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Human Monkeypox Virus; New Possible Viral Pandemic

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Abstract

The unexpected monkeypox outbreak and global increase have drawn attention due to the ongoing COVID-19 pandemic. With 3340 confirmed cases worldwide as of June 22, 2022, this is the biggest and most pervasive monkeypox outbreak outside of Africa. In addition to vertical transmission from mother to child, MPXV can spread from person to person through direct contact with infectious skin or mucosal skin lesions, respiratory droplets, or indirect contact with contaminated objects or materials. Additionally, it is most likely sexually transmitted through vaginal fluid or semen, and community transmission is a possibility. MPXV, an envelope, linear, double-stranded DNA virus that is a member of the Orthopoxvirus genus, Chordopoxvirinae subfamily, and Poxviridae family, is the causative agent of monkeypox, a viral zoonotic disease. The symptoms of monkeypox often go away on their own after two to four weeks, and the mortality rate has historically ranged from 0% to 11%.

Monkeypox is characterized by severe headaches, fever, lymphadenopathy, and lesions. Antiviral medications and smallpox vaccines have been authorized for use in a number of nations in response to the monkeypox outbreak, despite the fact that there is no particular treatment or vaccine for MPXV infection. Rapid action is required to control the local spread and, consequently, the multi-country monkeypox outbreak before the virus can be allowed to establish effective person-to-person transmission.

Keywords: Monkeypox virus, Outbreak, Infection, Prevention, Treatment

1. Introduction

The new multi-country epidemic of the Human Monkeypox virus (MOXV) has shocked the world as the COVID-19 pandemic continues as the world deals with the effects of the coronavirus 2019 sickness (WHO, 2022).

The UK Health Security Agency (UKHSA) announced on May 7, 2022, that a person with a history of travel to Nigeria had been diagnosed with MOVX (Hinch *et al.*, 2024). A large number of patients in this outbreak lacked the usual clinical signs and symptoms of monkeypox. Common symptoms in instances reported thus far include fever, enlarged lymph nodes, genital and perianal lesions, and difficulty swallowing.

Localized anogenital rashes (with blisters, pustules, or ulcerative lesions) can occasionally emerge initially and do not spread to other areas of the body, even if oral ulcers are still a common feature of fever and lymphadenopathy. The majority of cases were between the ages of 31 and 40 (792/1796), and 99.4% (1761/1771) of the 1796 confirmed cases recorded by the European Surveillance System were male. Of the 152 men interviewed, 151 identified as gay, bisexual, or men who have sex with men (GBMSM), according to the UKHSA (Luo & Han, 2022).

Several nations have released full-length or partial genome sequences of MPXV in an effort to pinpoint its origin and monitor its spread (https://virological.org). These sequences were homologous with a strain that was found in the UK three years ago, according to sequence comparisons. The strains are members of the West African strains whose mutation frequency has been established and which exhibit low virulence. The 2022 MPXV seemed to have a mean of 50 SNPs,

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which is significantly higher than earlier estimates of the Orthopoxvirus substitution rate (1–2 substitutions per site per year) when compared to the 2018–2019 MPXV. The genome's higher-than-expected mutation rate raises the possibility that MPXV is evolving into a more human-adapted virus (Isidro *et al.*, 2022). Since monkeypox has been reported in countries that have never experienced the disease before and have no epidemiological ties to countries that have previously reported cases of human monkeypox (such as the endemic countries in West and Central Africa), the transmission of the disease appears to be highly unusual in the global outbreak of 2022. The global monkeypox outbreak was deemed a public health emergency of international concern by the World Health Organization (WHO) on July 24, 2022 (Adegboye *et al.*, 2022).

Concerns have been raised recently by the sharp and quick increase in human monkeypox cases reported worldwide. Since May 2022, monkeypox has been recorded in almost 100 countries, with over 62, 000 cases confirmed. More than 99 percent of confirmed cases were male.

The majority of confirmed cases (>99%) were males, with an average age of 35–38 years (ranging from 18 to 67). The bulk of cases in the current widespread outbreak in countries not previously endemic are still predominantly male individuals who identify as men who have sex with men. Additionally, most of these cases have shown mild to moderate symptoms (WHO, 2022). To confirm the ability of MOXV to be transmitted sexually, semen and vaginal fluids were used in isolation (Noe *et al.*, 2022). So far, there have been reports of healthcare workers becoming infected through their work (WHO, 2022; Zachary & Shenoy, 2022). Before this outbreak, cases outside of Africa were linked to travel to areas where the virus was endemic or to contact with imported animals (Rao *et al.*, 2022). Although the natural host of MOXV remains a mystery, some studies suggest rodents might be the primary source (Reed *et al.*, 2004). Some experts believe that the recent increase in MOXV transmission could be due to the end of smallpox vaccination programs in the 1980s. However, smallpox vaccination did provide some level of protection against other orthopoxviruses, including monkeypox (primarily in the elderly) (Rimoin *et al.*, 2010). Moreover, the changing patterns of monkeypox in humans must be taken into account to effectively prevent its spread, which highlights the importance of healthcare professionals being well-informed about monkeypox to achieve this goal. This paper aims to provide a comprehensive overview of MOXV's history, clinical signs, spread, vaccination, and treatment.

1.1. History of monkeypox

The virus that causes monkeypox in humans was first identified in 1958 during an outbreak among captive cynomolgus macaque monkeys at a research facility in Copenhagen, Denmark. This led to the name monkeypox, as the monkeys were imported from Singapore for polio vaccine research (von Magnus *et al.*, 1959).

Subsequent research revealed monkeypox in various rodents like rats, mice, and squirrels, but the exact origins and how the virus spreads remain a mystery, making the term "monkeypox" somewhat misleading (Rao *et al.*, 2022). The first human monkeypox case was reported in Zaire (now the Democratic Republic of the Congo) in 1970, nine months after the country had successfully eradicated smallpox (Xiang & White, 2022).

In 1970, a 9-month-old child was brought to the hospital with symptoms similar to smallpox. Samples from the child were sent to the WHO Smallpox Reference Centre in Moscow, where the monkeypox virus was identified. The child recovered but later died from measles, which was unrelated to the monkeypox. All other family members had smallpox scars from previous vaccinations. There was no evidence of the virus spreading further. Since then, monkeypox has become a regular occurrence in the Democratic Republic of the Congo and has spread across Africa, particularly in Central and West Africa (Breman *et al.*, 1980).

The first monkeypox cases outside of Africa were reported in the United States of America in 2003. Over the next few years, there was a significant increase in human monkeypox cases (CDC, 2022).

2. Epidemiology of monkeypox

Over the last forty years, surprisingly, the occurrence of human monkeypox has been most frequent in impoverished communities located in far-off forests across Africa (Cohen, 2022).

2.1. Causative agent

Monkeypox is a rare illness that results from infection with MPXV. MPXV is a unique virus with an enveloped, linear, double-stranded DNA structure. It belongs to the Orthopoxvirus family, specifically the Chordopoxvirinae subfamily, and the Poxviridae family. It shares similar features with other orthopoxviruses, such as being ovoid or brick-shaped particles (Shchelkunov *et al.*, 2001; McCollum & Damon, 2014; Saxena *et al.*, 2022).

Monkeypox is caused by the monkeypox virus, a type of Orthopoxvirus found in the Poxviridae

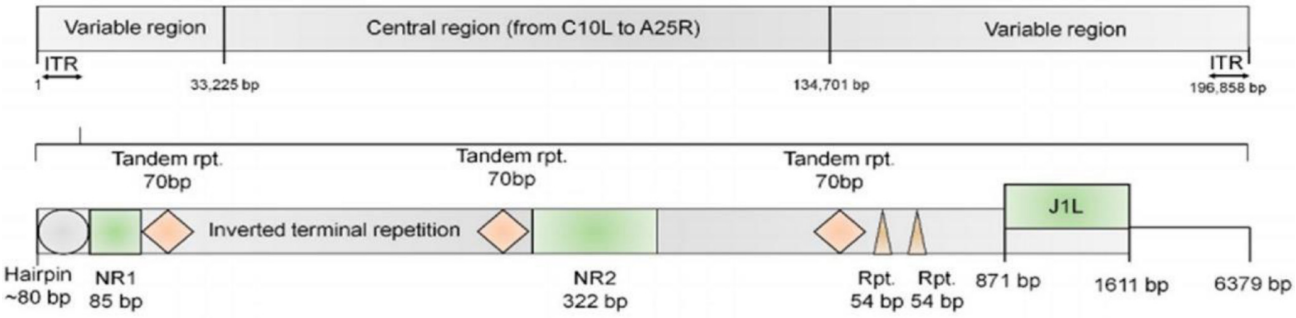

Fig. 1. The structure of the MPXV genome (Shchelkunov et al., 2002).

family, Chordopoxvirinae subfamily. Within the Orthopoxvirus family, there are other significant viruses that affect humans and animals, including the smallpox virus, vaccinia virus, and cowpox virus. In 2001, a study comparing the monkeypox and smallpox viruses identified 96.3% similarity in their central genome regions, which contain crucial enzymes and structural proteins. However, there were notable differences in the end regions responsible for virulence and the ability to infect hosts (Babkin, Babkina, and Tikunova, 2022).

MPXV is considered one of the largest and most complex viruses in the animal kingdom, measuring between 200 to 250 nm in size when viewed under an electron microscope. The virus is made up of four primary components: the core, lateral bodies, the outer membrane, and the outer lipoprotein envelope. Virions are surrounded by a geometrically corrugated lipoprotein outer membrane, with the core being biconcave and housing a large double-stranded DNA genome, each with lateral bodies on either side.

2.2. *MOXV genome*

The virus encodes 200 proteins and has a genome of about 197 kb. An identical but oppositely orientated region known as an inverted terminal repeat is found at the ends of the genome, Fig. 1, (Shchelkunov *et al.*, 2002). There are roughly 190 nonoverlapping open reading frames of >180 nt length in the genome, which features close hairpins on both ends. Since the inverted terminal repeat contains four open reading frames on the left side of the genome, they have corresponding sequences on the right side of the genome (Alakunle *et al.*, 2020). Despite being a DNA virus, MPXV spends its whole life cycle in the cytoplasm of cells that have been infected. The MPXV genome encodes every protein needed for transcription, virion assembly, egress, and viral DNA replication.

According to phylogenetic trees, MPXV sequences were divided into two genetic clades: the Central African clade (also known as the Congo Basin clade) and the West African clade. Because of the differences in virulence, the genomes of monkeypox strains from Central and West Africa were compared. The findings showed that there were nucleotide differences between the two strain types of 0.55% to 0.56%. MPXV is readily inactivated by formalin, methanol, and chloroform, but it is resistant to ether and drying. Furthermore, the virus is rendered inactive by heating it to 56°C for 30 minutes. The virus can be kept for a short time at 4°C or −20°C, or for a long duration at −70°C (McCollum & Damon, 2014).

3. Clinical manifestations

Monkeypox is normally a self-limiting infection, with symptoms recovering within 2–4 weeks. However, in certain people, such as toddlers, pregnant women, or those with weakened immune systems, the illness can be quite serious. There are two phases to the infection: the invasion phase and the skin eruption phase. A fever, severe headache, chills, fatigue, asthenia, lymphadenopathy (swelling of the lymph nodes), back pain, and myalgia are the hallmarks of the invasion period, which lasts from 0 to 5 days. Usually, the skin eruption phase starts one to three days after a fever appears. A rash may also occur prior to a fever, according to research conducted during this outbreak and in the past (Yinka-Ogunleye *et al.*, 2019).

Usually starting on the face, the rash spreads quickly and centrifugally throughout the body, concentrating more on the face and extremities than the trunk. In 95% of cases, the rash spreads to the face, 75% to the palms of the hands and soles of the feet, 70% to the oral mucous membranes, 30% to the genitalia, 20% to the conjunctivae, and the cornea, Fig. 2. Then, over the course of one to two days, monkeypox lesions go through multiple stages, from blister-like lesions to scabs.

The number of lesions varies from a few to several thousand, and the rash progresses in a sequential

Fig. 2. Low left photo belongs to Extensive papulo-pustular monkeypox rashes with crust and scar formation. (Courtesy of Nigeria Centre for Disease Control, Abuja, Nigeria.), upper (A, B) Papular-pustular monkeypox skin lesions on the hands, legs, and feet. (Courtesy of Nigeria Centre for Disease Control, Abuja, Nigeria.) lower right (A–D) explain Maculo-papular-vesicular-pustular monkeypox skin lesions of varying sizes on the face. (Courtesy of Nigeria Centre for Disease Control, Abuja, Nigeria) (Petersen et al., 2019).

manner from macules (flat-base lesions) to papules (slightly raised firm lesions), vesicles (lesions filled with clear fluid), pustules (lesions filled with yellowish fluid), and crusts that dry up and fall off. Lesions may clump together until sizable portions of skin peel off in extreme circumstances (WHO, 2022; Petersen *et al.*, 2019).

Furthermore, these many lesions could manifest simultaneously. The person is no longer contagious when the scabs from their lesion peel off and healthy tissue is exposed underneath, which typically occurs two to four weeks following the commencement of symptoms. Since monkeypox is a rash-producing disease, it must be recognized from other rash-producing disorders. Secondary infections, respiratory distress, bronchopneumonia, sepsis, encephalitis, corneal infection-related vision loss, gastrointestinal involvement, vomiting, and diarrhea with dehydration are among the complications that can arise from monkeypox (Petersen *et al.*, 2019).

The recent outbreak of MPXV seems to manifest differently. These patients may have minor prodromal symptoms or may go undiagnosed. The majority of cases in this outbreak had abnormal clinical features when compared to the clinical features of African monkeypox patients who have been previously documented.

Guys who have intercourse with other guys often come with a genital or perianal rash. Additionally, some cases have been reported as pustules preceded by lesions at various stages of development and constitutional symptoms (such as fever), both of which are unusual for presentations of monkeypox in the past. The majority of instances result in localized lesions, such as those on the genitalia, the anus, and the surrounding tissues, or on the oral mucous membranes. Proctitis can occur in certain patients (Durski *et al.*, 2018).

4. Sources of infection

A zoonotic infectious illness, monkeypox often strikes intermittently in Central and West African forests (Reynolds *et al.*, 2019). MPXV, a member of the Orthopoxvirus family, is the cause. Both touch and big droplets of inhaled fluid can transmit monkeypox. The majority of infections are caused by infected animals or reservoir hosts. Humans are the sole reservoir host of variola virus, with no known animal reservoirs, but MPXV has a wide variety of permitted animal reservoir(s), including rodents, mammals, and primates. Kenyan vervet monkeys, chimpanzees, African elephants, wild boar, antelope, Gambian poached rats, pet prairie dogs, West African squirrels, and anteaters are examples of specific animal reservoirs. The method of monkeypox transmission in nature is still unknown, as is the location of its natural reservoir.

Nonetheless, it is believed that African rodents contribute to the spread of monkeypox to people (Panchal *et al.*, 2023).

5. The mode of transmission

When an individual is exposed to MPXV by an infected person, animal, or virus-contaminated object, the virus can spread. MPXV is spread through both human-to-human and animal-to-human contact. Additionally, the virus can transfer from a mother's placenta to a developing fetus. Direct contact with blood, body fluids, or cutaneous or mucosal lesions from infected animal bites or scratches, treating wild animals, or using goods derived from sick animals can all result in the transmission of MPXV from one animal to another (van Saene, Stoutenbeek, & Stoller, 1992).

Direct contact with infectious ulcers, scabs, or bodily fluids, as well as objects like clothing or linen that have come into touch with bodily fluids or ulcers, are the main ways that monkeypox is spread from person to person. It can also be spread via respiratory secretions during prolonged face-to-face contact. Additionally, MPXV can spread through intimate contact, such as kissing, embracing, touching monkeypox-infected body parts, or sexual activity. Monkeypox was mostly found in Africa throughout history, and it was primarily spread by animals to humans. Human-to-human transmission was rare, with secondary human-to-human transmission making up only 28% of cases (Shchelkunov *et al.*, 2001).

However, human-to-human transmission is the mechanism of transmission during this outbreak, and GBMSM has been identified as the cause of the majority of cases. Inter-human transmission has been demonstrated by close contact, despite the fact that the disease is not typically thought of as a sexually transmitted infection. As a result, community transmission is a possibility (Nguyen *et al.*, 2021).

6. Susceptible population

Approximately 80% to 96% of the population is unvaccinated against the vaccinia virus, making up the majority of the susceptible population in the modern era. There is still a chance of infection even though the vaccinated population has some immunity to MPXV, and protection may have diminished over time. The case fatality rate for individuals who are not vaccinated against vaccinia is 9.8%, while vaccination against smallpox (vaccinia) has historically been demonstrated to be 85% effective in preventing MPXV (L'Vov *et al.*, 2008).

7. Natural reservoir of the virus

The monkeypox virus (as well as other Orthopoxviruses) can infect several animal hosts and transmit to humans, in contrast to the variola virus, which only infects humans (Parker *et al.*, 2007; Kmiec & Kirchhoff, 2022).

Three virus-positive African species linked to the importation of monkeypox into the United States in 2003 were rope squirrels (Funisciuris species), giant pouched rats, and dormice (Hutson *et al.*, 2007). Numerous wild animals, including non-human primates (orangutans, chimpanzees, sooty mangabeys, and cynomolgus monkeys), rodents (mice, rabbits, squirrels, hamsters, and groundhogs), anteaters, prairie dogs, southern opossums, marmosets, and

hedgehogs, can contract the disease in the wild, according to serological surveys (Nalca *et al.*, 2005). The natural animal reservoir for the monkeypox virus is still unclear, despite the fact that several animals have been identified as being vulnerable to it. Humans can contract the monkeypox virus by coming into touch with contaminated objects or an infected person or animal (WHO, 2022). The fact that there were only 54 cases of human monkeypox documented between 1970 and 1979 suggested that the virus still infects animals and that humans are merely incidental hosts. Transmission from animals to humans can happen through mucosal membranes, respiratory tract droplets, or torn skin (Alakunle *et al.*, 2020). The eating of undercooked meat and other animal products from infected animals may be a risk factor. Prior to the 2022 outbreak, human monkeypox infections were thought to be mostly caused by animal-to-human transmission through animal interaction. Nonetheless, outbreaks of human monkeypox in certain endemic nations were identified in which the index case was reportedly infected by an animal;Nonetheless, outbreaks of human monkeypox in certain endemic nations were identified, in which the index case was reportedly infected by an animal; still, the transmission persisted for up to a generation (Nolen *et al.*, 2016).

It is believed that the main ways that human-to-human monkeypox is spread are through direct contact with an infected person's skin lesions (like infectious rash, sores, or scabs), respiratory droplets (during close and prolonged face-to-face contact), or contact with recently contaminated objects, fabrics, or surfaces (WHO, 2022). Intimate contact (oral, anal, and vaginal sex, as well as touching an infected person's genitalia or anus), hugs, massages, and kisses, extended face-to-face contact, and touching unclean fabrics and objects used by an infected person during intercourse are all considered forms of direct contact (for instance, fetish gear, sex toys, beds, and towels). Healthcare workers, household members, and other close contacts of monkeypox sufferers are at increased risk due to transmission through respiratory droplets (Jezek *et al.*, 1986). There is little information on monkeypox infection transfer from mother to child during pregnancy and lactation. Neonatal monkeypox infection, miscarriage, stillbirth, and premature delivery are among the negative consequences of mother-to-child transmission of the monkeypox virus. Young adult males with genital ulcers accounted for the bulk of cases in the 2017 human monkeypox outbreak in Nigeria; some of these cases also had concurrent HIV and syphilis. However, there is no proof that human monkeypox is spread through sexual contact, and more research is needed to determine whether vaginal fluids play a part in transmission (Ogoina *et al.*, 2019).

8. Etiology

8.1. MPXV discovery

MPXV is a member of the genus Orthopoxvirus, which also contains the cowpox virus, vaccinia virus, and smallpox virus (Babkin, Babkina, and Tikunova, 2022). They all cause smallpox. In 1958, monkeypox was initially identified in a Danish laboratory. It was called "monkeypox" because there were two outbreaks of the disease among the laboratory monkeys at the time. While smallpox was being eradicated in the Democratic Republic of the Congo (DRC), the first human case was verified in 1970 in a 9-month-old boy who was suspected of having the disease. Since then, reports of monkeypox have surfaced in a number of other Central and West African nations, where it is prevalent and causes thousands of cases annually.

8.2. Outbreak before the global outbreak in 2022

The Democratic Republic of the Congo has been the only nation to consistently report human monkeypox cases for the past 50 years, with over 1000 cases documented annually for the previous three decades. There were 6257 suspected instances of human monkeypox there in 2020 alone. The Democratic Republic of Congo reported 1238 new cases in the first four months of 2022 (WHO, 2022).

The Central African clade was responsible for the majority of human monkeypox cases. It wasn't until an outbreak in the United States in 2003 that human monkeypox was documented outside of Africa. In this outbreak, no deaths occurred, and none of the 81 documented cases (40 percent verified in a lab) were linked to secondary transmission. Infected pet prairie dogs were the source of the monkeypox cases in the United States. Infected exotic animals (dormice and pouched rats) transported from Ghana were the source of the monkeypox virus in the prairie dogs. A number of reasons have probably contributed to the increase in human monkeypox since the 1970s.

These include the monitoring activities, environmental changes (such as deforestation and climate change), and urbanization in regions where the monkeypox virus is maintained in a high number of animal hosts, leading to an increase in incidental animal hosts or reservoirs. Following the end of smallpox vaccination in the early 1980s, the majority of people 40–45 years of age or younger do not have immunity to the smallpox virus. Last but not least, human behavior (such as coming into contact with live or dead

Fig. 3. 2022 Human monkeypox outbreak global map: Cumulative number of confirmed cases, by countries, data as of 19 September 2022.

animals or reservoirs, going to forested or recently deforested areas, hunting, sharing a home with an infected person, sleeping in the same room or bed as an infected person, preparing and consuming dead bush meat or monkeys, etc.), poverty, war, civil conflict, and displacements, travel, the exotic pet trade, and health care facilities are also significant factors (Bunge *et al.*, 2022).

8.3. Outbreak in 2022

For the first time since early May 2022, numerous human monkeypox outbreaks have been documented in European Region nations where the illness is not endemic. First, six instances of human monkeypox were recorded in the UK between May 13 and May 16, 2022. All of the cases self-identified as gay, bisexual, or other males who had sex with men, and there were no epidemiological connections to travel to Africa or imported animals (WHO, 2022).

The majority of confirmed human monkeypox cases included a history of travel to North American and European nations. In addition, there are still reports of human monkeypox cases in endemic nations. More than 62, 000 cases of human monkeypox have been documented globally since early May 2022, with nearly all of those cases occurring in non-endemic areas as of September 19 (Fig. 3) (Bunge *et al.*, 2022).

As of 19 September, 24, 017 cases had been reported in 44 European countries, accounting for 38.5% of all cases reported globally in the current outbreak. Spain had the highest number of cases (6947), followed by France (3898), Germany (3563), and the UK (3552), while Turkey and Ukraine each had one case. The US reported the most cases in this outbreak (23, 892), accounting for 38.3% of all cases reported globally. Variations in the size and population of the at-risk groups, socioeconomic position, underdiagnosis, and/or underreporting may all contribute to variations in the number of human monkeypox cases by nation. This outbreak revealed for the first time the persistent person-to-person transmission chains of human monkeypox that have been documented in Europe (Vivancos *et al.*, 2022).

A rash that appears before prodrome, a rash that manifests with only one ulcer or few lesions, a rash that is limited to the anogenital and/or perineal area, lymphadenopathy that is primarily inguinal, and the absence of prodrome or very mild prodrome symptoms are some of the clinical features observed in the current outbreak that are different from those previously described in the literature that is currently available (Bunge *et al.*, 2022).

The condition is classified as mild to severe in severity, and between 4 and 10% of cases require hospitalization (WHO, 2022). There have been 20 recorded monkeypox deaths in this multi-country epidemic thus far, with an equal number occurring in non-endemic and African nations (mostly as a result of encephalitis and comorbidities).

Only around 25% of cases in one UK cohort research had known interactions with a person who

had a confirmed monkeypox infection, despite some reports indicating a small number of asymptomatic cases. There hasn't been any verified human-to-animal or animal-to-human transmission in the continuing outbreak as of yet. The viruses that were isolated from this epidemic are members of the West African clade (Kmiec & Kirchhoff, 2022).

98% of the 99% of male monkeypox cases, according to a study done at 43 locations across 16 nations, self-identified as gay or bisexual males, or men who had intercourse with men. With a range of 18 to 50 years, the median age of the cases was 38 years.

41% of them were HIV positive, and most of them had well-controlled HIV infection. Of those who were HIV negative or were unsure of their status, 57% received preexposure prophylaxis. There were reports of concurrent sexually transmitted infections in 29% of those who were tested. Even though sexual transmission could not be verified, 95% of cases had a recorded sexual history, with a median of 5 sex partners over the previous 3 months (interquartile range 3–15); 20% reported having "chemsex," or sex related to drug use, in the previous month, and 32% reported going to a sex-on-site event this month (Thornhill *et al.*, April-June 2022).

84.1% of cases in the Spanish outbreak said they had sex without a condom or with several partners in the 21 days prior to the onset of symptoms, 8.1% said they had not, and 7.9% did not respond. Furthermore, 80.3% of cases in the same research did not know of or did not record contact with a known case of monkeypox (Martínez *et al.*, 2022).

While no cases reported traveling to Africa, a number of cases had a history of overseas travel in the month prior to diagnosis, including trips to Italy, Portugal, Belgium, Germany, the UK, Peru, etc.

Furthermore, a number of private parties also played a significant role (56.9% of cases reported dating through social networks, which resulted in sexual encounters in private apartments, cruise ships, and bars). Other cases reported attending a sauna in Madrid or the Gay Pride Maspalomas festival on the Spanish island of Gran Canaria. More research is required to determine whether human monkeypox can be sexually transmitted through genital fluids, even though the virus was discovered in samples of seminal fluid from cases during this outbreak and close physical contact in sexual networks is a significant contributing factor to the ongoing outbreak. Notably, numerous papers noted the absence of vaccination status information (Benites-Zapata *et al.*, 2022).

Out of the US monkeypox cases for which vaccination status was available, 14% said they had previously received the smallpox vaccine (of whom 23% had received one of the two doses during the current outbreak, 23% had received pre-exposure prophylaxis at an unspecified time prior to the current outbreak, and 54% did not specify when they received the vaccine) (Philpott *et al.*, 2022).

People who have been identified as close contacts of someone who has monkeypox, as well as those who find out that one of their sexual partners has been diagnosed with the disease within the last two weeks, are eligible to receive the vaccine during the current outbreak in the United States. Men who have sex with other men or who are transgender or gender nonconforming and have had sex with men within the last two weeks may also be eligible for the vaccine if they have had sex with several partners or in a group setting, or if they have had sex at a commercial sex location (e.g., a sex club or bathhouse), or if they have had sex at an event, location, or in an area where monkeypox is being spread.

The United Kingdom and other European Union nations, including Spain, France, Germany, and others, are vaccinating during the 2022 monkeypox outbreak in accordance with WHO guidelines (Ilic, Macuzic, & Ilic, 2022).

With the exception of Europe and the Americas, where the risk is rated as high, the WHO considers the monkeypox risk to be moderate worldwide and in practically every location. There are several ways in which the current worldwide pandemic is different from previous outbreaks: the unusual size; atypical global expansion; spread in nations where the virus has never been detected; rapid global expansion, primarily among young men (mostly between the ages of 18 and 44), with over 97% of them self-identifying as men who engage in condom-free sex with multiple sexual partners; the role of certain superspreading events associated with international gatherings, while asymptomatic infections and the absence or mild symptoms during the prodromal phase of disease facilitate spreading; and occurrence of a larger number of secondary cases.in conclusion, more investigation is required to comprehend and enhance the treatment of human monkeypox (WHO, 2022).

9. Diagnosis

Clinical and epidemiological features are necessary for the diagnosis of monkeypox. Typically, over the last 21 days, patients have either visited an endemic nation or come into contact with sick people and animals. Since early May 2022, outbreaks of MPXV infection have persisted in non-endemic nations. Furthermore, nearly every one of these sufferers had never visited an endemic nation. As a result, for the current monkeypox outbreak in

non-endemic nations, the WHO has created monitoring case criteria (Vivancos *et al.*, 2022).

10. Detection

A crucial component of diagnosing and monitoring this new virus is the prompt and precise laboratory examination of case samples. The kind of laboratory test used as well as the specimen's quality and type determine whether monkeypox is confirmed. Skin lesion material, such as swabs of the lesion surface, exudate, roof from many lesions, or lesion crust, is the suggested clinical specimen type for laboratory confirmation of MPXV. While blood specimens are typically not used for diagnostic purposes, nasopharyngeal swabs and saliva are also crucial items for detection (Hong *et al.*, 2023).

10.1. Nucleic acid amplification testing

Nucleic acid amplification testing is the foundation for identifying MPXV infection; real-time or traditional polymerase chain reaction is the main detection technique for identifying distinct MPXV viral DNA sequences. According to the WHO, in nonendemic countries, a positive polymerase chain reaction result for Orthopoxvirus is regarded as confirmation if a particular MPXV test is not available (Vivancos *et al.*, 2022).

10.2. Antibody detection

Serum or plasma antibodies shouldn't be used for diagnosis on their own. MPXV-specific immunoglobulin M and immunoglobulin G detection can be performed using acute and convalescent samples. Nonetheless, MPXV and other orthopoxviruses exhibit antigenic cross-reactivity (Martínez *et al.*, 2022).

10.3. Electron microscopy

Although MPXV cannot be distinguished from poxvirus using electron microscopy, it can be utilized to visualize possible poxvirus in a sample. Additionally, this approach only provides limited detection sensitivity, is very technical and complex, and necessitates costly facilities and equipment (Martínez *et al.*, 2022).

10.4. Virus isolation

To date, MPXV isolation from clinical samples has been the accepted diagnostic technique for infection. MPXV should only be carried out in labs with the necessary containment equipment and experience, nevertheless. As a result, this approach is not the best for routine diagnostics. P2-level biosafety labs should isolate viruses, but staff should wear personal protective equipment in accordance with P3-level lab requirements (CDC, 2022).

11. Treatment

As previously mentioned, many MPXV infections have a mild, self-limiting course of illness that doesn't require special care. However, a number of variables, including preexisting medical conditions, comorbidities, and prior immunizations, affect the prognosis of monkeypox. The following individuals may be eligible for treatment:

(1) those with severe illnesses (e.g., hemorrhagic diseases, confluent lesions, sepsis, encephalitis, or other illnesses necessitating hospitalization);
(2) the immunocompromised population (e.g., HIV/AIDS, tumors, transplant recipients, and those undergoing radiation therapy or high-dose corticosteroids);
(3) children, particularly those younger than eight years old;
(4) ladies who are nursing or pregnant;
(5) those who have had allergic dermatitis in the past or who now have it, as well as people who have other exfoliative skin conditions (such severe acne, burns, pustulosis, varicella-zoster virus infection, or herpes simplex virus infection);
(6) people who have one or more side effects (such as bronchopneumonia, secondary bacterial skin infection, coexisting illnesses, or other comorbidities);
(7) people who have abnormal MPXV infection, such as unintentional implantation into the mouth, eyes, or other anatomical areas (like the genitalia or anus), where MPXV infection may present unique risks. Currently, MPXV infection has no specific treatment (Khodakevich, Jezek, & Kinzanzka, 1986).

Antiviral medications created for smallpox victims, however, might be helpful. Primarily symptomatic and supportive, clinical treatment aims to reduce long-term effects, manage problems, and ease symptoms. It must also keep an eye on respiratory health and avoid secondary bacterial infections. The antivirals tecovirimat, brincidofovir, and cidofovir are possible choices for severe cases. The US Food and Drug Administration (FDA) has approved the antiviral medication tecovirimat, also referred to as tpoxx, to treat smallpox in both adults and children (Perez Duque *et al.*, 2022).

During monkeypox epidemics, the US Centers for Disease Control and Prevention permits "compassionate use" of stockpiled tecorvir to treat monkeypox. Although it is not listed in the US Strategic National Stockpile, brincidofivir, also marketed as tembexa, is another antiviral medication that has been authorized by the US FDA to treat smallpox in adults and children, including infants (Saxena *et al.*, 2022).

The US CDC also permits the use of cido fovir, often referred to as vistide, to treat orthopoxviruses, such as monkeypox, during epidemics. (Luo & Han, 2022). There is little information on the effectiveness of tecovirimat, the only medication approved by the European Medicines Agency to treat monkeypox, despite it having demonstrated safety in clinical trials (Saxena *et al.*, 2022).

12. Prevention

The COVID-19 pandemic and the multi-country monkeypox outbreak that is currently taking place in non-endemic nations have garnered international interest. Since international trade and tourism are expanding so quickly, infectious diseases are becoming more widespread. Monkeypox instances have been recorded in South Korea and Singapore in Asia, and on June 24, 2022, imported cases were reported in China. Therefore, Asian nations must closely monitor any developments in the epidemic.

To stop more cases of the disease being imported into China, strict import control and quarantine measures are in place in the interim ((Luo & Han, 2022).

13. Vaccination

Smallpox vaccination has stopped after the disease was eradicated in 1980. However, the number of unvaccinated cohorts is increasing, and the protection offered by the vaccine may diminish over time. As a result, the susceptible population is expanding worldwide, which could allow MPXV to infect people.

To prevent MPXV, the USA authorized the use of the JYNNEOS and ACAM2000 vaccinations, commonly referred to as imvamune or imvanex. The US FDA has approved JYNNEOS, a live attenuated virus vaccine, for use in certain people who may be at risk of contracting poxvirus. However, ACAM2000 is no longer permitted in the EU and has significant adverse effects. Close contacts of patients with monkeypox have primarily been vaccinated with these two vaccinations (Ilic, Macuzic, & Ilic, 2022).

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