Public Health Emergency of International Concern declared by the World Health Organization for Monkeypox

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ABSTRACT

Monkeypox (MPX) was a rare endemic disease in western and central Africa. In 1970, the first detected case of human MPX was reported in the Democratic Republic of Congo, and it was detected outside Africa in 2003. Currently, there are about 31,799 confirmed MPX cases which led the WHO to declare the disease a public health emergency of international concern which is considered the seventh deceleration by the WHO between 2009 and 2022. Herein, we aim to review the history behind the outbreak of the disease, its mode of transmission, and the target of WHO deceleration, while providing recommendations for disease prevention. The disease is prevalent mostly in the United States with a total case number of 10,676 which is considered a high-risk country. Meanwhile, other countries are at moderate risk. The disease can be transmitted directly through contact with different body fluids, infectious lesions, or sexual activity. We conclude that there should be public health awareness to stop the transmission of the disease. In addition, there is a great need to follow the instructions provided by public health institutions since vaccines, till now, are available only for high-risk populations secondary to their shortage.

INTRODUCTION

Monkeypox (MPX) is a double-stranded DNA virus of the orthopoxvirus genus which is related to the Poxviridae family (Oregon Health Authority, 2022). This family includes the variola virus which causes smallpox disease, the monkeypox virus (MPV) which causes human MPX disease, and other viruses (Sale et al., 2006). The first human case of MPX was detected in the Democratic Republic of Congo in 1970, two years after the last case of smallpox was reported in the same country. The disease is mainly endemic in this region and has two genetic variants, namely the central African (Clade1) and west African (clade2) clades (Sale et al., 2006). The strain present in central Africa is more severe than that of west Africa as the disease is capable of evading immunity by inhibiting T-cell activation, deterring the production of pro-inflammatory cytokines, and inhibiting the action of complement enzymes which are likely to be present in the central Africa strain (Estep et al., 2011; Hammarlund et al., 2008; Hudson et al., 2012). MPX is a zoonotic disease transmitted from animals to humans through natural reservoirs that are yet not confirmed; however, tree squirrels, rope squirrels, Gambian pouched rats, and non-human primates are considered potential reservoirs for the virus (Murphy, 2022; World Health Organization, 2022a).

The disease can be transmitted from animals by direct contact with infectious lesions on the animal’s body, through contact with bodily fluids, and through the ingestion of undercooked meat. On the other hand, transmission between humans can occur through direct contact with the body of the infected individual (i.e. touching the genital organs of infected patients, such as the penis, vagina, or anus) or contact with body fluids, contaminated objects with the virus, or aerosols during extended face-to-face contact. It can also be transmitted from infected pregnant women to their offspring through the placenta (CDC, 2022a; Petersen et al., 2019; World Health Organization, 2022a).

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The incubation period of the disease ranges from 7–17 days and starts with a prodromal stage of symptoms including fever, malaise, headache, and lymphadenopathy, which is considered characteristic of MPX disease that distinguishes it from smallpox. This prodromal period extends between 1–4 days and is followed by, in most cases, a skin manifestations stage which involves the development of a maculopapular rash on the face, head, and neck during the early stage of the disease. The rash then becomes centrifugal and progresses in its shape between papular, vesicular, pustular, and crusts in a stepwise process within 14–21 days (Damon, 2011; Di Giulio & Eckburg, 2004a).

**History of MPX Outbreaks**

The first detected case of human MPX was in the Democratic Republic of Congo (DRC) which is considered the most affected country with this disease in Africa. Nigeria comes in second place regarding the number of infected patients with an outbreak in September 2017 resulting in 181 confirmed cases (Bunge et al., 2022). The disease is endemic in Africa, and given the fact that it is a zoonotic infection, animals play an important role in its transmission and spread outside endemic regions. This led to the first outbreak outside Africa in the United States (US) in 2003 (Ligon, 2004). This occurred due to animal-to-human transmission of the virus through the importation of animals such as tree squirrels, rope squirrels, striped mice, Gambian pouched rats, Dormice, and bushtail porcupines with prairie dogs from Ghana. Of all these animals it is reported that infected dogs transmitted the infection to other animals (i.e. rabbits) which were considered the source of human transmission leading to an outbreak of 81 cases (CDC, 2003; Di Giulio & Eckburg, 2004b; Reynolds et al., 2004).

After that, most of the detected cases were related to travelling to African countries without a significant outbreak as these cases were sporadic in nature. One case had a travel history to Nigeria and the other case was a clinician who developed the infection during the hospitalisation of one of the infected cases (Vaughan, Aarons, Astbury, Balasegaram et al., 2018; Vaughan, Aarons, Astbury, Brooks et al., 2018). The third case was also a traveller to Nigeria who was in contact with a rodent during his visit. He was later diagnosed with MPX upon his arrival in Israel (Erez et al., 2019).

Nigeria experienced a large outbreak of the disease in 2017 where 200 cases of human MPX were identified (Yinka-Ogunleye et al., 2019). In addition, in May 2019, a case of MPX was identified in Singapore that also had a history of travel to Nigeria without any contact with wild animals or infected humans; however, the case reported having barbecued bushmeat during his travel (Yong et al., 2020). Therefore, travelling to African countries was perceived as the cause of disease transmission outside Africa as the three cases that were detected in London reported a history of travel to Nigeria. In this regard, we should apply restriction and isolation policies to regulate the return of travellers from African countries to their homelands (World Health Organization, 2022b).

In May 2022, several cases of MPX were reported in non-endemic countries, sparking the outbreak. In the past, MPX was restricted to Central and West African countries until 2003 when a major outbreak occurred in the US. The current multi-country outbreak has affected countries in Europe, North America, and Africa, with most cases linked to travel to endemic countries. The Democratic Republic of the Congo and Nigeria had the most cases of MPX in early 2022 (Farahat, Abdelaal et al., 2022). It spread gradually to other African countries, including Cameroon, Ghana, and the Central African Republic. It also made its way to Europe, where the United Kingdom (UK), Spain, and Germany were severely affected (Farahat, Ali et al., 2022).

As of 24 August 2022, and according to the Centers for Disease Control and Prevention (CDC), 44,116 out of 44,503 confirmed MPX cases were reported in countries that had no previous cases in the past, which reveals the spread of the disease outside Africa. Moreover, 12 MPX-associated deaths were reported, out of which five occurred in non-endemic counties (CDC, 2022b). The rapidity with which the disease has spread among the younger age group especially males could also be due to the fact most of them were born after the eradication of smallpox and therefore are not vaccinated against the same. USA has the maximum number of cases in the world followed by Spain and Germany. Among the South-east Asian countries Singapore lead the way with 15 cases followed closely by India with 9 cases (Table 1; CDC, 2022b; Sah, Mohanty et al., 2022).

**Monkeypox As a Public Health Emergency**

The world has been fighting COVID-19 for the past two years and has seen more than 6 million people losing their lives due to this emerging disease (Worldometer, 2022). It was on 30 January 2020, when the World Health Organization (WHO) declared COVID-19 a public health emergency of international concern (PHEIC), and later, on March 11, as a global pandemic (World Health Organization, 2022c). A PHIEC, according to the WHO, constitutes an extraordinary event that forms a public health risk to other states through the
international spread, potentially requiring a coordinated global response.

On 23 July 2022, following an urgent meeting of the International Health Regulations (IHR) Emergency Committee, the WHO declared the multi-country MPX outbreak a PHEIC, one step below that of a pandemic (World Health Organization, 2022d). PHEIC diseases have a serious public health impact, are unexpected, pose a significant risk of international spread, and are likely to affect travel and trade worldwide. This WHO declaration also indicates a global public health risk that necessitates a coordinated international response in an attempt to prevent the disease from becoming a pandemic.

The WHO has declared a global public health emergency for the second time in two years (World Health Organization, 2022c, 2022e; Worldometer, 2022). Despite the committee’s failure to reach a consensus on whether the outbreak was a PHEIC, the decision was made to raise awareness to the highest level possible with strong political commitment in addition to reducing discrimination since the majority of cases are reported among men who have sex with other men (MSM), and that is associated with a stigma that could further complicate the health care seeking behaviour of those individuals (World Health Organization, 2022e). Except for Nigeria, all of the remaining countries reported that most of the reported cases were MSM, primarily among those with multiple partners. The number of cases in West and Central Africa has also increased significantly, with more women and children affected. The basic reproduction number ($R_0$) is estimated to be greater than one in MSM populations and less than one in others. In addition, few cases have been reported among healthcare workers, and although investigations into any possible link are still ongoing, recent evidence suggests the potential for occupational transmission (Global Health, 2022).

### WHO Risk Assessment of Countries

Although the number of cases and countries experiencing outbreaks of MPX appear to be increasing, the WHO risk assessment still considers the risk moderate at a global level, except for the European region, where it is considered high. A set of recommendations has been established for all countries as part of the temporary PHEIC declaration, which is reviewed every three months. All countries are classified into four categories. The first category includes those who have not yet reported cases or where the most recent case was reported in the past 21 days. The second category includes those who have recently imported cases and are still experiencing human-to-human transmission. The third category includes countries where cases are being reported and have a history of the presence of the virus. The fourth category includes states with medical countermeasure manufacturing capacity. These guidelines instruct countries to increase surveillance, raise awareness about this multi-country outbreak, and ensure that risk groups are not stigmatised (World Health Organization, 2022e).

### Rate of Transmission

The rate at which the disease spreads worldwide is currently a concern. However, the actual number is thought to be much higher because testing is now being revamped. The longer the outbreak lasts, the greater the chances for the virus to spread from infected people to animal populations. It could last ages and trigger sporadic human infections, resulting in disease endemicity. Many cases report no source of infection, indicating undetected community spread (World Health Organization, 2022f). More research is required to assess the complexities of transmission routes of the virus during the current multi-country outbreak. Deforestation, globalisation, and climate changes have all served as vectors for these viruses, allowing them to spread across species and continents to become a global threat.

### Recommendation to Hinder the Transmission

There are a group of recommended preventive strategies that should be implemented to reduce the risk of

| Sl No | Country                      | Confirmed Cases |
|-------|------------------------------|-----------------|
| 1     | United States of America     | 10,676          |
| 2     | Spain                        | 5270            |
| 3     | Germany                      | 3063            |
| 4     | United Kingdom               | 3017            |
| 5     | France                       | 2601            |
| 6     | Brazil                       | 2293            |
| 7     | Netherlands                  | 1025            |
| 8     | Canada                       | 1008            |
| 9     | Portugal                     | 710             |
| 10    | Peru                         | 632             |
| 11    | Italy                        | 599             |
| 12    | Belgium                      | 546             |
| 13    | Switzerland                  | 368             |
| 14    | Austria                      | 186             |
| 15    | Israel                       | 174             |
| 16    | Democratic Republic of Congo | 163             |
| 17    | Nigeria                      | 157             |
| 18    | Mexico                       | 146             |
| 19    | Denmark                      | 135             |
| 20    | Sweden                       | 126             |
| 21    | United Arab Emirates         | 16              |
| 22    | Singapore                    | 15              |
| 23    | India                        | 09              |
transmission, which include: (1) avoiding direct contact with an infected MPX patient by avoiding skin lesions touch, (2) avoiding contact with wild animals, kissing, and hugging, (3) limiting the use of sharable items (i.e. cups, utensils, clothes) among infected or exposed cases as these objects might become the source of transmission, (4) following proper hand hygiene techniques after the contact with others or any usual practice, (5) proper cooking of food not only to prevent MPX but also to prevent other parasitic diseases from being transmitted if the meat was not properly cooked, and (6) wearing a protective mask in crowded areas (CDC, 2022c; Cleveland Clinic, 2022).

Recommendations to reduce the risk of disease transmission during sexual activities can include (1) promoting a thorough discussion between partners about the disease and if any one of them experiences one of the disease symptoms they should seek medical care and stop any sexual contact during this period, (2) reducing the number of sexual partners, (3) encouraging the use of protective equipment such as condoms and gloves during different sexual activities, (4) implementing proper hand hygiene after practicing any sexual activities, and (5) washing and disinfecting any contaminated objects or clothes used during the sexual contact (CDC, 2022d).

Vaccination is now available for certain people (i.e. high-risk populations) due to its shortage. These people include individuals who are exposed to the virus and those who are expected to develop the disease as public health specialists who have constant contact with infected cases, laboratory technicians who are in contact with the specimens of infected patients, individuals who have sex with a partner known recently to have MPX, and individuals who have multiple sexual partners (CDC, 2022e). The application of ring vaccination would be of great value in breaking the chain of transmission as well as in preventing the occurrence of severe disease (Sah, Abdelaal et al., 2022).

The most recommended vaccine is JYNNEOS which provides protection within 14 days from receiving the second dose. Meanwhile, ACAM2000 can be used as an alternative vaccine, and although it can provide protection within 28 days after a single dose, it can lead to adverse effects in people with weakened immunity. Thus, it is not recommended for use in such populations (CDC, 2022e). Of note, these vaccines can prevent the development of the disease if given before exposure or within 4 days from being exposed to the infection (if given within 4–14 days of contact with the infected individual). In addition, these vaccines can prevent the occurrence of severe disease form if given after exposure; however, in this case, they might not be able to prevent the disease from occurring (CDC, 2022f).

The devastation of the COVID-19 pandemic and the ease with which the MPX virus spread serve as a warning to governments to prepare for future epidemics. Global vaccine and therapeutic production, as well as effective response coordination among nations, are urgently required (Abdelaal et al., 2022). That would go a long way towards ending the disease and clearing the various uncertainties regarding the outbreak.

**Conclusion**

Monkeypox is a self-limiting viral disease associated with a low case fatality rate. The WHO declared it a public health emergency to drive coordinated efforts across countries to properly contain the disease before it becomes a pandemic. Monkeypox vaccination is recommended nowadays for health care professionals, public health specialists, laboratory technicians dealing with patients’ specimens, and individuals with an infected sex partner, and all of them should ask their health authority about the suitable vaccine to be taken. In the light of the current outbreak, prevention of MPX is much more effective than active treatment, which can be done by following hand hygiene, promoting health care seeking behaviour (reporting any lesions that appear for early detection, diagnosis, and prevention), avoiding sex with multiple sexual partners, and other measures. Monkeypox, like many other infectious diseases, can be limited by adhering to proper infection control measures provided by public health specialists and health care professionals.

**Authors Contribution**

RS draw the draft, BIL, AA, AS, AM, AR, NZA and AJRM review the literature, and critically edit the manuscript. All authors read and approve the final manuscript.

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