AMJ
ISSN: 0005-2523

ISSN: 0005-2523
Volume 62, Issue 08, October 2022

A COMPREHENSIVE OVERVIEW OF THE CURRENT UNDERSTANDING ON MONKEYPOX VIRUS

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ABSTRACT
Human monkeypox is a zoonotic orthopoxvirus with symptoms similar to smallpox. Monkeypox spreads accidentally to people when they come in contact with sick animals. According to the reports, the infection can also be transmitted via physical contact (sexual or skin-to-skin), respiratory droplets, or via fomites such as towels and bedding. Multiple medical countermeasures are on hand; While most incidences of monkeypox is a minor and self-limiting disease that can be treated with supportive care and antivirals (e.g., tecovirimat), JYNNEOSTM, ACAM2000® and replication inept vaccinia virus which were originally designed for smallpox are also affective towards monkeypox. More effective, treatments include brincidofovir (cidofovir) and vaccinia immune globulin intravenous (VIGIV). Antivirals can be considered in severe disease, immunocompromised individuals, pediatrics, pregnant and breastfeeding women, complex lesions, especially when lesions occur around the mouth, eyes, or genitals. The goal of this brief overview is to detail each of these countermeasures. Following two instances of monkeypox virus infection in people returning from Nigeria to the United States, one in Texas (July 2021) and the other in the Washington, DC region (November 2021), the number of monkeypox infections has skyrocketed.

KEY WORDS: Monkeypoxvirus (MPV); Covid-19; PCR; Molecular Diagnosis; Standardisation; Pathogenesis; Therapies; Transmission; VARV; ADE; SORMAS

1. Introduction

Monkeypox virus (MPV) is a *viral zoonosis* (a virus transmitted to humans from animals) [1]. Symptomatically, it is difficult to distinguish MPV patients from smallpox patients, but fortunately, the former is clinically milder [1]. Even through its mind severity, MPV has emerged as the prominent orthopoxvirus for public health since the eradication of smallpox and its vaccine's subsequent cessation. Public health experts are concerned that the emergence of this new outbreak of the MPV could pose a new threat while the world continues to be challenged by the coronavirus disease 2019 (COVID-19) pandemic [2].

In the beginning, MPV was found in monkeys, but now, we have found it in dormice, tree squirrels, rope squirrels, and gambian pouched rats too. Monkeypox is brought on by a pox virus (Poxviridae family) that is closely linked to the smallpox virus and spreads through intimate contact between humans and animals. Rodents, rabbits, and non-human primates are the main hosts of poxviruses, which can occasionally be passed to humans, aiding in the occurrence of human-to-human transmission [3].

2. Pathogenesis

MPV is an enveloped linear double-stranded DNA virus in the Poxviridae family's orthopoxvirus genus. It has two distinct genetic clades (parental origin): central African (Congo Basin) and west African. The Congo Basin clade has historically caused more severe disease and was thought to be more transmissible. So far, the only country where both virus clades have been found has been Cameroon [4].

MPV can infiltrate its host via the oropharynx, nasopharynx, or intradermal routes. The virus replicates at the site of inoculation before spreading to regional lymph nodes. It then spreads to other body organs after a period of initial viremia (virus as guest in our body). One could see that MPV resembles other orthopoxviruses in its morphology [4].

MPVs are oval or brick-like in shape, with a lipoprotein-based membrane surface. Poxviruses enter host cells through macropinocytosis, endocytosis, and fusion. MPV, being a "DNA virus", one could mistake its presence in nucleus. But in fact, they reside in the cytoplasm. The reason is that the virus DNA replication, transcription, and virion assembly require the presence of several proteins which is mostly abundant in the cytoplasm [4].

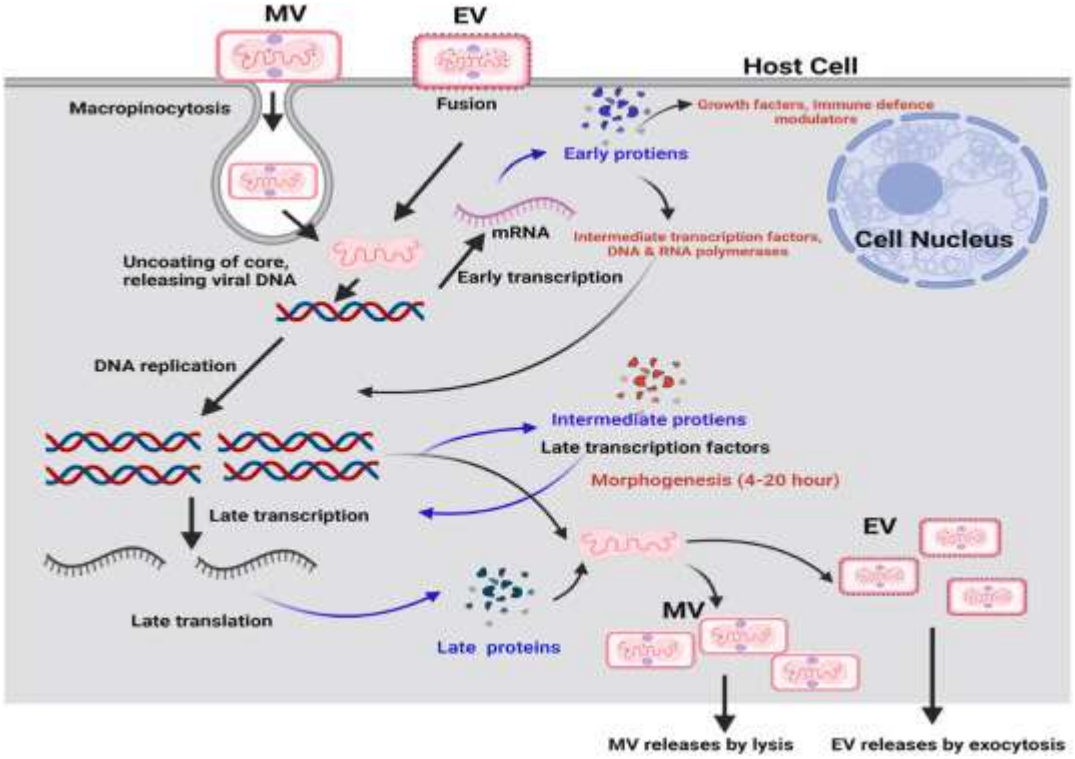

Figure 1: Pathogenesis of MPV in human (host) cell

Whether the virus is transmitted from human to human or from animal to human, the aetiology and pathophysiology of monkeypox start with this transmission [2]. The diagram above shows a brief and yet precise pathology of the MPV.

3. Transmission

The MPV is thought to have several modes of transmission, all of which are linked to direct contact

with infected animals or humans [3]. Direct contact with the blood, body fluids, cutaneous or mucosal lesions of infected animals can result in animal-to-human (zoonotic) transfer [5]. Numerous animals in Africa, including rope squirrels, tree squirrels, Gambian pouched rats, dormice, various species of monkeys, and others, have shown signs of MPV infection. Rodents are the most plausible candidates for the monkeypox natural reservoir, though this has not yet been determined [6,14]. Eating undercooked meat and other diseased animal products is a potential risk factor. People who live in or close to forests may be indirectly or minimally exposed to diseased animals [4]. Close contact with respiratory secretions, skin sores on an infected person, or recently contaminated objects can cause human-to-human transmission [2]. Health professionals, family members, and other close contacts of current patients are more at risk because droplet respiratory particles typically require extended face-to-face contact [7,8,9]. The number of person-to-person infections in a community's longest documented chain of transmission has increased from 6 to 9 in recent years [7] [10]. This might be an indication of a general decline in immunity brought on by the end of smallpox vaccination campaigns. Congenital monkeypox can result through transmission through the placenta, which can also happen during intimate contact during labour and after delivery [8]. Despite the fact that intimate physical contact is an established risk factor for transmission [8].

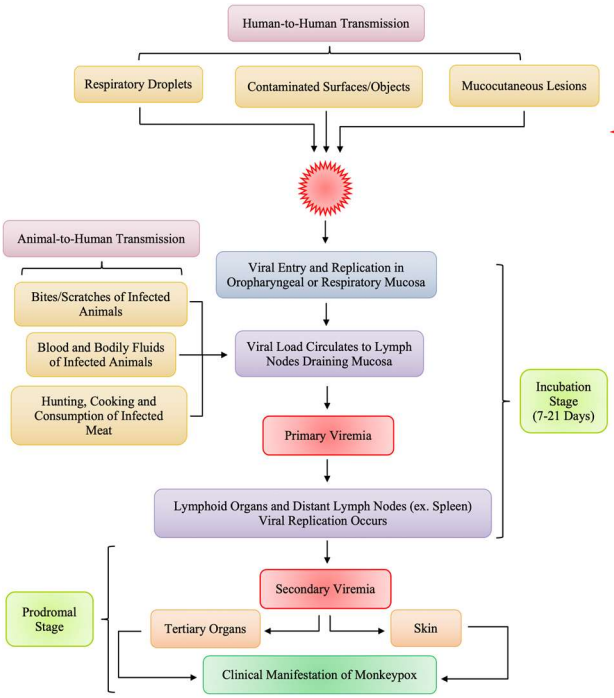

Figure 2: Virus Pathogenesis in Human to Human in Animal to Human

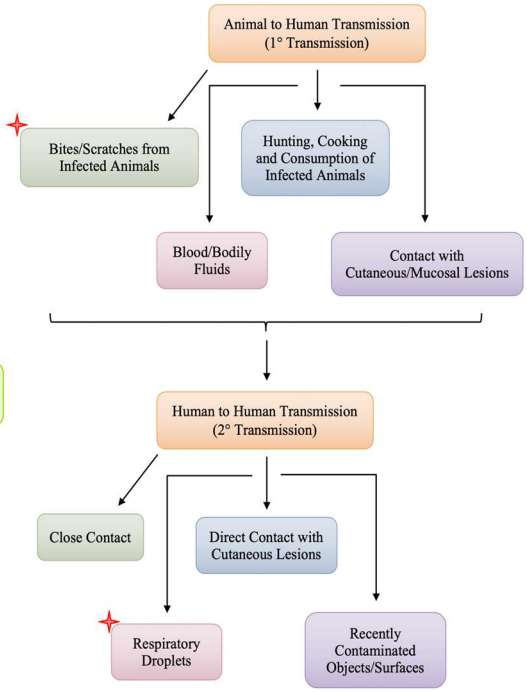

Figure 3: Virus Transmission

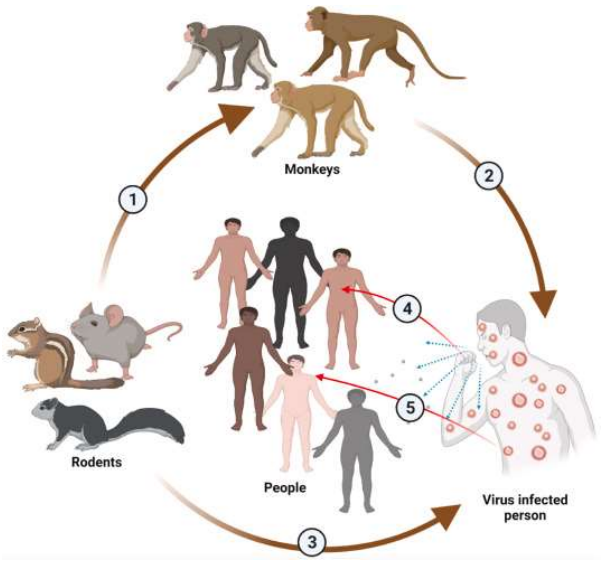

Figure 4: Virus Transmission cycle

4. Sign and Symptoms

The incubation period (the time it takes from infection to the onset of symptoms) for monkeypox is typically 6 to 13 days, but it can range from 5 to 21 days [1].

The infection can be divided into two periods:

a. The invasion period (which lasts between 0 and 5 days) is characterised by fever, severe headache, lymphadenopathy (lymph node swelling), back pain, myalgia (muscle aches), and severe asthenia (lack of energy). Lymphadenopathy distinguishes monkeypox from other diseases that may initially appear similar (chickenpox, measles, smallpox) [3].

b. After the onset of a fever, the skin eruption often starts one to three days later. Instead of the trunk, the rash is more frequently found on the face and limbs. In 95% of cases, it affects the face, and in 75% of cases, it affects the palms of the hands and the bottoms of the feet. Along with the cornea, oral mucous membranes, genitalia, and conjunctivae are all also impacted in 70% of instances. The progression of the rash goes from macules (flat, firm lesions) to papules (slightly raised, firm lesions), vesicles (clear fluid-filled lesions), pustules (yellowish fluid-filled lesions), and crusts that dry up and break off. Lesions can range in number from a few to several thousand. Lesions may combine in extreme circumstances [3].

Typically, monkeypox is a self-limiting illness with symptoms that last between two and four weeks [1]. Children are more likely to experience severe cases, which are connected to the level of viral exposure, the patient's condition, and the type of problems [4]. The results could be worse if immunological deficits were present. Although smallpox immunisation proved protective in the past, people under the age of 40 to 50 (depending on the country) may now be more susceptible to monkeypox due to the worldwide discontinuation of smallpox vaccine campaigns after the illness was eradicated [7]. Monkeypox complications can include secondary infections, bronchopneumonia, sepsis, encephalitis, and corneal infections with subsequent vision loss. It is unknown how widespread an asymptomatic infection might be.

Monkeypox case fatality rates have historically ranged from 0% to 11% in the general population,

with young children being more vulnerable. Recently, the case fatality ratio has hovered around 3-6% [14].

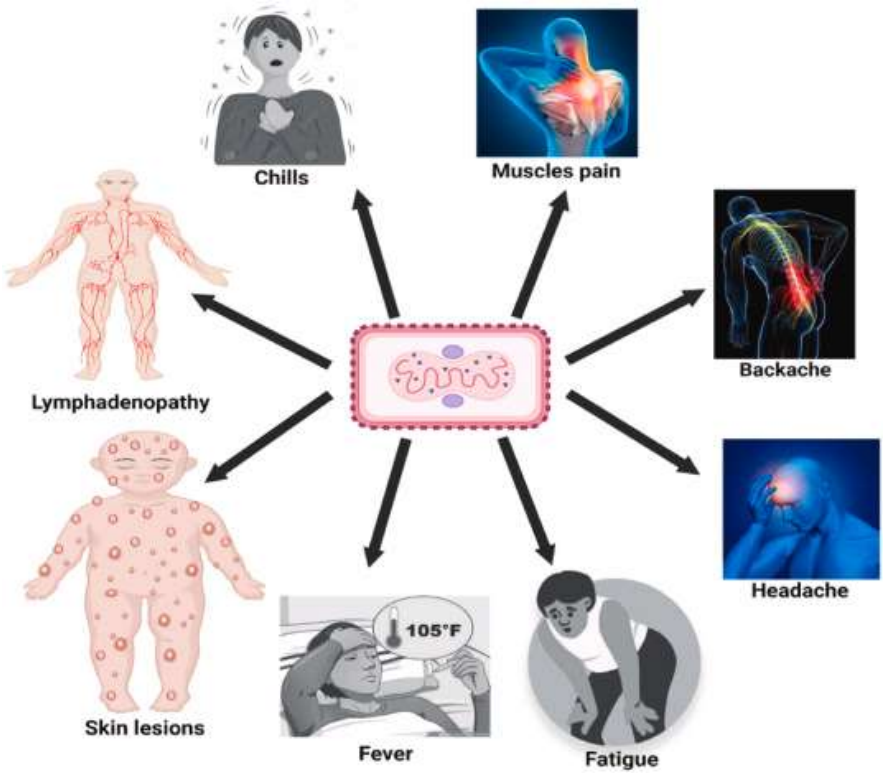

Figure 5: Sign and Symptoms of MPV

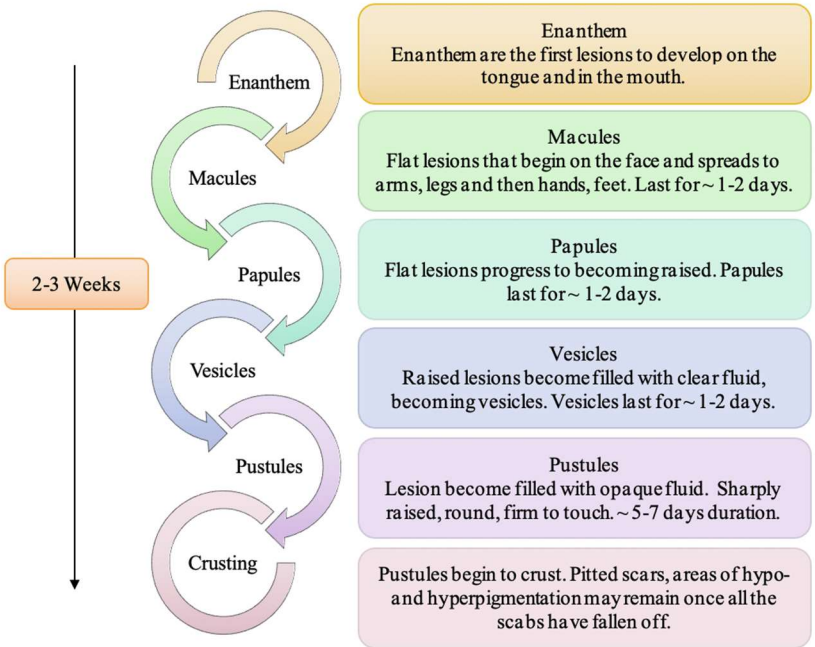

Figure 6: Stages of Vesiculo pustular in MPV

5. Diagnosis

Diagnostic tests are required to confirm MPV infection and must be correlated with clinical and

epidemiological data [3]. The history, clinical symptoms, and laboratory tests are used to diagnose MPV infection. The latter include immunohistochemistry, western blotting, PCR, and ELISA [4]. To rule out other potential infectious disorders like smallpox, a confirmatory diagnosis is essential [3]. A swab is used to collect crust or exudate from the lesion in order to isolate viral nucleic acids for diagnosis [5]. The MPV genome-specific real-time polymerase chain re[1]action (RT-PCR) assay is then performed using viral DNA. The western blot method, on the other hand, uses MPV proteins to verify the presence of the MPV. The preferred test for identifying MPV during an acute infection, according to the WHO, is the RT-PCR test [5,6].

Other rash disorders, such as chickenpox, measles, bacterial skin infections, scabies, syphilis, and medication-associated allergies, must be taken into account when making a clinical differential diagnosis. As a clinical characteristic, lymphadenopathy during the prodromal stage of the illness can help differentiate monkeypox from chickenpox or smallpox [8].

If monkeypox is suspected, health workers should collect a suitable sample and have it safely transported to a laboratory with the necessary capabilities. The type and quality of the specimen, as well as the type of laboratory test, are used to confirm monkeypox. As a result, specimens must be packaged and ship [5,6].

The best diagnostic samples for monkeypox come from skin lesions, such as dry crusts and the liquid that comes from vesicles and pustules. Biopsy is a possibility when it is possible [8]. Lesion samples must be maintained cool and stored in a dry, sterile tube without viral transport medium. Due to the short period of viremia in relation to the date of specimen collection after symptoms begin, PCR blood tests are typically inconclusive and should not be regularly obtained from patients.ped in accordance with national and international standards [5,6,8]. Because of its accuracy and sensitivity, polymerase chain reaction (PCR) is the preferred laboratory test. Antigen and antibody detection techniques do not offer proof of monkeypox-specific infection because orthopoxviruses are serologically cross-reactive [25,29]. Therefore, in cases where resources are scarce, serology and antigen detection procedures are not advised for diagnosis or case inquiry. Furthermore, recent or distant immunisation with a vaccinia-based vaccine (for example, anyone immunised prior to the eradication of smallpox, or more recently due to heightened risk, such as orthopoxvirus laboratory employees) may result in false positive results.

In order to interpret test results, patient information such as: a) date of onset of fever, b) date of onset of rash, c) date of specimen collection, d) current status of the individual (stage of rash), and e) age must be provided with the specimens [30].

6. Prevention

Some precautions can be taken to avoid MPV infection. This includes, but is not limited to, avoiding direct contact with animals suspected of harbouring MPV [13,27], particularly in regions where monkeypox disease is common, isolating infected patients in a negative-pressure environment to stop the virus from spreading from person to person, isolating and euthanizing the animals suspected of being the virus' reservoirs, and avoiding contact with any objects that have come into contact with sick people or animals. The proper personal protective equipment (PPE),

such as an N-95 mask, water-resistant gowns that cover the entire body, double-layered gloves, and other items, should be worn by front-line staff caring for MPV-infected patients and other high-risk individuals who are anticipated to come into contact with the infected people [13].

The smallpox vaccine is expected to provide some protection against MPV infection due to their genetic similarities [8]. Because of the virus's long incubation period, prevention of MPV is expected if the vaccine is administered within four days of exposure to MPV [9,13]. It is reasoned that such vaccination should provide complete disease protection. Health departments have implemented regulations to give smallpox immunizations to front-line staff caring for the afflicted patients in numerous countries in order to stop the current MPV outbreak [13]. For people who are at a high risk of coming into contact with MPV, the US CDC chose to distribute some of its JYNNEOS vaccine, a live vaccinia vaccine that was initially authorised for smallpox virus in 2019 [11,13]. The general population is not advised to use this vaccine, nevertheless. The German government announced an intention to purchase 40,000 doses of Bavarian Nordic's smallpox vaccine in a news statement on May 25. The United Kingdom Health Security Agency announced on May 26 that it had already produced 20,000 doses of smallpox vaccine to combat the rise in MPV cases [27]. The Modified Vaccinia Ankara (MVA) vaccine is a third-generation smallpox vaccine. MVA has been approved for use against monkeypox in the United States and Canada. Bavarian Nordic is working with the European Medicines Agency (EMA) to get the MVA vaccine approved [8,9].

The primary preventative method for monkeypox involves increasing public knowledge of risk factors and teaching individuals about the steps they may take to lessen virus exposure [1]. A scientific evaluation of the viability and suitability of vaccination for the prevention and control of monkeypox is now being conducted. Some nations have policies in place or are creating them to provide vaccines to people who may be at risk, including laboratory staff, members of quick reaction teams, and healthcare professionals [13,27,45].

7. Treatment

The symptoms of monkeypox sickness are often moderate, and the majority of patients recover without treatment.

Aid and Comfort [13]

Monkeypox patients typically recover without any medical intervention. anyone experiencing digestive symptoms. To reduce gastrointestinal fluid losses, patients who experience (e.g., vomiting, diarrhoea) will need oral/intravenous rehydration.

Antivirals [13]

A number of antivirals may be effective in treating monkeypox infections, despite the fact that they were initially licenced for the treatment of smallpox based on animal models, studies on dose because human testing for these medications has not been done in order to fully determine their efficacy.

(i) Tecovirimat: The first antiviral approved for the treatment of smallpox in adults and children weighing at least 3 kg is tecovirimat, commonly known as TPOXX or ST-246, and it is

regarded as the preferred method.Dual therapy with tecovirimat and brincidofovir may be utilised in patients with advanced illness. Tecovirimat blocks the viral envelope to function. Inhibited by the protein VP37 [1,6], which prevents the last stages of viral maturation and release from the infected cell, the virus's ability to propagate within an infected host While the efficacy of this drug against monkeypox in people has not been studied, studies have shown enhanced survival. Infections with the deadly MPV in tecovirimat-treated patients mice were compared to placebo-treated animals at various disease phases The placebo side-effect profile was generally comparable to that of tecovirimat in an enlarged safety study with 359 human volunteers given the medication. Tecovirimat [13] and vaccinia immune globulin (VIG) were combined in modest studies to treat patients with consequences from the smallpox vaccine, including eczema and developing vaccination disease The use of tecovirimat for infections caused by non-variola orthopoxviruses, such as monkeypox, is permitted by the CDC-held Emergency Access Investigational New Protocol. The protocol also provides room for breaking open an oral capsule and combining its contents with liquid or soft food in kids under the age of 13 kg [15]. The Strategic National Stockpile offers Tecovirimat as an oral capsule formulation or an intravenous vial.

(ii) Brincidofovir and Cidofovir: [1] Since June 2021, brincidofovir has been authorised in the US for the treatment of smallpox. An oral counterpart of the injectable medication cidofovir called brincidofovir may have a better safety record, including reduced kidney toxicity cidofovir. These medicines function by preventing the viral a DNA polymerase [28]. The effectiveness of brincidofovir against orthopoxvirus infection has been demonstrated, despite the paucity of studies examining its usage in treating monkeypox infections in animal models [24]. Despite the lack of clinical evidence for cidofovir's effectiveness against monkeypox in people, the drug has shown in vitro activity and efficacy against animals have experienced fatal infections with the MPV published [23]. It is necessary to administer cidofovir together with probenicid treatment and intravenous normal saline. For before and during therapy with brincidofovir, liver function tests must be performed as brincidofovir may induce increases in serum bilirubin and serum transaminases. These treatments are accessible through an EUA or IND.

(iii) Vaccinia Immune Globulin (VIG) [6]: The FDA has authorized the use of VIG, a hyperimmune globulin, to treat specific vaccine-related side effects. Vaccinia [25] infections in people with eczema vaccinatum, progressive vaccinia, severe generalized vaccinia, and cutaneous problems, abnormal infections brought on by the vaccinia virus, and individuals with these conditions (save in rare, isolated situations) keratitis, such as eye infections The effectiveness of VIG as a treatment for monkeypox and smallpox has not been evaluated in people, despite the fact that it is a possible cure [26]. Due to the contraindications of receiving the vaccinia virus vaccine exposure history may also be used to treat patients with severe immunodeficiency in T-cell function VIG be given. It is necessary to administer VIG therapy through an IND application [28].

8. Epidemiology

Human MPV [3,7] was discovered in a 9-month-old boy in the Democratic Republic of the Congo in 1970, in a region where smallpox had been eradicated in 1968. Since then, the majority of cases have been recorded from the Congo Basin's rural, rainforest regions, mainly in the Democratic

Republic of the Congo, with human cases increasingly being reported from across central and west Africa. Since 1970, 11 African countries have recorded human cases of monkeypox: Benin, Cameroon, the Central African Republic, the Democratic Republic of the Congo, Gabon, Cote d'Ivoire, Liberia, Nigeria, the Republic of the Congo, Sierra Leone, and South Sudan [11,12]. The exact impact of monkeypox is unknown. In 1996-97, for example, an outbreak in the Democratic Republic of the Congo was recorded with a lower case fatality ratio and a greater attack rate than typical [25]. A concurrent epidemic of chickenpox (produced by the varicella virus, which is not an orthopoxvirus) and monkeypox was discovered, which could explain real or perceived variations in transmission dynamics in this case. Nigeria has been experiencing a major outbreak since 2017, with over 500 suspected cases and over 200 confirmed cases, with a case fatality ratio of about 3%. Cases have been reported up to the present day [23,24,25]. Given that it affects the rest of the world in addition to countries in west and central Africa, monkeypox is a disease of worldwide public health significance. The first monkeypox outbreak outside of Africa occurred in the United States of America in 2003, and contact with pet prairie dogs that had the disease was to blame. These pets had been kept with dormice and pouched rats from Ghana that were imported from the Gambia. Over 70 monkeypox cases were brought on by this outbreak in the United States. Additionally, monkeypox cases have been documented in travellers from Nigeria to Israel in September 2018, the UK in September 2018, December 2019, May 2021, and May 2022, Singapore in May 2019, and the United States of America in July and November 2021 [40]. In a number of non-endemic nations in May 2022, several cases of monkeypox were found. The epidemiology, infection origins, and transmission patterns are the subject of studies that are now being conducted [6].

Re-emergence of the virus

In Portugal, Spain, and Canada, respectively, there were 14, 7, and 13 cases of MPV infection recorded on May 18, 2022 [11,20]. The first MPV cases were confirmed in Belgium, Sweden, and Italy on May 19, 2022. Two incidents were reported by Australia on May 20. Both came from Sydney and Melbourne, respectively. Recently, both patients have returned from Europe. On May 20, France, Germany, and the Netherlands all reported their initial cases. On May 20, the Health Secretary of the United Kingdom (UK) revealed an additional eleven MPV cases, bringing the total to 71. The first nation to impose a 21-day MPV quarantine requirement was Belgium . On May 21, Israel and Switzerland both verified their initial cases. On May 18, 2022, Spain reported the first case. The Republic of Spain recently reported an increase in cases of 20 on June 3, bringing the overall number of cases to 186. Denmark's first incidence was reported on May 23. Someone who had just returned from the Canary Islands sent this. On May 24, 2022, Quebec in Canada announced the confirmation of 15 instances; at that time, the Czech Republic had only confirmed one case. The alleged offender attended a concert event abroad in Belgium. A traveller from West Africa, age 29, who was in the United Arab Emirates at the end of May, was the country's first confirmed case. Slovenia also verified its initial incident. 19 nations have reported MPV cases as of May 24. The origin of the present MPV outbreak, however, is yet unknown. According to the MPV's changing nature, it may be transmitted from person to person or from animal to person.

Travelers from the endemic areas of Africa to North America and Europe brought infections with them, which started in them and subsequently spread [11,40].

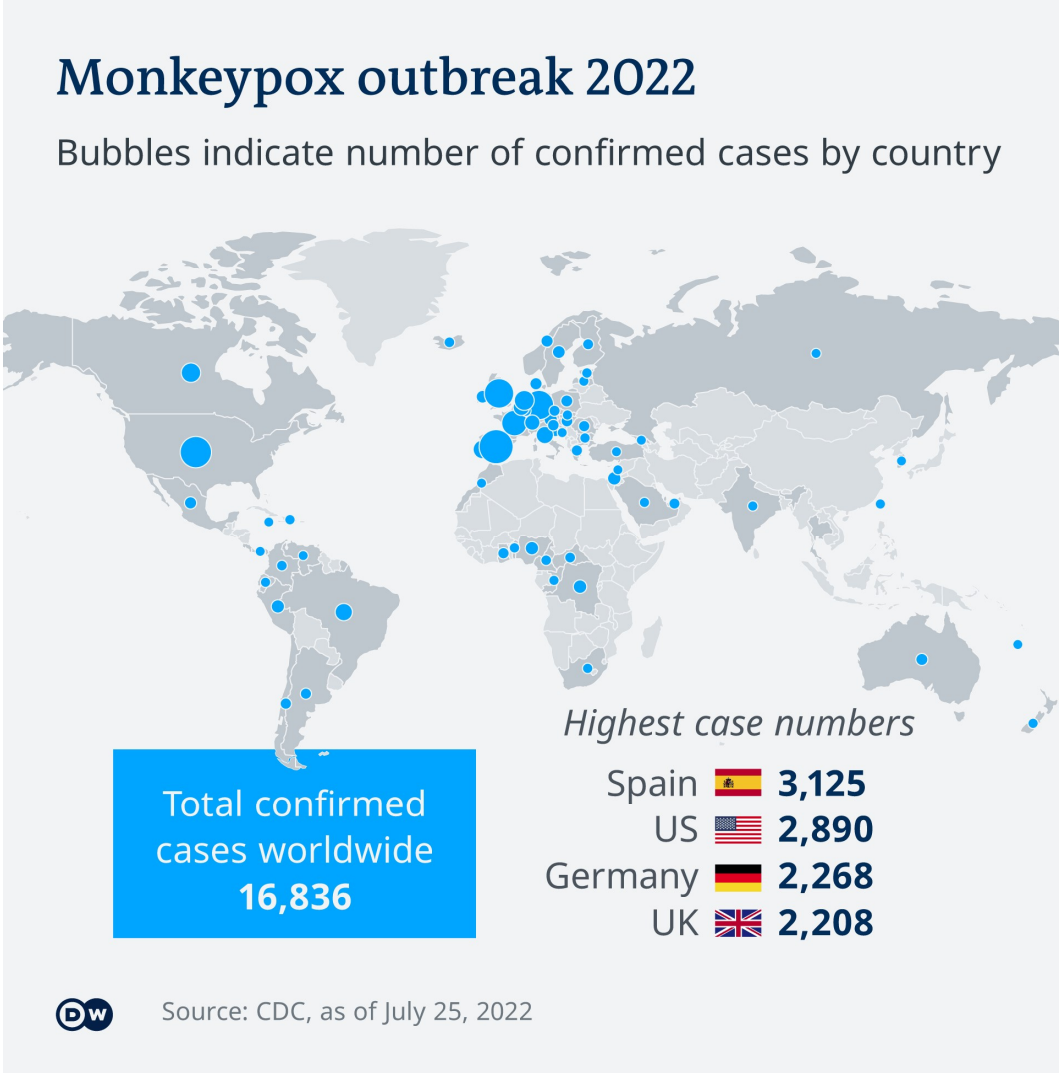

Figure 7: World representation of MPV outbreak in 2022

Infection in the US

In 2003, the US received its first report of an MPV case. In six states, there have been confirmed cases of 47 MPV cases (Illinois, Indiana, Kansas, Missouri, Ohio, and Wisconsin) [24,29,32,34]. Each of these patients contracted MPV after coming into contact with pet prairie dogs. These pets from Ghana were infected by imported tiny animals. The virus outbreak was probably caused by animals that were brought from Ghana to Texas in April 2003 [15]. 800 small mammals, including African giant pouched rats, rope squirrels, tree squirrels, brush-tailed porcupines, striped mice, and dormice were included in this wildlife cargo. Three rope squirrels, nine dormice, two enormous African pouched rats, and nine of them were all MPV-positive, according to the Centers for Disease Control (CDC) [38]. Prairie Dogs, an Illinois animal shelter, has few affected animals living nearby. Before any indications of infection, these animals were sold [24,38]. Following interaction

with the prairie dogs, people had an MPV infection. One MPV infection case involving a US resident was confirmed by the CDC and the Maryland Department of Health on November 16, 2021. The patient was an American who had travelled back to Nigeria. A second instance of monkeypox was also documented by the CDC in Texas in July 2021, and this individual had also come to the US from Nigeria [3].

In the US, MPV is not an innate phenomenon. Nonetheless, there have been occurrences linked to international travel or interaction with imported animals from regions where the illness is more prevalent. The CDC confirmed a case of a recent Canadian immigrant on May 18 in Massachusetts. In addition, the CDC has reported that monkeypox clusters were discovered in early- to mid-May in a number of nations, including Europe and North America, which don't generally report MPV . Infection with MPV has been confirmed in 49 instances in the US as of June 10 [3,24].

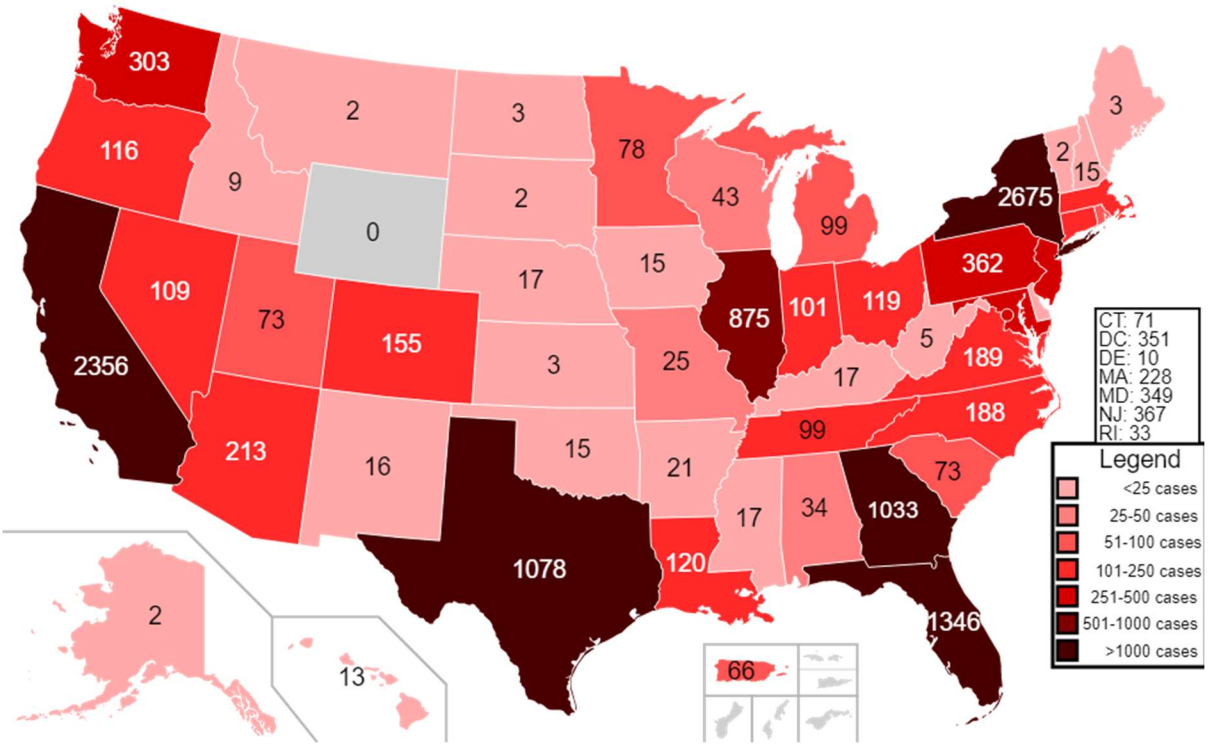

Figure 8: USA representation of MPV outbreak in 2022

Epidemiology of MPV in Nigeria

In Nigeria, a four-year-old girl was the first person to contract MPXV, and her mother became the second person to contract the virus two years later. The mother was thought to have been infected by her child [10]. The affected people were residents of Ihie Umduru, which is in the current state of Abia. Similar to the second instance, the third MPXV infection in Nigeria was discovered in 1978 in a 35-year-old male living in Omifunfun (Oyo state) [9,10,20]. Only three of the ten instances that were reported between 1971 and 1978 were confirmed, and there were no deaths. In September 2017, MPXV cases were reported in Nigeria for the first time in over 40 years. A suspected MPXV case in an 11-year-old boy with an 11-day history of fever, widespread rash, headache, malaise, and sore throat was reported to NCDC by the Niger Delta University Teaching Hospital (NDUTH)

[19,20]. Since the MPXV outbreak began in September 2017 and ended in December 2017, 157 suspected cases have been reported in 23 states of Nigeria. Bayelsa, Rivers, Lagos, Cross River, and Akwa Ibom had the largest number of suspected cases, with 40, 29, 21, 22, and 15 cases, respectively. In 2017, there were 68 verified cases, with two deaths reported from two states. Only nine of the 23 states with suspected cases had no confirmed cases, whereas 14 had between one and twenty confirmed cases. NCDC had documented 104 suspected cases as of November 13th in 19 states, 38 confirmed cases in 12 states, and one fatality in Imo state. The states of Rivers, Cross River, Bayelsa, and Akwa Ibom make up 68% of suspected cases, whereas the states of Rivers, Bayelsa, Delta, and Oyo make up 66% of confirmed cases [20,22,40]. Lagos, Rivers, and Delta states led the 2019 MPXV cases with 35, 20, 15, and 14 suspected cases, respectively, and 14, 10, 8, and 8 confirmed cases. Nigeria generally has 424 MPXV suspected cases and 155 confirmed cases, with the 2017 outbreak having the most confirmed cases. The number of confirmed and suspected cases decreased in 2018, which would indicate that Nigeria's attempts to battle MPXV were successful, but the 2019 data revealed otherwise [22, 23, 25]. Between 2017 and 2019, MPXV cases were recorded in people aged 21 to 40 (median age: 30), with a verified male-to-female ratio of 3:1. After more than three decades of no cases being reported, MPX has returned to Nigeria. This could be because a large portion of the population is immunologically unprepared for OPV infection because they have not received the smallpox vaccination, which also provides protection against monkey pox, or because the smallpox vaccine's effects on induced immunity have worn off in those who have received the vaccination [40]. Other factors that will contribute to the virus's re-emergence include I increased human encroachment on the wildlife habits of human and non-human primates due to urbanization and hunting, (ii) increased trade in rodents and other species of wildlife fuelled by increased demand for and consumption of barbequed rodents/wildlife mammals (referred to as "bush meat") in Nigeria, (iii) heavy rainfall and flooding that brought humans and MPXV-infected animal hosts. As the trade in rodents exported MPX to the USA in 2003, as well as human travellers from Nigeria who exported the disease to Israel, Singapore, and the United Kingdom in 2018 and 2019, the re-emergence is not just a public health concern for Nigeria but has implications for global health. The fact that there is now proof of the West African clade of MPXV spreading from person to person in both the United Kingdom and Nigeria is more concerning. Overall, MPX should no longer be regarded as an uncommon condition that only affects nations in West and Central Africa. In order to understand the zoonotic hosts, the epidemiological variables that maintain and perpetuate the virus in ecosystems, as well as the viral and host factors that modify animal-to-human transmission and human-to-human transmission, significant efforts must be made [9,10,19].

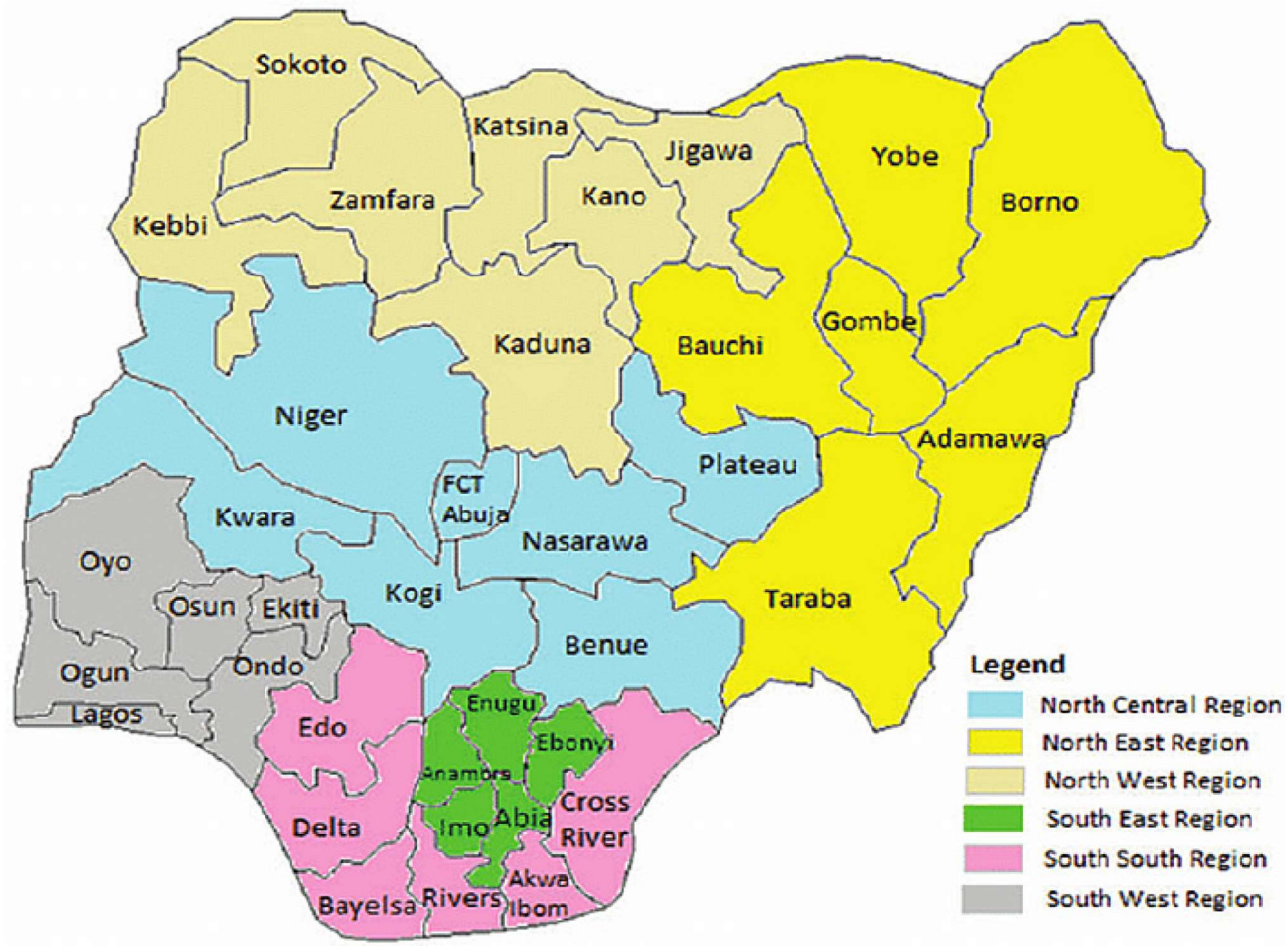

Figure 9: Nigeria representation of MPV outbreak in 2022

9. Knowledge Gaps, Omitted Research

Reservoir Host Species and Tissue Tropism

Although rodents and non-human primates have been identified as potential natural hosts, there is no clear reservoir or host for MPXV [19,20,21]. The lack of information about the virus's natural reservoirs and maintenance hosts may be the cause of the difficulty in comprehending pathogen-host associations. Identifying the exact natural host of MPXV could lead to its specific tissue tropism. Future study should concentrate on finding the viral and host characteristics that influence zoonotic spillover occurrences, human-to-human transmission, and animal/human transmission [22].

Co-infection and recombination

During the smallpox pandemic, MPXV co-infected or superinfected the same human host with VARV. Recombination of MPXVs and other OPVs during Co-infection or Superinfection in a host is not well understood. The MPXV virus may have helped to eradicate smallpox in West Africa in Nigeria and other monkeypox-endemic areas of West and Central Africa. Superinfection or co-infection with VARV is unlikely because MPXV is an acute rather than a chronic infection. The next generation sequencing and proteomic analyses of historical/retrospective samples will

provide new insights into the biology of the MPXV virus. To verify this assertion, particularly in Nigeria, more research is required [45,46].

MPV Infectome

Both cell cultures and animal models have been used to conduct lobal analyses of viral and host gene expression patterns in MPXV-infected cells. Transcriptomic, proteomic, and system kinomics data all reveal that host anti-viral responses are downregulated in the CB clade when compared to the WA clade. Although MPXV possesses a shortened form of those genes, studies have shown functional redundancy of some genes in MPXV since immune evasion tactics against the host antiviral arsenal were triggered [40,45]. While data on virus and host gene expression patterns are available, information on the functional implications of these gene expression profiles to virus infection biology and the molecular basis of MPXV pathogenicity is lacking. The MPXV Zaire and MPXV WRAIR7-61 strains were used in the majority of published work on the MPXV infectome. While this may have provided insight into inter-clade specific heterogeneity in virus infection biology, it provided no answers regarding intra-clade specific variability. As a result, there is no reason to believe that MPXV WRAIR7-61 infection biology will be comparable to that of Nigerian isolates simply because they are members of the same WA lineage [47]. More isolates from the two major clades should be used in future infectome analyses. This will provide a more complete view of MPXV infection biology and may help to identify species-specific antiviral therapies [10,19,24,25].

Antibody-Dependent Enhancement (ADE) of Infection

Antiviral antibodies, a key element of the host immune response against viral infections, work to prevent and neutralize viral infection. An acquired viral infection (ADE) develops when these antibodies promote viral reproduction and uptake into target cells and tissues. According to Kulkarni's theory, antibodies produced by immunization could lead to ADE and make the condition worse [6]. Despite the fact that IgM and IgA antibodies, together with their complement, have a tendency for ADE and have been seen in several viruses such the Zika virus, Dengue virus, and Ebola virus, no MPXV cases have been documented. However, circumstances in which populations of people, domesticated animals, and wild animals already have antibodies to MPXV or other naturally occurring OPVs and are then exposed to the smallpox vaccine or a natural superinfection with OPVs could theoretically increase infectivity and alter the host range, tissue, and cell tropism of MPXV [34,40]. In order to better understand the risks associated with using new generation smallpox vaccines, vaccine-induced antibodies, and antiviral immunoglobulins as therapy against MPX, we must examine ADE in MPXV during natural and experimental infections [19, 35].

10. Conclusion

In Nigeria and other nations in the tropical rain forest belt, MPXV may have been able to reemerge due to factors including the decline in herd immunity brought on by the end of smallpox vaccination, increased human-potential MPXV animal reservoir host contact as a result of climate change and deforestation, consumption of bush meat, and inadequate health and research

infrastructure. Travelers have recently transferred MPX from Nigeria and Ghana to the USA, the UK, Israel, and Singapore, so it is no longer restricted to areas where it is endemic. Due to its global reach, MPXV is a very dangerous re-emerging pathogen. National and international research efforts should be increased to identify virulence markers of disease, host and viral factors that modulate MPXV evolution, human behaviours that support zoonotic spill over events, surrogates for asymptomatic infection, as well as virus and host determinants of immunity, in order to stop MPXV from occupying the ecological niche vacated by VARV and potentially evolving into a much deadlier pathogen than it is at present. Preventive MPXV epidemiological surveillance in humans and possible host species should be carried out in Nigeria, meaning it should be done regularly rather than only in response to an epidemic. An example of MPXV monitoring in Nigeria can be found in the comprehensive CPXV surveillance in Fennoscandia and Germany. It's a step in the right direction that NCDC recently deployed and put into use the Surveillance Outbreak Response Management and Analysis System (SORMAS) for the MPX outbreak in Nigeria. We support the inclusion of routine, periodic epidemiological surveillance for MPXV in humans and animals into SORMAS.

The CDC is creating preliminary recommendations for treating monkeypox. Even in the most severe cases, the monkeypox virus frequently causes moderate, self-limiting sickness in infected persons.

Despite the lack of specific treatment, the outcome of monkeypox patients may vary depending on a number of circumstances, including prior the presence of comorbid conditions, starting health state, and vaccination status. Consequently, personal growthized therapies according to each patient's risk of developing the most logical plan seems to be a serious illness.

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