

Monkeypox 2022: Can We Contain This Dangerous Outbreak?

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Has monkeypox become the next public health emergency of international concern after the COVID19?. The world health organization (WHO) is likely to come up with the answer soon. Meanwhile, the world health network (WHN), a global collaboration of scientific and citizen teams urged the WHO to declare monkeypox a pandemic. Monkeypox is a rare zoonotic smallpox-like infectious disease in humans caused by the monkeypox virus, a member of orthopoxvirus genus, in the family of Poxviridae, and subfamily of chordopoxvirinae [1]. It is recognized as the most important orthopoxvirus infection after the eradication of smallpox. It was first isolated and discovered in Monkeys in a Danish laboratory in 1958 [2]. The first case in humans was documented in the 1970s in a 9-year-old boy suspected of smallpox-like illness in the Democratic Republic of the Congo (Central Africa). Since that time, most cases have been restricted to the endemic areas including the tropical rainforests of Central and Western Africa [3]. Higher mortality rate was reported for infections in the Congo basin (11% including Central Africa) than in the Western Africa region (4%) [4]. Outside of Africa, the virus was first identified in the Midwestern United States (US) in 2003 but no fatalities have been reported [5]. Currently, As of June 25, 2022, over 3400 laboratory confirmed cases of monkeypox including 1 death have been reported across 50 countries where the virus was not seen earlier [6]. The size of the present outbreak is rapidly expanding across multiple continents including Europe and North America. Over 80%

of cases were in European nations. The reason for the outbreak is being investigated. Lack of smallpox vaccination due to the eradication of smallpox in 1980 (vaccine was 85% protective against monkeypox) [7], forest area encroachment, and growing international travel or imported animals seems to play an important role in the epidemiology of an outbreak [8]. Therefore, the pattern of geographical dispersal of the monkeypox is much larger compared with past outbreaks that were more localized and limited to resource constraint communities (Figure 1) [9]. The potential threat of this pathogen virus is likely an underestimate because of the underreporting of suspected cases from rural endemic areas in view of limited surveillance, and a lack of widely available diagnostics.

Monkeypox is a typical example of a combination of emerging zoonotic spillover and anthropogenic drivers that cause epidemic potential over the world. It is a zoonotic virus with primary transmission through direct contact with infected animal's blood, body fluids, or cutaneous/mucosal lesions or possibly by eating inadequately cooked flesh or other products of infected animals. The natural reservoir of monkeypox has not yet been discovered. Although, non-human primates (such as monkeys) and African rodents may harbor the virus and subsequently infect humans. In the 1996-1997 outbreak, the secondary or person-to-person transmission was found to be another possible route. In recent years, the chain of transmission of virus infection in a

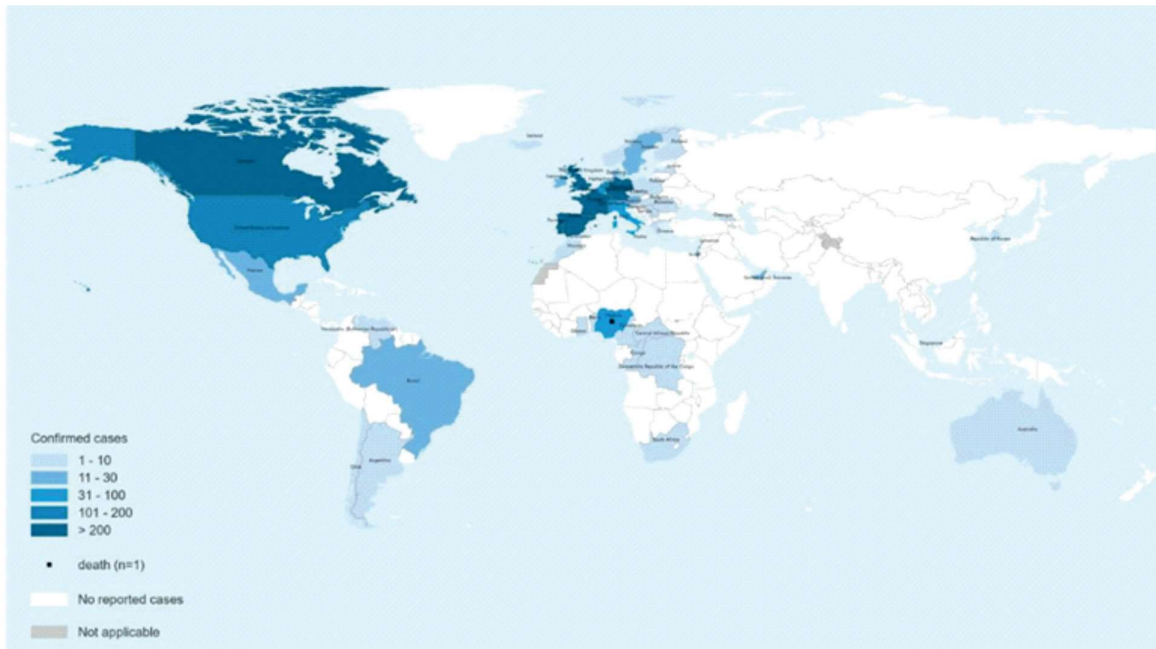


Figure 1: Geographic distribution of cases of monkeypox [adopted from WHO [10].

community has risen from 6 to 9 successive person-to-person [10]. Close physical contact is a well-known risk factor for transmission. However, it has not clear if monkeypox is transmitted through the sexual transmission route. The virus is likely to spread from human-to-human through a). Direct contact with infectious body fluid, skin rash, cutaneous lesions b). respiratory droplets secretions during prolonged face-to-face contact or during physically close contact such as kissing or sex, c). touching recently contaminated objects, and d). from mother to fetus transmission may also occur via the placenta.

The incubation period of the virus is usually 1 to 2 weeks (ranging from 5 to 21 days). The clinical symptoms of monkeypox are similar to smallpox symptoms but overall monkeypox is less infectious and rarely fatal. Usually, the infection can be divided into two phases. The invasion period (0 to 5 days) is an early set of symptoms (prodrome) including

febrile illness often accompanied by intense headache, chills, myalgia, intense asthenia, and lymphadenopathy. The skin eruption phase usually begins within 1 to 3 days of the appearance of febrile illness and the rash appears as blisters, or pimples more concentrated on the face (in 95% of cases), and extremities rather than the trunk (fig. 2). It also affects the other part of the body such as the soles of the feet and palms of the hands (in 75% of cases), oral mucous membranes (in 70% of cases), and genitals (in 30% of cases) [10].

The rash goes into various stages before healing completely (fig. 3). The illness is usually self-limiting and typically lasts 2 to 4 weeks. Severe infection occurred more frequently among children and depends on the extent of virus exposure, comorbidities, and nature of complications. CDC has proposed case definitions (Table 1) [11]. Polymerase chain reaction (PCR) using samples from skin lesions is the preferred laboratory test for monkeypox.



Figure 2: Clinical pictures of monkeypox.

Table 1: Monkeypox Case Definitions [11].

Type of case	Definition
Suspect	<ul style="list-style-type: none"> Presence of new characteristic rash/lesions that is well-circumscribed, deep-seated, and often develop central umbilication (dot on the top of the lesion). Rash evolves through particular sequential stages from macules (1-2 days), to papules (1-2 days), vesicles (1-2 days), pustules (5-7 days), and scabs (7-14 days) which dry-up and fall-off. This can be confused with other diseases such as secondary syphilis, herpes, and varicella-zoster. <p style="text-align: center;">OR</p> <ul style="list-style-type: none"> Meet one of the epidemiological criteria* and has high clinical suspicion (illness confused with secondary syphilis, herpes, and varicella-zoster) for monkeypox.
Probable	<ul style="list-style-type: none"> No suspicion of other <i>Orthopoxvirus</i> exposure, AND presence of - <ul style="list-style-type: none"> <i>Orthopoxvirus</i> DNA by PCR laboratory test OR <i>Orthopoxvirus</i> by electron microscopy or immunohistochemical laboratory test OR Anti-orthopoxvirus IgM antibody detection between 4 to 56 days after onset of lesion.
confirmed	<ul style="list-style-type: none"> Presence of Monkeypox virus DNA by PCR laboratory test or clinical specimen having Next-Generation sequencing OR <i>Monkeypox virus</i> isolation in a culture of clinical specimen
<p>*Epidemiologic Criteria: Meet the followings criteria within 21 days of onset of illness:</p> <ul style="list-style-type: none"> Evidence of contact with a person or people with a similar-appearing rash or who have been diagnosed with a confirmed or probable case of monkeypox. OR Had close physical contact with an individual in a social network experiencing monkeypox, including men who have sex with men who come in contact via online social media, websites, social events, or parties. OR Person travelled from the area where monkeypox virus is endemic. OR Had contact with an infected wild animal (African endemic species) or used a product derived from these animals (e.g. meat, lotion, powder). 	

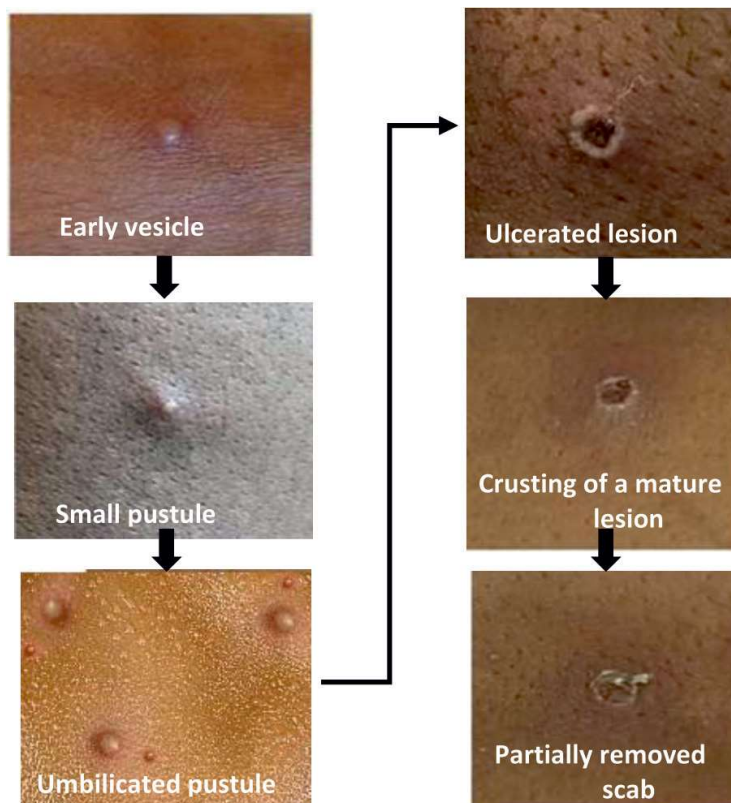


Figure 3. Stages of rash in monkeypox.

Clinical Characteristics of Monkeypox

- Skin Rash/Lesions: well circumscribed, deep seated, with central umbilication.
- Relatively same size lesions having same stage of development on a single site of the body such as vesicles on legs, and pustules on face.
- Fever before rash
- Lymphadenopathy
 - It is distinguishing characteristics of monkeypox from smallpox and usually may swell submandibular, cervical, inguinal or axillary.
 - Usually occur with onset of fever, or 1-2 before the development of rash, or rarely with rash onset
- More lesions on face, extremities – centrifugal disseminated rash
- Lesions on palms of the hands and soles of the feet.
- Painful lesions until the healing completely when they become itchy.

Transmission of Monkeypox is not as rapid as COVID19 as we have options to treat and prevent the monkeypox virus infection, unlike the COVID19 infection when it emerged. However, there is no safe and proven treatment for monkeypox infection, but the spread of the infection can be controlled. The management goal should be focused on reducing the symptoms, treating secondary bacterial infections, maintaining adequate nutrition status, addressing the complications, and preventing long sequelae. Possible complications may include permanent skin scarring, secondary bacterial infection, hyperpigmentation/hypopigmentation, blindness, corneal ulceration, bronchopneumonia, dehydration, septicemia, and encephalitis. As per CDC, available options for the management of a monkeypox outbreak may include smallpox vaccines (live, non-replicating virus), antiviral drugs such as Tecovirimat, Cidofovir, Brincidofovir, and vaccinia immune globulin (VIG) [12]. Antiviral Tecovirimat has been approved by European Medicine Agency for treating monkeypox and cowpox infection in 2022 and registered by USA-FDA for smallpox in 2018 [13]. There is no proven effect of these antiviral agents in managing monkeypox in humans. These agents have shown proven activity against poxvirus in animal studies. There is also no proven benefit of using VIG in the management of monkeypox complications. It may be used prophylaxis therapy in an exposed patient with immunodeficiency in T-cell function for which the smallpox vaccine is contraindicated.

Recently, FDA approved a non-replicating, live, modified attenuated vaccinia virus vaccine (Ankara strain) for the prevention of monkeypox in adults 18 years of age and older who are at high risk [14]. This vaccine is two-dose subcutaneous injections administered four weeks apart.

Vaccination can be given after exposure to the monkeypox virus. CDC recommends the administration of vaccines within 4 days from the date of exposure to prevent the onset of disease. Vaccination between 4 to 14 days after exposure may reduce the severity of infection but may not prevent the disease. With respect to revaccination, it is recommended in those exposed to the monkeypox virus and who have not taken the smallpox vaccine within the last 3 years.

In view of the larger geographical dispersal of the monkeypox, there is utmost need for the implementation of a preventive strategy that includes decreasing human contact with infected animals, and contaminated objects and limiting the human-to-human spread of infection. In addition, practicing good hand hygiene and the use of personal protective equipment (PPE) during caring for patients can help in preventing the spread of infection among healthcare workers. A person diagnosed with monkeypox should isolate themselves at home and avoid contact with others until the lesions have healed completely.

Epidemic preparedness is the key to prevent the spread, so close surveillance of ongoing outbreaks when and where they occur rather than waking up when it knocks our doors. We must ignore the stigma about where the disease comes from, who is infected with this, and how. Inevitable neglect of the disease that primarily affects the low-income countries and global disregard shown in this matter is the real culprit of the outbreak. Support for medical innovation is not just a subject of health equity and justice, but also it is important for global health security because it is critical to solving the obstruction before it gets out of hand. Novel effective interventions must be made accessible and affordable to low-income countries endemic to monkeypox. Thus, priority

should be on better diagnostics, education, engagement of local community, comprehensive approach and research on vaccines and therapeutic agents.

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