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Review Article

Outbreak Over Monkey Pox Virus in Human: Immediate Countermeasures from the Endemic to Non-Endemic Regions

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Abstract

A zoonotic orthopoxvirus called human monkeypox has symptoms that resemble smallpox. When people come into contact with diseased animals, they may unintentionally contract monkeypox. According to reports, the virus can also spread through close physical contact, such as skin-to-skin contact or sexual contact, respiratory droplets, and by household items like towels and blankets. There are numerous medical countermeasures on hand for orthopoxviruses like monkeypox. Monkeypox, which originated in western and central Africa, has lately been found in a integer of nations, counting Spain, Canada, Australia, and the United Arab Emirates. Despite its extremely low incidence rate, it nonetheless poses a serious concern that needs to be addressed as soon as possible because of the strong likelihood that it will spread to many other nations. Outside of endemic areas, the danger of monkeypox transmission in medical settings is not well known. One recorded instance of transmission was found after a quick assessment of the literature from 2000 to 2022, which also included cases outside of areas where monkeypox is endemic. It is unusual for monkeypox to recur in non-endemic nations. It is a zoonosis that can extend from animal to human and from human to human, and it has clinical characteristics comparable to smallpox. The latest outbreaks may be attributed to lowered resistance to the orthopoxviruses, movement of people from widespread to non-endemic areas, hereditary alterations in the viral genome, and diminished observation. Transmission and pathogenicity could be avoided with the use of a multifaceted strategy that includes health education, monitoring human mobility, the development of diagnostic tools, and an efficient vaccination.

Keywords: Monkeypox, Outbreak, Orthopoxvirus, Epidemiology, Vaccination, Virology, Public health, Preventive measures

INTRODUCTION

A viral zoonosis called monkeypox is endemic to some regions of Africa. Its primary symptoms, like those of other illnesses brought on by pox viruses, are illness and skin grazes. Though, a small percentage of patients may experience harsh, multisystemic illness that is frequently deadly. A sudden increase in instances that were found outside of the endemic region, monkeypox has recently attracted attention and worry on a global scale. The monkeypox and the smallpox (variola) virus are both enclosed doublestranded DNA viruses belonging to the Poxviridae family. Monkey pox was originally discovered in the Democratic Republic of the Congo in 1970[1]. Numerous outbreaks have occurred since then, primarily impacting African nations. Gradually, cases outside of Africa were also reported, and the disease gained importance for public health. The World Health Organization (WHO) recently announced the confirmation of an unusual monkeypox outbreak originating from several non-endemic nations, with new cases being reported every day[2]. This increases the possibility that, as was the case with COVID-19[3-5], anaesthetists will once more be required to provide frontline treatment to critically ill patients with infectious infections that could be lethal. The term "monkeypox" is inaccurate. Although it was initially discovered in monkeys brought from Denmark to Africa for research, Later, it was found in approximately 14 species of African rodents, including huge Gambian pouched rats, dormice, and squirrels. It is still unknown what the monkeypox's natural host reservoir are[6]. The primary route of spread is from animal to human when infected animals are directly touched or their uncooked meat is handled. Sexual contact, respiratory droplets, saliva-containing body fluids, and mother-to-child transplacental transmission are all ways that human-to-human transmission can occur. Monkeypox is categorized in the UK as a High Consequence Infectious Disease (HCID)[7]. Monkeypox has been reported in two distinct strains: West African and Central African (or Congo basin). Compared to the West African clade's 3% case fatality rate, the Central African strain has a 10% higher case fatality rate[8,9]. Between May 13 and June 2, 2022, the current comeback saw 780 cases have been

confirmed in 27 non-endemic countries, surpassing past outbreaks[2]. Unknown factors may have contributed to the unexpectedly rapid rate of dissemination compared to earlier observed epidemics. Further investigation is required to determine whether the virus has changed to improve human transmission. Monkeypox cases with peri-anal or genital rash have been found in large numbers among males who have sex with men in sexually transmitted infection clinics. This suggests that monkeypox might use sexual transmission to target particular social groups. However, this initial finding requires confirmation and should under no circumstances result in homophobia[2]. Preventing occupational exposure and illness spread requires early detection of the disease's signs and symptoms. Monkeypox normally takes 6 to 13 days to incubate. Fever, headache, myalgia, body soreness, and chills are some of the initial non-specific symptoms. The early viral invasion stage is characterised by prominent cervical and axillary lymphadenopathy, which separates monkeypox from smallpox. Within one to three days of the onset of the fever, centrifugal rashes begin to develop and advance via macules, papules, vesicles, pustules, and scabs. The scalp, trunk, limbs, face, soles, palms, nail beds, and anogenital regions can also develop lesions[2]. Patients may also experience ulcerated inguinal lymph nodes, severe subungual lesions, eyelid oedema, pharyngitis, conjunctivitis, deep abscesses, and aching oral sores. Permanent opacities could be the outcome of corneal involvement. Emotional lability and depression are two neuropsychiatric signs that patients frequently experience. The condition normally gets better in 2-4 weeks, but considerable scarring is frequently left behind and can be both disfiguring and incapacitating[8-10].Using a polymerase chain reaction, viral DNA can be isolated from body fluid samples or lesions-related samples to provide a diagnosis. Urine, blood, fluid from open sores, and swabs of the upper respiratory tract are among the samples utilized for detection[11]. Throughout the monkeypox outbreak in the USA in 2003, additional methods used during the outbreak included immunohistochemistry, electron microscopy, culturing samples from lesions, and serological testing for specific antibodies. The most frequent differential diagnoses for monkeypox are measles, scabies, chickenpox, smallpox, allergic skin reactions, and syphilis. Non-specific blood test results include increased liver enzymes, low blood urea nitrogen levels, increased total leukocyte counts, and low albumin levels[12].

HISTORY OF MONKEYPOX

In a Danish laboratory, monkeypox was initially identified in 1959 as a primate infection[13]. Between 1958 and 1968, eight more laboratory outbreaks were linked to monkeypox[14]. The first human case was found in a village inside a tropical rain forest in August 1970 in Equateur province, Democratic Republic of the Congo[15]. Clinically, the illness is very similar to smallpox. However, the majority of individuals show cervical, axillary, and occasionally inguinal lymphadenopathy, which is nearly never seen with smallpox. It is believed that the illness was widespread for a long time, going unnoticed until smallpox transmission was stopped throughout the rain forest regions and surveillance for diseases similar to smallpox was considerably increased. More than 400 cases of monkeypox in humans were reported between 1970 and 1995, mostly in Zaire. Although the cases were dispersed and mostly manifested as lone cases in a community, in a select few cases it was evident that human-to-human transmission might take place. Investigations showed that humans and monkeys were simply incidental hosts for the virus, which had a natural reservoir in ground squirrels and possibly other rodents. A monkeypox outbreak in central Zaire in 1996-1997 that may have resulted in more than 300 cases first made people wonder if human–human virus transmission would be more common than previously believed. However, it was discovered that there was also a varicella outbreak in the same area, and it was evident that many of the reported cases of monkeypox were actually varicella cases[16]. The majority of monkeypox patients in the 2003 U.S. outbreak indicated exposure to wild or exotic species, including prairie dogs. Some of the patients were also close household contacts of those with the illness. However, no instances of monkeypox could be solely linked to interpersonal contact[17].

MONKEYPOX EPIDEMIOLOGICAL AND CLINICAL CHARACTERISTICS

A double stranded DNA virus with an envelope, the monkeypox virus can infect a variety of animal species, primarily rodents[18, 19]. Transmission from person to person can happen when skin lesions, respiratory secretions, or bedding that has recently been contaminated. Direct contact with bodily fluids, blood, cutaneous or mucosal lesions of infected animals might result in zoonotic transmission of the virus. As respiratory droplets may only travel a short distance between people, human-to-human transmission by these means necessitates extended face-to-face contact[20,21]. Rash, fever, chills, and lymphadenopathy are among the clinical symptoms that distinguish monkeypox from smallpox. These symptoms typically appear early on in the illness' progression. The virus can incubate for 5 to 21 days, but the average incubation period is between 6 and 13 days[22]. In most cases, despite the fact that monkeypox is a self-limiting virus, some demographic categories, such as children, pregnant women, and those who are immunosuppressed[23]. Geographically separated, the virus has been split into two distinct genetic clades: the West African clade, which has a case fatality rate of less than 1% and limited transmissibility, and the more severe Congo Basin clade (the Central African clade), which has a case fatality rate of approximately 11%[24].

EXPANSION OF HUMAN MONKEYPOX FROM ENDEMIC TO NON-ENDEMIC REGIONS: IMPACT MEASURES

It is unusual for monkeypox to have recently spread to areas where it is not endemic. A zoonosis known as monkeypox is brought on by the monkeypox virus (MPXV), a kind of orthopoxvirus. The MPXV is similar to the smallpox virus, Variola. In the Democratic Republic of the Congo (DRC), MPXV was first recognised as a human disease in 1970[25]. So far, MPXV has been classified into two genetic clades: Central African and Western African. The Central African clade has a greater case fatality rate (11%) and more human-to-human transmission than the Western African clade, which has a lower case fatality rate (1%) [26]. The clinical characteristics of human monkeypox and smallpox are quite similar. After a 10 to 14 day incubation period, the majority of people experience prodromal disease, which includes fever, malaise, and enlarged lymph nodes. The typical human monkeypox rash develops over the course of the following 14–21 days as maculopapular lesions, moving through vesicular, pustular, papular, and crust phases prior to sloughing off and leaving dyspigmented scars[27]. It is possible for complications to occur, comprising secondary skin infections, sepsis, encephalitis, bronchopneumonia, and corneal infections that can result in blindness[28]. There are two MPXV transmission modes that could be used: human-human and animal-human. An infected person's skin lesion, contact with bodily fluids, respiratory droplets, a contaminated patient's surroundings or possessions, an infected person's skin lesion, and sexual transmission from an infected person with groyne and genital lesions have all been related to inter-human transmission. Animals to human's transmission can occur through direct contact with or consumption of natural viral hosts.

Additionally, zoonotic transmission may occur as a result of direct contact with the blood, bodily fluids, or inoculation through mucocutaneous lesions of an infected animal[29]. Although the diagnosis is mostly clinical, laboratory testing is also required for an accurate diagnosis. These tests include viral isolation, culture, immunohistochemistry for the identification of viral antigens, ELISA for the detection of antibodies (IgG and IgM), and specific viral DNA detection using PCR[30]. Most of the time, symptoms are treated. There is currently no approved antiviral medication for MPXV infection. The eradication of MPXV may be facilitated by vaccination in conjunction with a rigorous surveillance effort[27]. Concerns regarding the geographic distribution and continued return of monkeypox are growing. In recent years, outbreaks of monkeypox have been documented in 11 African nations, with the DRC coverage the majority of cases. The DRC started disclosing many suspected cases in 2000, and since then, the number of cases has increased steadily, from 2000 to 2009, there were over 10,000 cases; from 2010 to 2019, there were over 18,000 cases, and in the first nine months of 2020 alone, there were 4594 more suspected cases. Between 2017 and 2019, there were 181 cases in Nigeria, a sharp increase from the three cases there were in the 1970s[31]. The only human case of monkeypox exterior of Africa was reported in the US in 2003 and was linked to rats imported from Ghana. When three passengers carrying the MPXV virus left Nigeria and arrived in 2 different countries-two instances in the UK and one case in Israel-this was the first instance of human-to-human transmission[32]. A Nigerian national contracted MPXV in Singapore in 2019. In 2021, a small number of cases were also shipped to the US and the UK. Several cases of monkeypox were found during the most recent outbreak, which started in May 2022, in a number of non-endemic nations. According to the World Health Organization (WHO), 92 laboratories confirmed cases and 28 suspected cases from 12 non-endemic countries had been reported to WHO[33] as of May 21, 2022. A total of 257 laboratory confirmed cases and around 120 probable cases for MPXV from 23 non-endemic countries have been reported to WHO[34] after 5 days, on May 26, 2022.It is unknown what specifically is causing this increased incidence in endemic and non-endemic areas. Many explanations have been put up to explain the increase in instances of monkeypox. First, the Smallpox vaccination programme was stopped in 1980, which led to a loss of immunity to the Orthopoxviruses. Monkeypox occupied an immunological gap created by the suspension of vaccination following the elimination of smallpox and waning immunity. Second, significant anthropogenic and demographic shifts that have taken place in the DRC since 1980 may have increased locals' exposure to MPXV reservoir species. Additionally, civil unrest, persistent warfare, and poverty force the affected population to flee and ultimately seek sanctuary more deeply in the rainforest, heavily relying on wild foods, which significantly boosts the spread rate. Third, an expanded return in people, particularly in immune-compromised hosts, may allow MPXV to gain genetic alterations that improve its fitness in people, thereby leading to increased transmission, virulence, and pathogenic potential. Fourth, it can be difficult to monitor human monkeypox infections in endemic places. Challenges that the surveillance framework faces include limited resources, poor infrastructure, a lack of diagnostic instruments, and a lack of clinical facilities for diagnosing monkeypox sickness. Endemic and non-endemic regions, the burden of human monkeypox infection can be reduced by a multifaceted strategy. In particular in endemic areas, the seminars, health education campaign, brochures, and workshops would be helpful in distributing information. Establishing quarantine zones and isolating the diseased person is strictly necessary. In order to regulate the traveling behaviours of animals from endemic areas, the trade in wildlife should be outlawed. Traveling from endemic to non-endemic places needs to be closely controlled as international travel keeps growing. Public health authorities should assess potential dangers and keep an eye on travellers or other individuals who may have come into contact with an infectious patient while travelling. Few laboratories worldwide have the tools necessary to verify monkeypox infection. To improve early detection, adequate diagnostic facilities must be offered. Although vaccination remains a feasible control method, it would be extremely logistically challenging to reinstate the Vaccinia vaccination as a component of regular immunisation programmes. No longer considered a rare illness, monkeypox. Its recent outbreak has made it a threat to the safety of the world's health, needing more attention to stop it from spreading. To prevent transmission and pathogenicity, appropriate measures and proactive surveillance activities are urgently required. It is imperative that international organisations engage with national organisations, national health agencies, healthcare professionals, researchers, and the media to develop and establish a strategy plan for spreading knowledge about and preventing monkeypox.

PREVENTIVE ACTIONS TAKEN BY COUNTRIES TO REDUCE MONKEYPOX RELATIONSHIP

More cases are anticipated to be reported as the monkeypox virus spreads internationally, thus all nations-even those that have not yet reported any cases-need to start putting the required health promotion strategies in place to stop and stop the epidemic. Countries with confirmed cases began tracing contacts and monitoring the contacts for the emergence of symptoms. The first nation to mandate mandatory 21-day quarantine for infected individuals was Belgium[35]. Contacts are not required to segregate themselves but are required to be attentive and keep an eye out for the emergence of any symptoms. However, the UK is encouraging anyone with family or close friends to isolate themselves for 21 days[36]. The government ordered smallpox vaccines from Bavarian Nordic Company, which are also effective against monkeypox, for $119 million US after the confirmation of the country's first case of the disease[37]. The JYNNEOS vaccine was authorised by the U.S. Food and Drug Administration (FDA) in 2019 for use in adults 18 years of age and older who are at high risk of contracting smallpox or monkeypox infection. Both the European Medicines Agency and the European Medicines Agency approved the vaccine in 2013 and 2019, respectively[38]. It is based on a live, attenuated vaccinia virus that has been grown in fibroblast cells from chicken embryos. The monkeypox virus is 85% successfully prevented by the vaccination[39]. In the UK, IMVANEX was first administered to as post-exposure prophylactic, close contacts of confirmed cases[40]. For post-exposure prophylaxis, the immunisation needs to be given during the first four days following exposure. Giving it between 4 and 14 days after revelation can lessen the indications but not the infection[41]. To deal with monkeypox, many nations began preparing their emergency preparedness plans. The UAE created a thorough manual for surveillance, early illness identification, clinically infected patient management, and other preventative measures. All medical professionals employed in the nation were asked to report any suspicious cases to the appropriate health authorities in a circular distributed by the Ministry of Health and Prevention[42]. Similar to this, the public and private sectors were questioned by the Ministry of Public Health in Qatar to keep an eye out for possible patients exhibiting symptoms that could indicate monkeypox and to notify the health authorities of any suspected cases[43]. It also published a route on how to handle suspected instances brought into medical amenities. The WHO has cautioned that stigmatising those who have the infection can impede efforts to contain the outbreak and may discourage others who exhibit symptoms from seeking

medical attention, ultimately causing undiscovered spread[44]. As of May 29, no nations had enacted any restrictions or travel bans to stop the illness from spreading.

CONCLUSION

Every day, there are more confirmed cases of monkeypox, and more instances are anticipated. Men make up the majority of the cases, and several have come out as gay or bisexual. The majority of cases were seen by a doctor after developing symptoms, primarily rash. The chains of transmission documented in Europe for the first time have no epidemiological connections to Central or West Africa, wherever the illness is widespread. In order to prevent or stop the spread of the disease, nations must apply the lessons learnt during the COVID-19 pandemic. Modern methods are being used to investigate human monkeypox epidemics in order to better understand the disease's epidemiology and ways to stop and contain outbreaks. Continued research is necessary, and as new knowledge comes to light, it should be utilised to parameterize epidemiological models and recommend the relative efficacy of measures including isolation, safe burial, contact tracking, antivirals, and immunizations.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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DATA AVAILABILITY

All datasets generated or analyzed during this study are included in the manuscript.

ETHICS STATEMENT

This article does not contain any studies with human participants or animals performed by any of the authors.

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