Perspectives

Neglected Zoonotic Monkeypox in Africa but Now Back in the Spotlight Worldwide

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On July 23, 2022, the World Health Organization (WHO) Director-General, Dr. Tedros Adhanom Ghebreyesus claimed monkeypox a Public Health Emergency of International Concern (PHEIC), the 7th such an event in the 21st century (*1*). This is an alarming challenge to the world while we are still combating the coronavirus disease 2019 (COVID-19) pandemic. Until mid-August, approximately 40 thousand cases had been reported in more than 89 nations and regions worldwide (*2*).

Monkeypox was named upon its first discovery in monkeys in 1958 and was first identified in humans in 1970 (*3*). Monkeypox is usually a self-limiting disease caused by monkeypox virus (MPXV), a member of the *Orthopoxvirus* genus in the family *Poxviridae* (*4*). MPXV is phylogenetically divided into two clades: West African clade as Clade two (II) and Congo Basin (Central Africa) clade as Clade one (I). The Clade II strain of MPXV is linked to the current monkeypox outbreak. Monkeypox presents with fever, an extensive characteristic rash and usually swollen lymph nodes (*4*). However, the largest study of 2022 confirmed monkeypox cases to date identified new clinical symptoms that were similar to those of syphilis and other sexually transmitted infections and could easily lead to misdiagnosis (*5*). MPXV is not so tightly host restricted and employs wild rodents as primary reservoirs with occasional spillover leading to cases of MPXV infections in humans (*4*). Animal-to-human (zoonotic) transmission can occur from direct contact with the blood, bodily fluids, or cutaneous or mucosal lesions of infected animals. Human-to-human transmission can result from close contact with respiratory secretions, skin lesions of an infected person, or recently contaminated objects (*4*). Detection of viral DNA by polymerase chain reaction (PCR) is the preferred laboratory test for monkeypox. The best diagnostic specimens are directly from rashes — skin, fluid, or crusts, or biopsy where feasible (*6*).

Monkeypox is a viral zoonotic disease that occurs primarily in tropical rainforest areas of Central and West Africa and is occasionally exported to other regions (*4*). In 2003, the first monkeypox outbreak outside of Africa was in the United States of America and was linked to pet importation from Africa (*4*). In recent years, the monkeypox epidemic in Central and West Africa has been relatively active, and multiple cases of monkeypox have also been identified in several non-endemic countries (*4*). MPXV in Africa was grossly neglected by international community for over five decades prior to the global outbreak that has affected wealthy countries in North America and Europe since May 2022 (*1*). With these cases spreading worldwide, without epidemiological links with outbreaks among men who have sex with men (MSM), it warrants urgent public health control measures to contain the spread of the MPXV and investigate the underlying pathophysiology, including genetic modification of the virus (*6*).

In 1980, smallpox was eradicated under vaccination, and its related vaccine programs were gradually discontinued. Vaccination against smallpox with a first generation vaccinia virus-based smallpox vaccine was shown to be 85% effective in preventing monkeypox in the past (*4*). Since the smallpox vaccine can also prevent monkeypox, the termination of the smallpox vaccine program at the time also caused a surge in monkeypox-endemic areas.

The recent gradual lifting of COVID-19-related travel restrictions in West and Central Africa may have contributed to an increase in monkeypox cases. No cases of monkeypox infection have been found in the mainland of China, nor has the virus been found in animal hosts. However, on June 24, 2022, the first confirmed case of monkeypox appeared in Taiwan, China, which sounded the alarm for us. Most of the population in China (especially those born after 1981) have no history of smallpox vaccination and lack immune protection background against MPXV, which results in a large population susceptible to monkeypox. With the country's trade with Africa and the increasing number of African workers and tourists, the risk of importation of monkeypox has also increased objectively. In addition, MPXV is a zoonotic virus that can infect rodents and a variety of wild animals, recent reports indicated that the establishment of a reservoir of MPXV in animal populations in a previously non-

endemic region is now a distinct possibility and would make control and eradication much more challenging (*4*,*7*). The clinical symptoms of some people infected with MPXV are very similar to those of smallpox, and the pathogens are not easy to distinguish. The possibility of smallpox or monkeypox bioterrorism in the world increases the threat to public health and social security. We can learn from the experience of the COVID-19 pandemic, prepare technical reserves as early as possible, take the initiative to respond, and prevent endemic monkeypox before it occurs in China. Therefore, in order to effectively control and prevent monkeypox in China, specific real-time PCR and serological detection techniques have been successfully established in China CDC, which were successfully applied in the China-Sierra Leone Joint BSL-3 Laboratory to detect monkeypox cases and conduct molecular traceability in 2017 (*8*). In 2018, the experts in China CDC compiled and formulated the "Technical Plan for Emergency Response to Monkeypox Epidemic". On June 6, 2022, China CDC released: "Monkeypox Prevention and Control Technical Guidelines (2022 Edition)". In addition, "Guidelines for the Diagnosis and Treatment of Monkeypox (2022 Edition)" was jointly issued on June 14, 2022 by the National Health Commission and the State Administration of Traditional Chinese Medicine. The prevention of monkeypox in China should focus on the quarantine of entry personnel and imported animals. At present, it is recommended to control the human-to-human transmission of monkeypox through early detection and diagnosis of cases, isolation, and contact tracing as much as possible, and mass vaccination of the population is not currently recommended to prevent monkeypox. We should seriously study and treat monkeypox, but people should not panic.

Neglected zoonotic monkeypox has been restricted in Africa for fifty years but now it is back in the spotlight worldwide. Many questions surrounding the basic biology of MPXV demand answers to lay the foundations for developing effective strategies and tools to manage the disease. Scientists have always attached importance to the basic research on *Orthopoxvirus* and the research and development of prevention and control products. In recent years, several specific diagnostic reagents, novel therapeutic drugs, and preventive vaccines for monkeypox have been approved for commercial use in Europe and the USA. While vaccines and specific therapies have been approved to prevent and treat monkeypox, they are not currently used worldwide. It is imperative to strengthen relevant basic research funds, especially cooperation between industry, academia and research, and to strengthen the R&D and application reserves of safe and effective vaccines and drugs for monkeypox. In addition, assessment of potential routes for zoonotic and reverse-zoonotic transmission of MPXV is encouraged based on the clear One Health framework. To our knowledge, we are currently facing many challenges and difficulties against the global monkeypox epidemic, such as different economic and technological levels among nations and regions, uneven vaccine and drug reserves and distribution, difficulty in monitoring and management of MSM activities, atypical clinical manifestations and the risk of cryptic spread, so the MPXV evolution in large populations brings a lot of uncertainty to prevention and control. These challenges also shed light on global preparedness for future emerging infectious diseases or unknown Diseases X or even pandemics.

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