Editorial: Current Status of Non-Endemic Global Infections with the Monkeypox Virus

Dinah V. Parums, MD PhD
Science Editor, Medical Science Monitor, International Scientific Information, Inc., Melville, NY, USA
e-mail: dinah.v.parums@isi-science.com
Conflict of interest: None declared

Abstract

Monkeypox is caused by an orthopoxvirus, which is a DNA virus. Monkeypox is a zoonotic viral infection that has been endemic in West Africa and Central Africa for over a decade. Between 1 January and 22 June 2022, the World Health Organization (WHO) reported 3,413 laboratory-confirmed cases of monkeypox from 50 countries. Most cases (86%) were reported from Europe, with 2% from Africa and 11% from North and South America. In the US, the Centers for Disease Control and Prevention (CDC) identified an outbreak of monkeypox on May 17, 2022. In 99% of cases, the patients were men, 94% reported male-to-male sexual contact or intimate contact in the three weeks before they experienced symptoms of infection, 46% reported one or more genital lesions, and 41% had HIV infection. This initial data from the US showed widespread community transmission of monkeypox that mainly affected bisexual, gay, other men who had sex with men, and also ethnic and racial minority groups. Therefore, public health efforts in the US aim to prioritize these specific demographic groups for infection prevention and testing. By August 4, 2022, the US Department of Health and Human Services declared the monkeypox outbreak a public health emergency. This Editorial aims to present the current status of non-endemic global infections with the monkeypox virus, and current strategies for its prevention and management.

Keywords: Orthopoxvirus • Monkeypox • Zoonosis • Epidemic • Pandemic • Editorial

In the mid and late 1980s, a new retrovirus was identified, with high mortality, rapidly becoming a globally endemic disease. The retrovirus was later termed the human immunodeficiency virus (HIV) and the disease it caused became known as acquired immunodeficiency syndrome (AIDS) [1]. HIV-1 and HIV-2 resulted from the zoonotic transfer from African primate viruses [1]. This viral infection was not contained in the outbreak and epidemic stages and rapidly became a global pandemic and then a global endemic infection, representing an epidemiological failure in infection control [1]. Over forty years on, despite advances in highly active antiretroviral therapy (HAART), HIV is still associated with significant morbidity and mortality in most countries [1].

In the 1980s, medical school examination questions asked students and trainees to compare the epidemiological factors associated with successfully controlling and eradicating viral infections, such as smallpox, with HIV. At that time, the success of smallpox eradication was attributed to the control of contact transmission without socially difficult control associated with sexual transmission, lack of airborne spread, an effective vaccine, and the lack of viral animal reservoir [2]. Population smallpox vaccination ceased in 1980 [2].

It is possible that unless lessons have been learned and implemented from the recent COVID-19 pandemic, geographically localized epidemic zoonotic viral infections will continue to cause pandemic disease and, ultimately, global endemic disease [3]. In 2004, human monkeypox was identified in the US and was stated at that time to be the most important human orthopoxvirus infection since the eradication of smallpox [4].

In the US, the Centers for Disease Control and Prevention (CDC) identified an outbreak of monkeypox on May 17, 2022 [5]. By August 4, 2022, the US Department of Health and Human Services declared the monkeypox outbreak a public health emergency [5]. Following the first human case detection in the US, the CDC and health departments implemented case detection and reporting [5]. By July 22, 2022, there were 2,891 cases reported by 43 states, the District of Columbia (DC), and Puerto Rico, and the CDC received case report forms for 41% of cases (1,195 patients) by July 27, 2022 [5]. In 99% of cases, the patients were men, and 94% reported male-to-male sexual contact or intimate contact in the three weeks before they experienced symptoms of infection [5]. Also, 46% reported one or more genital lesions, and 41% had HIV infection [5]. This initial data from the US showed widespread community transmission of monkeypox that mainly affected bisexual, gay, and other men who had sex with men, and also ethnic and racial minority groups [5]. Therefore, public health efforts in the US aim to prioritize these specific demographic groups for infection control.
prevention and testing [5]. The current situation with monkeypox may represent yet another example of the failure of epidemiological control unless global action is urgently taken. Monkeypox is caused by an orthopoxvirus, which is a DNA virus. Monkeypox is a zoonotic viral infection that has been endemic in West Africa and Central Africa for over a decade [6,7]. Following an incubation period of between 4 and 21 days, the symptoms of monkeypox are similar to, but milder than, those for smallpox and include fever, impaired lung function, skin rash, and skin vesicles but without lymphadenopathy [6,7]. In immunocompetent individuals, the symptoms reported in endemic areas in West Africa were mild, with rarely reported cases of transmission between humans [6,7]. However, monkeypox virus infection may cause severe disease or mortality in children, the elderly, immunocompromised individuals, pregnant women, and patients with co-morbidities such as diabetes and HIV/AIDS [7].

In West Africa, the recent increase in the number of cases of monkeypox virus infection in the past three years may have been due to the diversion of public health resources due to the COVID-19 pandemic and recent outbreaks of Lassa fever [7]. At the same time, the movement of populations to forested areas and expansion of urban areas may have brought humans closer to the animal hosts, which will drive zoonotic viral transmission [7]. Data regarding the interhuman transmission of the monkeypox virus in Africa is lacking. However, identifying new cases of monkeypox in non-endemic areas was the first sign of interhuman viral transmission because no new animal reservoirs of infection have been identified outside Africa [7]. A further concern regarding contact tracing and identifying the source of monkeypox cases in non-endemic countries is that it has commonly presented as a sexually transmitted disease with genital and peri-anal lesions but mild generalized symptoms [7]. A recent phylogenomics study by Isidro et al. has shown that no new variants of the monkeypox virus have been identified [8]. Therefore, it is still unclear why the monkeypox virus has accelerated transmission to humans [8]. One hypothesis is that cessation of global smallpox vaccination since 1980 has resulted in reduced population immunity that has driven the emergence of monkeypox [8]. Several critical epidemiological observations support this theory that reduced herd immunity from smallpox vaccination drives the current wave of global infections [8,9]. Firstly, monkeypox has mainly been diagnosed in individuals aged 50 years or less. Also, animal studies have shown that vaccination with a vaccine containing live modified vaccinia virus Ankara (MVA-BN) (Imvanex®) protects against infection [7]. Animal studies and the previous success of using vaccines to eradicate smallpox support the hope for effective vaccines to prevent infection with the monkeypox virus. However, replicating smallpox vaccines should not be used due to their risk in immunocompromised individuals and the risk of recombination between the monkeypox virus and the vaccine strain [9,10]. Recombination among orthopoxviruses is a significant driver of their evolution [9,10]. It is important to note the current presentation patterns, transmission and spread of non-endemic monkeypox between humans. In July 2022, a study was reported by Blanco and colleagues from an international case series that described the clinical presentation, course, and outcomes of monkeypox virus infections that were all confirmed using the polymerase chain reaction (PCR) [11]. Between April and June 2022, 528 confirmed cases of monkeypox virus infections were confirmed at 43 sites in 16 countries [11]. In 98% of cases, non-endemic monkeypox infection was diagnosed in gay or bisexual men, of whom 75% were Caucasian with a median age of 38 years, and 41% had HIV infection [11]. The clinical presentation was a rash in 95%, and 73% had anogenital lesions, with sexual transmission likely from the patients’ history in 95% of cases [11]. The clinical presentation was a rash in 95%, and 73% had anogenital lesions [11]. Systemic symptoms preceded the rash, including fever in 62%, lethargy in 41%, myalgia in 31%, and headache in 27% [11]. Lymphadenopathy was identified in 56% of patients with a confirmed diagnosis of monkeypox [11]. Concomitant sexually transmitted infections (STIs) were reported in 29% of patients who were tested for STIs [11]. In this recent study, 5% of cases were given antiviral treatment, 70 (13%) were hospitalized due to a requirement for pain ano-rectal management, soft tissue infection, and pharyngitis, but no deaths were reported [11].

Between 1 January and 22 June 2022, the World Health Organization (WHO) reported 3,413 laboratory-confirmed cases of monkeypox from 50 countries, which resulted in one death [12]. Most cases (86%) were reported from Europe, with 2% from Africa and 11% from North and South America [9]. One death was reported from a patient in Nigeria in early 2022 [12]. The WHO continues to update the number of monkeypox cases worldwide and developments in prevention and treatment [12,13]. Currently, monkeypox is not classified as an STI. Infection with human monkeypox in non-endemic areas occurs incidentally through direct sexual or skin-to-skin contact, respiratory droplet spread, and from fomites such as towels [14].

Two live inactivated vaccinia virus vaccines are currently available, JYNNEOSTM and ACAM2000® [14]. Supportive care is sufficient for mild and self-limited cases of monkeypox [14]. Vaccinia immune globulin intravenous (VIGIV) is also available when supportive care is inadequate to relieve symptoms [14]. At this time, the US Food and Drug Administration (FDA) has approved two antiviral drugs for the treatment of monkeypox under the FDA expanded access program [14]. Preliminary phase 1 and open label clinical trial data have supported the use of tecovirimat (NCT00728689) and cidofovir (NCT01143181) [14].
Antiviral treatment is recommended for patients with severe infection, children, pregnant and breastfeeding women, immunocompromised patients, and when severe lesions are present around the eyes, mouth, and genitals [14].

Strategies should be urgently implemented to prevent the global spread of the monkeypox virus. These strategies should be driven by current knowledge of the epidemiology and pathogenesis of the monkeypox virus combined with lessons learned from the eradication of smallpox and the recent COVID-19 pandemic [11]. Non-replicating smallpox vaccines may provide cross-protection for individuals at high risk of infection or following exposure to any contacts. Active infection surveillance in humans and their contacts may be required. Also, infection surveillance in potential animal reservoirs in non-endemic areas may be necessary [7,11]. Finally, both COVID-19, due to SARS-CoV-2 infection, and monkeypox, due to monkeypox virus infection, should have taught us to ensure public health resources and protocols are established in endemic areas to predict and prevent endemic and pandemic zoonotic virus disease outbreaks [11].

Conclusions

Several important lessons should be learned from the recent COVID-19 pandemic to prevent the interhuman spread of the monkeypox virus and to prevent it from establishing in domesticated animals and wildlife in non-endemic regions. Public health strategies should be implemented to identify infected patients and their contacts and to implement vaccination programs in susceptible groups, which have now been identified.

References:

1. Sharp PM, Hahn BH. Origins of HIV and the AIDS pandemic. Cold Spring Harb Perspect Med. 2011;1(1):a006841
2. Henderson DA. The eradication of smallpox – an overview of the past, present, and future. Vaccine. 2011;29(Suppl. 4):D7-9
3. Pivetta E. The COVID-19 pandemic: A stress test for clinical epidemiology. Epidemiol Prev. 2020;44(5-6 Suppl. 2):28-29
4. Di Giulio DB, Eckburg PB. Human monkeypox: An emerging zoonosis. Lancet Infect Dis. 2004;4(1):15-25
5. Philpott D, Hughes CM, Alroy KA, et al; CDC Multinational Monkeypox Response Team. Epidemiologic and clinical characteristics of monkeypox cases – United States, May 17-July 22, 2022. MMWR Morb Mortal Wkly Rep. 2022;71(32):1018-22
6. Mahase E. Monkeypox: What do we know about the outbreaks in Europe and North America? BMJ. 2022;377:e1274
7. Alakunle E, Moens U, Nchinda G, Okeke MI. Monkeypox virus in Nigeria: Infection biology, epidemiology, and evolution. Viruses. 2020;12:1257
8. 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;28(8):1569-72
9. Otu A, Ebenso B, Walley J, et al. Global human monkeypox outbreak: Atypical presentation demanding urgent public health action. Lancet Microbe. 2022;3(8):e534-55
10. Olayinka A, Bayrak E, Kaya E, et al. Another epidemic in the shadow of Covid 19 pandemic: A review of monkeypox. Eurasian Journal of Medical Oncology. 2022;6:95-99
11. Blanco IL, Florence E, Moschese D, et al., SHARE-net Clinical Group. Monkeypox virus infection in humans across 16 countries – April-June 2022. N Engl J Med. 2022 Jul 21. doi: 10.1056/NEJMoa2207323 [Online ahead of print]
12. World Health Organization (WHO). Multi-country monkeypox outbreak: Situation update. 27 June 2022. Available at: https://www.who.int/emergencies/disease-outbreak-news/item/2022-DON396
13. World Health Organization (WHO). Update on monkeypox. 4th Aug 2022. Available at: https://www.who.int/news-room/questions-and-answers/item/monkeypox
14. Rizk JG, Lippi G, Henry BM, et al. Prevention and treatment of monkeypox. Drugs. 2022;82(9):957-63