveillance and management. Chinese researchers have recently generated two pseudovirus reference materials for the monkeypox viral wild-type *B6R* gene and mutant *F3L* gene. These two reference materials can be used to develop monkeypox virus detection kits, to verify their performance confirmation, to validate their methodology, to control quality in the laboratory, and to provide a "biological scale" for monkeypox virus diagnostic results, providing technical support to effectively reduce "false negatives" (14).

In light of the current strategy of "dynamic zero COVID-19" in China, the risk of monkeypox spreading in China is still low. Despite these favorable conditions, the harm caused to the population and society by the monkeypox epidemic should not be underestimated. The average symptomatic period after infection with monkeypox is three weeks, and the proportion of asymptomatic patients is low. At least 3 weeks of isolation are required for people infected with the monkeypox virus. COVID-19 is still rampant around the world. The spread of the monkeypox epidemic will have a negative impact on the labor supply and the provision of goods and services.

### Conclusion

We are now faced with high inflation globally, which will also have a huge impact on overall social efficiency. The risk of imported monkeypox cases should be kept in mind by the government. Public education about monkeypox prevention and related knowledge for the general public, including MSM, can help with early detection and reporting of cases and reduce transmission. The establishment of a comprehensive disease surveillance system, and particularly the establishment of sentinel sites in relevant institutions such as dermatology and sexual health clinics, will facilitate the early detection of monkeypox cases and close contact tracing.

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## References

1. Moore MJ, Rathish B, Zahra F. Monkeypox. <https://www.ncbi.nlm.nih.gov/books/NBK574519/> (accessed on July 23, 2022).
2. UN News. Monkeypox not presently a global public health emergency: WHO. <https://news.un.org/en/story/2022/06/1121362/> (accessed on July 25, 2022).
3. Thornhill JP, Barkati S, Walmsley S, *et al.* Monkeypox virus infection in humans across 16 countries - April-June 2022. *N Engl J Med.* 2022; doi:10.1056/NEJMoa2207323.
4. Bunge EM, Hoet B, Chen L, Lienert F, Weidenthaler H, Baer LR, Steffen R. The changing epidemiology of human monkeypox-A potential threat? A systematic review. *PLoS Negl Trop Dis.* 2022; 16:e0010141.
5. Fine PE, Jezek Z, Grab B, Dixon H. The transmission potential of monkeypox virus in human populations. *Int J Epidemiol.* 1988; 17:643-650.
6. World Health Organization. Monkeypox. <https://www.who.int/news-room/fact-sheets/detail/monkeypox> (accessed July 25, 2022).
7. Isidro J, Borges V, Pinto M, *et al.* Phylogenomic characterization and signs of microevolution in the 2022 multi-country outbreak of monkeypox virus. *Nat Med.* 2022; doi:10.1038/s41591-022-01907-y.
8. Petersen BW, Kabamba J, McCollum AM, Lushima RS, Wemakoy EO, Muyembe Tamfum JJ, Nguete B, Hughes CM, Monroe BP, Reynolds MG. Vaccinating against monkeypox in the Democratic Republic of the Congo. *Antiviral Res.* 2019; 162:171-177.
9. Keckler MS, Salzer JS, Patel N, Townsend MB, Nakazawa YJ, Doty JB, Gallardo-Romero NF, Satheshkumar PS, Carroll DS, Karem KL, Damon IK. IMVAMUNE® and ACAM2000® provide different protection against disease when administered postexposure in an intranasal monkeypox challenge prairie dog model. *Vaccines (Basel).* 2020; 8:396.
10. Liu X, Jiang XQ, Zhu Z, Sun L, Lu HZ. The novel monkeypox outbreak: What should we know and reflect on?. *Zoonoses.* 2022; DOI: 10.15212/ZOONOSES-2022-0022.
11. Liu X, Zhu Z, He Y, Lim JW, Lane B, Wang H, Peng Q, Sun L, Lu H. Monkeypox claims new victims: The outbreak in men who have sex with men. *Infect Dis Poverty.* 2022; 11:84.
12. Wei Q. Is China ready for monkeypox? *Animal Model Exp Med.* 2022 Jul 27. doi: 10.1002/ame2.12259.
13. Monkeypox Diagnosis and Treatment Guidelines. <https://baijiahao.baidu.com/s?id=1735900860873446404&wfr=spider&for=pc> (accessed July 29, 2022). (in Chinese)
14. China Institute of Metrology successfully developed monkeypox virus pseudovirus standard material. [https://www.cqn.com.cn/zgzlb/content/2022-07/28/content\\_8846463.htm](https://www.cqn.com.cn/zgzlb/content/2022-07/28/content_8846463.htm) (accessed July 29, 2022).

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