ISSN 2664-3987 (Print) & ISSN 2664-6722 (Online)
South Asian Research Journal of Medical Sciences
Abbreviated Key Title: South Asian Res J Med Sci

| Volume-6 | Issue-2 | Mar-Apr -2024 | **DOI: 10.36346/sarjms.2024.v06i02.002**

Case Report

Mpox and HIV, a Review and a Case Report of an a Forgotten Epidemic

María de los Ángeles Pérez-Rodríguez[1*], Ángela Rodríguez-Trujillo[2]

[1]Resident Physician of Internal Medicine at "Hospital Regional Pesidente Juárez, I.S.S.S.T.E." Oaxaca de Juárez, Oax
[2]Dermatologist Physician at the "Hospital Regional Poza Rica de Hidalgo, S.S.A." Poza Rica, Ver

***Corresponding Author:** María de los Ángeles Pérez-Rodríguez
Resident Physician of Internal Medicine at "Hospital Regional Pesidente Juárez, I.S.S.S.T.E." Oaxaca de Juárez, Oax

Article History
Received: 12.03.2024
Accepted: 24.04.2024
Published: 27.04.2024

Abstract: People living with HIV have accounted for 38–50% of those affected in the 2022 multicountry mpox outbreak. Most reported cases were in people who had high CD4 cell counts and similar outcomes to those without HIV. Emerging data suggest worse clinical outcomes and higher mortality in people with more advanced HIV [1, 2]. The first report of mpox that led to the discovery of the global outbreak was made to WHO on May 13, 2022. The outbreak spread to 110 countries and was declared a public health emergency of international concern. The Director-General of WHO called on member states to ensure respect for human rights and to address stigma and discrimination. As of Jan 31, 2023, there were 85 549 confirmed cases of mpox reported by 110 countries, including 89 deaths [3, 4].

Keywords: Mpox, sexually transmitted infection, HIV, emerging infectious disease, orthopoxvirus, poxviridae, vaccines, WHO.

INTRODUCTION

Mpox is caused by the species monkeypox virus (MPXV), genus Orthopoxvirus, discovered in 1958 in a primate research facility in Denmark, with the first human case reported in 1970. Two virus clades were identified: the Congo Basin (or central African) clade and the west African clade. Although stigma became a concern during outbreaks in Africa, the 2022 global outbreak reignited discussion with proposals to rename virus clades. Although the nomenclature of virus variants is the remit of scientists, reaching consensus quickly was important. On Aug 8, 2022, WHO convened an ad hoc expert meeting to discuss characteristics of MPXV clades and propose names for them. Participants included orthopoxvirologists, evolutionary biologists, and other scientists from WHO collaborating centres on orthopoxviruses at the US Centers for Disease Control and Prevention and the Russian State Research Centre of Virology and Biotechnology; the WHO Technical Advisory Group on SARS-CoV-2 Virus Evolution; the WHO Advisory Committee on Variola Virus Research; the Poxviridae study group of the International Committee on the Taxonomy of Viruses; research and public health institutes in Africa and around the world; and public virus-sequence databases [3-5].

Objective:

Present a review and a case of coinfection of Mpox and HIV, with the aim of promoting vaccination mainly in risk groups. Encourage the coordinators of this editorial and request their support to make visible the public health situation that we are experiencing in our country, and thus promote vaccination against MPOX in Mexico. Recommend intentional screening for HIV infection in patients when diagnosed with Mpox infection.

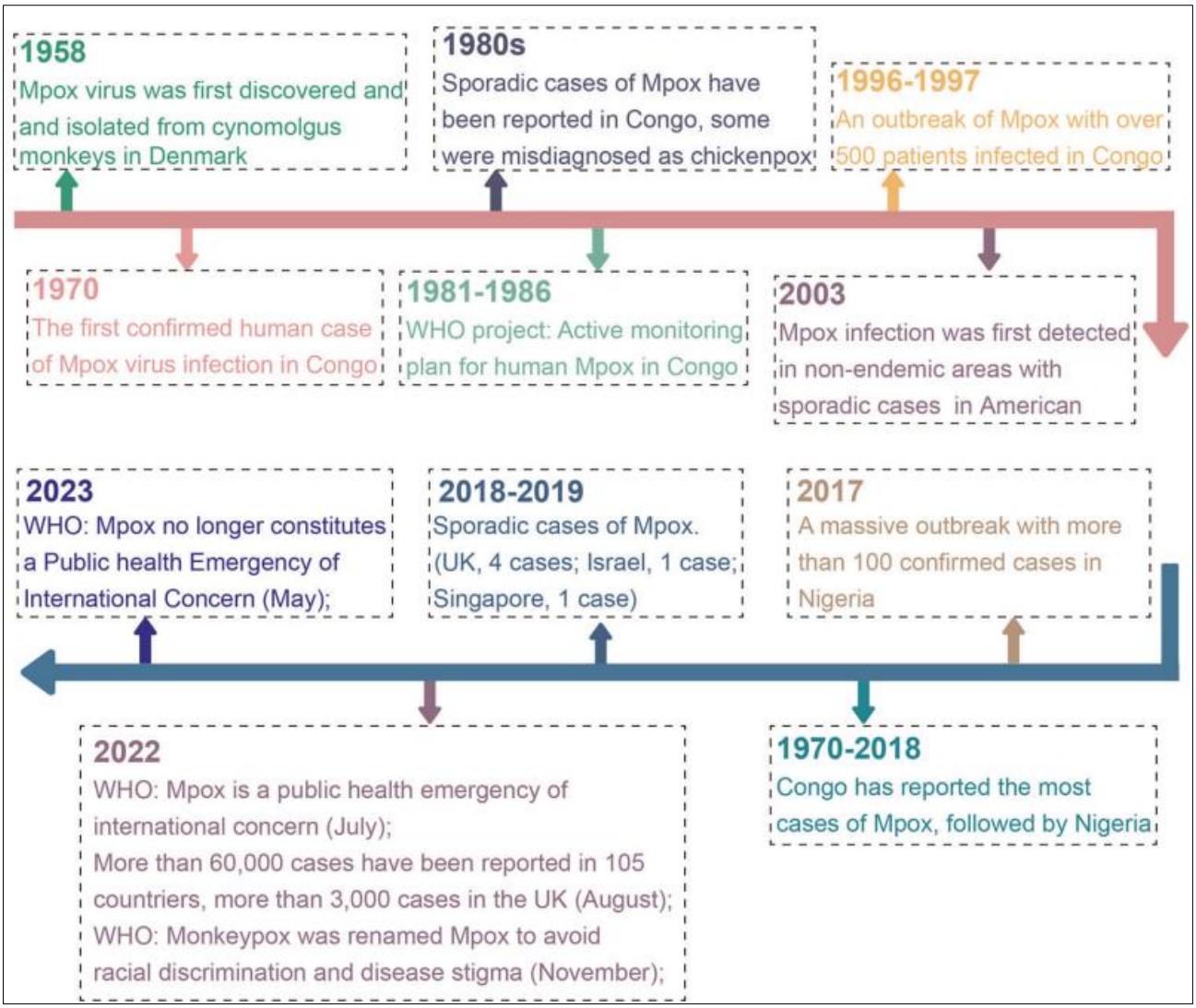

Figure 1: The timeline of the historical review and major milestones in Mpox [5]

The meeting reviewed the phylogeny and characteristics of MPXVs and proposed a neutral naming convention. MPXV phylogeny shows two distinct clusters corresponding to the previously recognised clades. Consensus was reached for nomenclature of a Roman numeral for each clade with lowercase Latin characters for subclades; the Congo Basin clade became Clade I and the west African clade became Clade II, encompassing two phylogenetically distinct subclades, IIa and IIb [3-5].

There are appreciable genetic differences between Clades I and II, showing nearly twice the divergence as that between subclades IIa and IIb. Nonetheless, both subclades include genomes from the 1960s and 1970s and appear to have evolved separately from a most recent common ancestor dating back hundreds of years. Neither subclade is descended from the other. Although the current global outbreak is related primarily to Clade IIb, new cases related to Clade IIa continue to be reported, requiring the tracking of numerous clades and lineages [3, 5].

Pathophysiology:

MPXV is a dsDNA virus and is reported to cause Mpox disease in humans and several other animals (Figure 2). MPXV is a member of the genus OPXV in the Poxviridae family that is known to have a large and complex DNA content amongst all animal viruses. The MPXV has four elements in its virion that include the core, outer membrane, lateral bodies, and the outer envelope made of lipoproteins. The dsDNA genome and fibrils are encapsulated within the core. The MPXV dsDNA genome is 197 kb in size, while the central genomic region is 101 kb. Other genomic elements consist of 6379 bp terminal inverted repetition (ITR, at both terminal variables regions) with ~80 bp long hairpin loop, short tandem repeats (70 or 54 bp), and exclusive ITR regions NR1 and NR2 and the existing coding region. The MPXV genome has ~190 nonoverlapping open reading frames (ORFs), while four are located in the ITR sequence. As consistently seen in OPXVs, the central genomic region consists of genes that have functions in viral transcription, replication, virion assembly, and its release (Figure 2). Both ends of the MPXV genome consist of genes responsible for virulence that have functions in

immune evasion, essentially by interrupting the signaling, antigen presentation and recognition, and cell death. The dsDNA structure, aided by DNA polymerase 30 -50 exonuclease activity, probably contributes to a lower frequency of genomic mutations in the MPXV. However, the 2022 variant of MPXV is reported to be different from the genomes of earlier reported MPXV by approximately 50 single-nucleotide polymorphisms (SNPs). Interestingly, these SNPs indicate increased frequency for GA > AA and TC > TT alterations. Several studies have highlighted that RNA editing could speed up the variations in the MPXV genome and induce mutations. The mechanisms presumed to contribute include the apolipoprotein B mRNA-editing catalytic polypeptide-like 3 (APOBEC3) enzymes. A phylogenetic analysis by Wang and colleagues indicates that the MPXV-2022 strain has 46 novel consensus mutations, which comprises 24 nonsynonymous mutations as compared to the MPXV-2018 strain. Further investigations may shed light on which specific mutations may help the virus evade the host immunity.

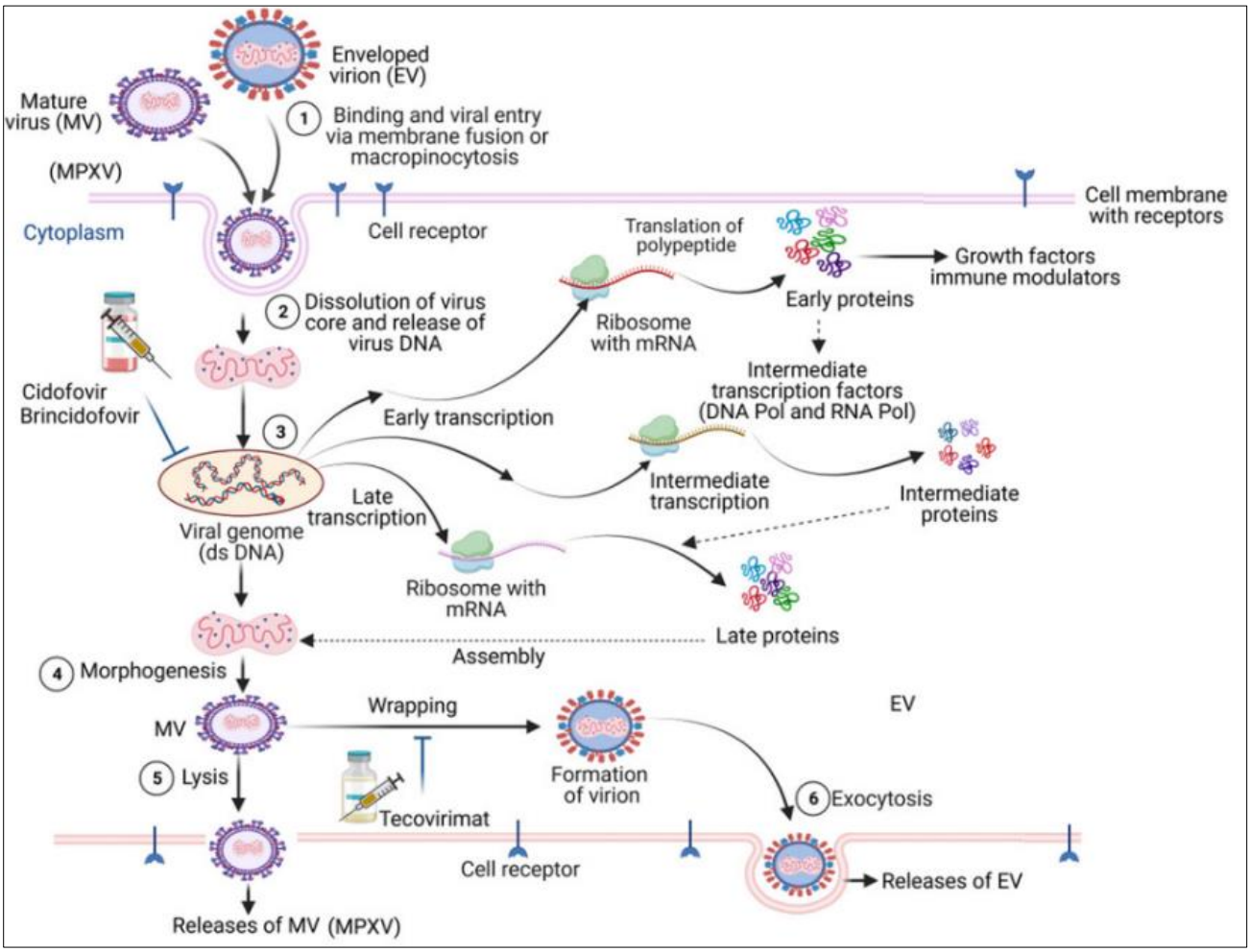

Figure 2: Schematic overview of the mechanism of MPVX infection in human cells

MPVX mature viruses (MV) and enveloped viruses (EV) bind and make an entry (step-1) to the cells via membrane fusion or micropinocytosis. MPXV releases its genome on arriving in the cytoplasm (step-2), where it executes transcription programs (step-3) early (synthesizing polypeptides/proteins that function as growth factors and immune modulators), intermediate (synthesizing intermediate transcription factors including DNA pol and RNA pol), and late (synthesizing proteins involved in MPVX genome assembly) stages. Antiviral medications Cidofovir and Brincidofovir target this step to inhibit MPVX infection. Assembly of the MPVX genome and core elements subsequently undergoes morphogenesis (step-4) and produces MV, which can either release from the host cell membrane directly (step-5) or may undergo wrapping to produce EV that is released by exocytosis (step-6). The later step is the therapeutic target of Tecovirimat [6].

MPXV executes its replication cycle in the host cell cytoplasm. MPVX mature viruses (MV) and enveloped viruses (EV) bind and make entry via membrane fusion or micropinocytosis. Though not exactly clear, viral proteins like D8L, A27L, A34R, A26L224, and H3L were believed to have a function in cell surface binding. Subsequently, MPXV releases its core into the host cytoplasm which has enzymes and key factors that instigate the transcription of viral genes. Viral transcription is initiated by DNA-dependent RNA polymerase, while the translation of early (polypeptides/proteins

that function as growth factors and immune modulators), intermediate (intermediate transcription factors including DNA pol and RNA pol), and late (proteins involved in MPVX genome assembly) proteins is mediated by the host cell ribosomes. Assembly of viral particles produces intracellular MV that resides in the cytoplasm as mature virions and are then released as extracellular enveloped viruses (EV) at the stage of cell lysis. Wrapping of the MV with a Golgi-derived covering to form an EV may also occur, mediated by the VP37 protein. The EV is then released by exocytosis. The later step is therapeutically targeted by the antiviral Tecovirimat [6].

Transmission:

Despite the original name for mpox, monkeys are not thought to be a common animal reservoir. Mpox has been described in squirrels, Gambian pouched rats, sooty mangabeys, prairie dogs, hedgehogs, pigs, and mice found in the African regions whence it was previously widely reported. The name of monkeypox was officially changed to mpox by the WHO on November 28, 2022. The primary routes of mpox transmission involve direct contact with the infectious rash, scabs, crusts, or fluids from sores, saliva, or other infected bodily fluids, including respiratory secretions. Before the 2022–2023 outbreak, close contact with infected animals was thought to be the primary route of mpox transmission; however, cases of human-to-human transmission were also described. Overall, the secondary attack rate (the proportion of unvaccinated contacts of primary cases who become infected) was reported to be 0–11%. Transmission in healthcare settings has also been documented [7].

The suspected route of transmission in the vast majority of cases in the 2022–2023 outbreak has been through close physical human contact, primarily sexual activity, and particularly among Men Who Have Sex with Men (MSM). Mpox has been consistently detected in genital fluids—both seminal fluid and vaginal fluid. In one case, prolonged shedding of mpox virus DNA in semen was noted for weeks after symptom onset, with evidence of replication-competent virus at day 6. Viable mpox virus has also been cultured from the anal and urethral swabs of people with mpox. Mpox has been detected in anorectal swabs from people without symptoms, highlighting the potential for asymptomatic spread. While mpox is not exclusively a sexually transmitted infection, the recent clinical presentations in Europe and the Americas fulfill many of the criteria for it to be considered as such, and consensus is growing for its inclusion as a sexually transmitted infection to allow the development of focused public health interventions [7].

The majority of mpox transmissions in the 2022–2023 outbreak have been among MSM; however, the proportion of all people with mpox who identify as MSM worldwide has decreased during the course of the outbreak, highlighting the need to consider other at-risk groups. An international case series of mpox in cis and trans women and non-binary individuals has been published in November 2022, demonstrating the potential for misdiagnosis and nonsexual transmission in cis women and identifying specific risks, including current sex work and injecting drug use among trans women. Furthermore, childhood infection has been described from exposures typically occurring at home or in school (via close contact), and vertical transmission from mother to fetus during pregnancy has also been described, although fortunately it has been a very rare feature of the multicountry outbreak [7].

Clinical Symptoms:

Most cases after the 2022 outbreak are also men (98%) who had sexual intercourse with other men—gay or bisexual men—and are in their thirties. 96% of the cases have rashes, while 69% also show flu-like symptoms. Respiratory distress/bronchopneumonia, sepsis, gastrointestinal/mouth, and throat ulcers, fever, superinfection skin, inflammation/lymphadenopathy, corneal infection, and skin scarring/cellulitis/skin lesions are amongst the most common symptoms and complications. Clinical signs that last two to four weeks can appear suddenly and proceed mildly. Nevertheless, the severity and progression of the MPX disease differ between individuals (Figure 3).

Following the entrance of the MPX virus into the cell throughout respiratory mucosa, examining the clinical signs of MPX takes approximately 7–21 days of the incubation period. Non-specific and common symptoms were reported in all MPX cases: fever, headache, myalgia, backache, lymphadenopathy, chills, exhaustion, and rashes. Following infection, some probable complications were estimated as bacterial superinfection in lesion regions, corneal infection, sepsis, dehydration, bronchopneumonia, and respiratory distress [8].

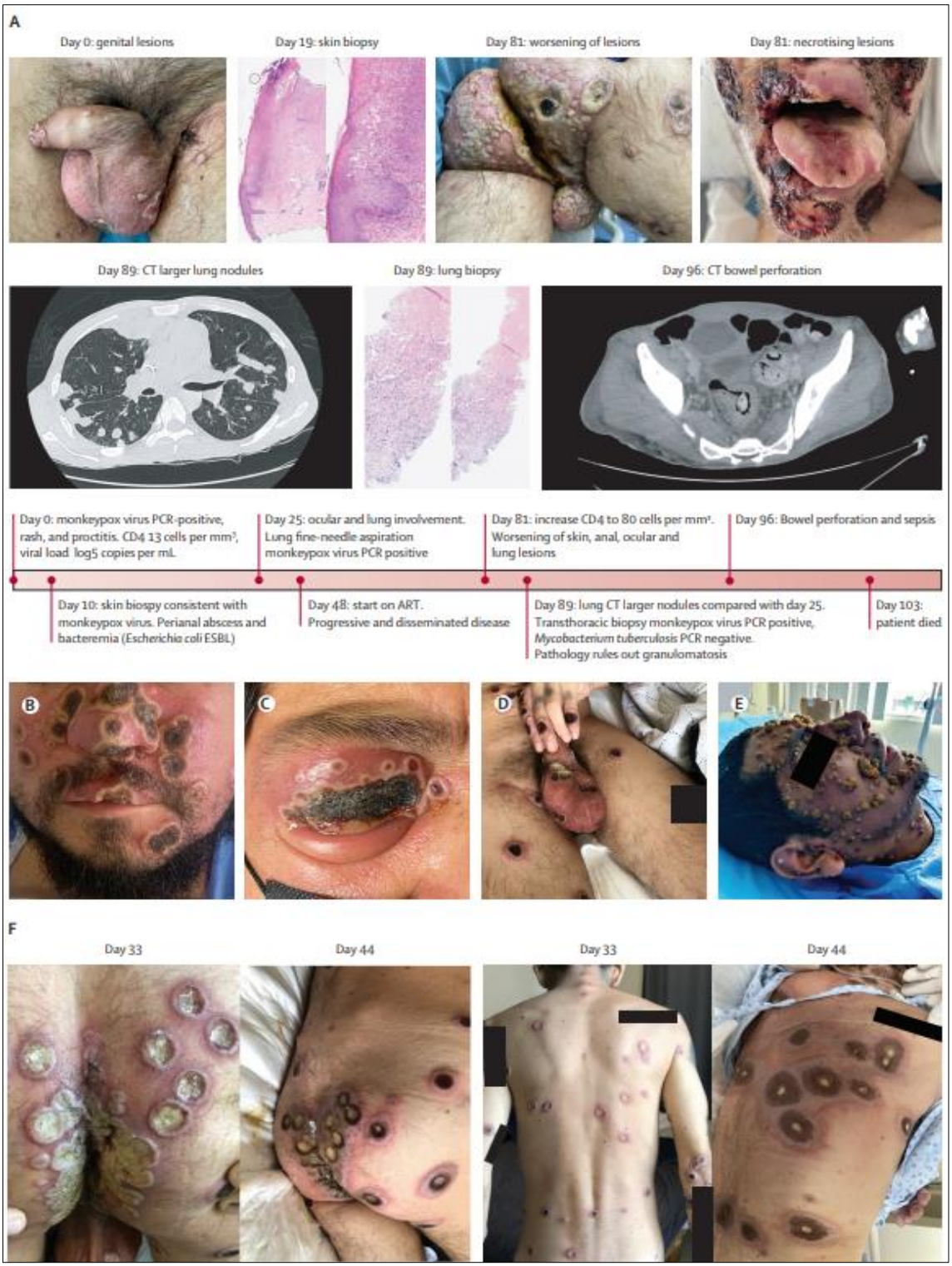

Figure 3: Skin presentation of mpox in advanced HIV disease (A) Disease progression in a patient with a CD4 cell count of 13 cells per mm³ and HIV viral load log5 RNA copies per mL, with PCR-confirmed lung involvement, bowel perforation, immune reconstitution inflammatory syndrome, and death, despite having received two courses of intravenous tecovirimat and one course of intravenous cidofovir. (B–E) Photographs of necrotising lesions (lesions of the skin and mucous membranes) in multiple patients. (B) Necrotic ulcers in the perilabial and nasal areas, and ulcer with tissue destruction on the right upper lip. (C) Umbilicated vesiculopustular-like lesions on upper eyelid surrounding an extensive necrotic ulcer, and eyelids and nasal radix with oedema and erythema. (D) Necrotic ulcers with raised edges, some confluent, on the scrotum, dorsum of the fingers, groin, and thighs. (E) Numerous verrucous, excrescent, yellowish facial lesions. (F) Before and after lesions, with progression to severe confluent target-shaped ulcers with dark necrotic centre surrounded by a vesiculopustular halo and peripheral oedema, in the perianal area and back. ART=antiretroviral therapy. ESBL=extended spectrum β-lactamase Escherichia coli [1]

Testing / Diagnosis

Clinical diagnosis of mpox is more than 90% sensitive but only 9% to 26% specific. To confirm the diagnosis, a viral swab vigorously obtained from active skin lesions should be sent in viral transport media for mpox DNA-specific polymerase chain reaction testing, which is available from major laboratories. Other supportive tests include serum studies for anti–mpox virus immunoglobulins and immunohistochemical staining for viral antigens on skin biopsy specimens. When evaluating suspected and confirmed mpox cases, dermatologists should wear a gown, gloves, a fitted N95 mask, and eye protection to prevent infection [9].

Treatment and Vaccines

Symptomatic mpox infection can last for up to 2 to 5 weeks. The patient is no longer infectious once the lesions have crusted over. The majority of cases require supportive care only. However, mpox remains a potentially fatal disease. High-risk populations include children younger than 8 years, pregnant women, and individuals who are immunocompromised. Tecovirimat, an antiviral medication approved by the US Food and Drug Administration (FDA) for smallpox, is available via the expanded access Investigational New Drug (EA-IND) protocol to treat severe mpox cases but is not widely available in the United States. Brincidofovir, a pro-drug of the antiviral cidofovir, possesses single-patient emergency use Investigational New Drug (e-IND) status for treatment of mpox but also is not widely available in the United States. Intravenous vaccinia immune globulin is under consideration for high-risk individuals, but little is known regarding its efficacy against mpox.

Two smallpox vaccines—JYNNEOS (Bavarian Nordic) and ACAM2000 (Emergent Bio Solutions)—are available for both preexposure and postexposure prophylaxis against mpox virus in the United States, but no in Mexico. At this time, only JYNNEOS is FDA approved for the prevention of mpox; ACAM2000 can be used against mpox under the FDA's EA-IND protocol, which involves additional requirements, including informed consent from the patient. ACAM2000 is a live, replication-competent vaccine that carries a warning of increased risk for side effects in patients with cardiac disease, pregnancy, immunocompromise, and a history or presence of eczema and other skin conditions. JYNNEOS is a live but replication deficient virus and therefore does not carry these warnings [9] (Figure 4).

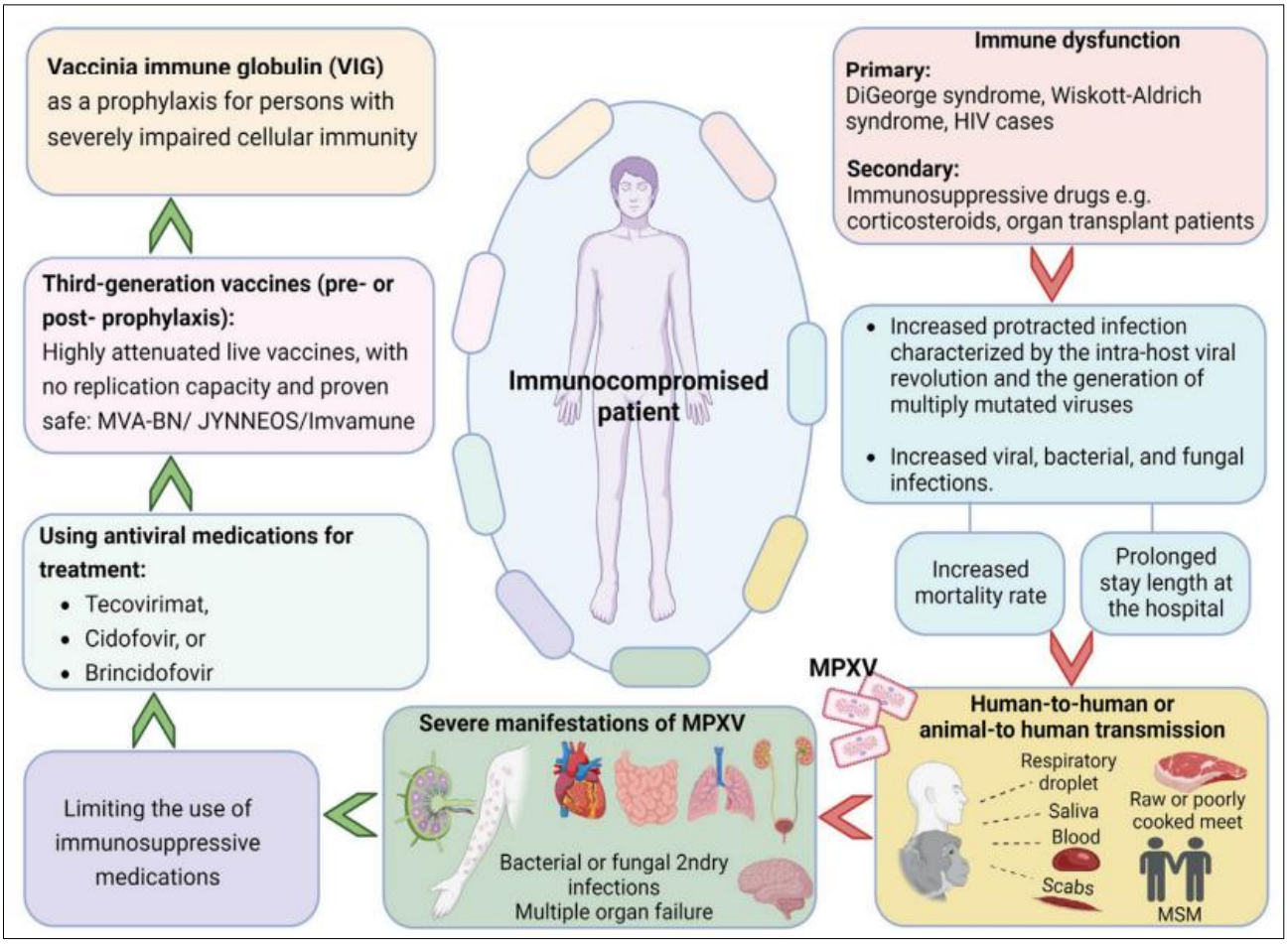

Figure 4: An overview on monkeypox in immunosuppressed patients, prevention and clinical management [10]

CASE REPORT

Male, 38 years old, history of living with HIV infection, on HAART. He presents with a febrile syndrome of 3 days of evolution, accompanied by bilateral disseminated dermatosis with a tendency to symmetry, affecting the head on the face on the right cheek, the left nostril and chin, the anterior trunk in the pubis, the base of the penis, and the lower extremities in inguinal region, characterized by umbilicated pustules surrounded by erythematous-violet halo, variable size approx. 5-15mm (Figure 5).

He presents submandibular lymphadenopathy, predominantly right, as well as painful inguinocrural lymphadenopathy. PCR for detection of Mpox virus with POSITIVE result.

It was decided to hospitalize him for close surveillance. Upon having adequate clinical and biochemical evolution, it was decided to discharge him with symptomatic treatment. The patient continues to send photos of his progress at home (Figure 6).

Symptomatic treatment and isolation measures were indicated, obtaining a favorable evolution despite the immunocompromise (Figure 7).

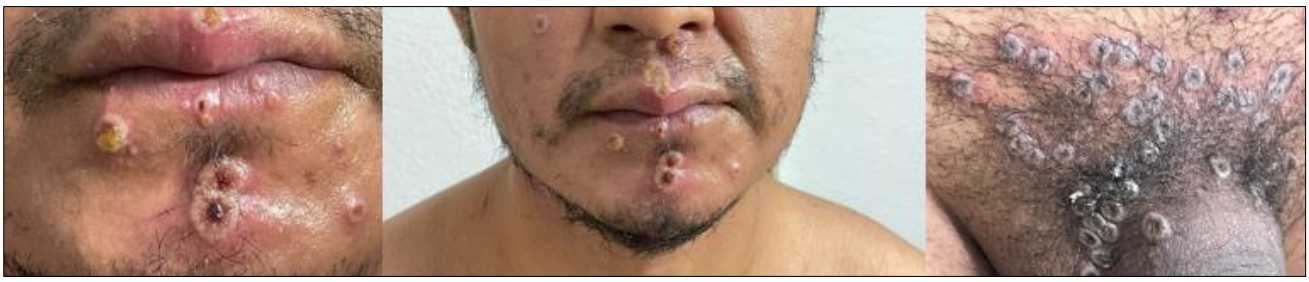

Figure 5: Bilateral disseminated dermatosis with a tendency to symmetry, characterized by umbilicated pustules surrounded by erythematous-violet halo, variable size approx. 5-15mm [11]

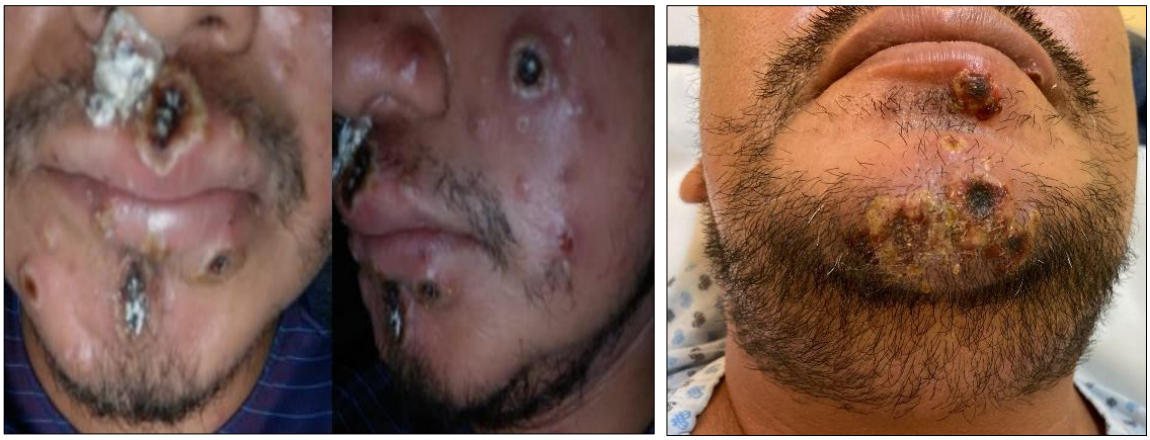

Figure 6 and 7: Necrotic ulcers in the perilabial and nasal areas, and ulcer with tissue destruction on the central upper lip [11]

DISCUSSION

On July 23, 2022, the WHO declared the current MPOX outbreak a Public Health Emergency of International Concern. Despite over 3508 officially reported cases to date, which has placed Mexico among the top-ten countries with the most cumulative cases and number one globally with the most daily cases, the MPOX vaccine has not been authorized for use in Mexico. We believe it is important for these authors to serve an international audience through the South Asian Research Journal of Applied Medical Sciences. The purpose of this publication is to encourage the authors to use their power to disseminate and thus pressure the corresponding authorities to authorize the use of the MPOX vaccine in Mexico [2-12].

Where do we go from here? We need a comprehensive, equity-based effort to address vaccine hesitancy and trust across the lifespan. It is necessary to promote connections between basic, social and public health sciences [13].

Partnerships should be encouraged between governments, community organizations and a wide range of sites where vaccines can be safely administered. We need an infusion of new ideas and an exchange of interdisciplinary knowledge that extends far beyond traditional healthcare. As evidence-based approaches evolve, we must train the next generation of healthcare providers to perform better [2-13].

CONCLUSION

The 2022 outbreak was the most widespread Mpox epidemic to date, significant not only for the large number of cases but also for the disproportionate burden of disease among MSM and non-MSM [14].

At the time of writing, the incidence is already low, however, there remains a significant risk of resurgence in communities where immunity from vaccination is lower. Therefore, the purpose of making this publication is to occupy this space to make visible to organizations with influence in public health the need for vaccination and support with the resource in our country.

The diseases do not distinguish sexual orientation, although the outbreak has been predominant in MSM, anyone can be affected. Despite the decrease in cases, it is important to recognize the epidemiological characteristics and raise awareness, without discriminating and without losing public interest, thinking that it only affects a minority.

Cases of coinfection of Mpox with HIV have been reported in the literature, which is why they recommend the intentional search for HIV infection. As doctors, we have the social responsibility to know the epidemiological chain of emerging diseases and disseminate information about available vaccines according to age groups and risk groups. Different vaccines against Mpox have been marketed (ACAM2000, MVA-BN7 and mainly JYNNEOS, among others), however, we do not have any in Mexico. Continued efforts to vaccinate at-risk individuals are critical to preventing new cases of widespread transmission [15].

ACKNOWLEDGMENTS

The main author thanks Dr. Angela Rodriguez, Dermatologist Phisycian of the Regional Hospital of Poza Rica de Hidalgo, Veracruz, for providing the clinical photographs recorded of one of the first cases of a patient with coinfection of Mpox and HIV in the state of Veracruz, Mexico, at the beginning of the Mpox Outbreak in 2022 and for patient who gave permission to take the photos and authorization to publish them.

REFERENCES

1. Mitjà, O., Alemany, A., Marks, M., Mora, J. I. L., Rodríguez-Aldama, J. C., Silva, M. S. T., ... & Paredes, M. T. (2023). Mpox in people with advanced HIV infection: a global case series. *The Lancet*, *401*(10380), 939-949. ttps://doi.org/10.1016/s0140-6736
2. Hazra, A., Zucker, J., Bell, E., Flores, J., Gordon, L., Mitjà, O., ... & Marchetta, L. (2024). Mpox in people with past infection or a complete vaccination course: a global case series. *The Lancet Infectious Diseases*, *24*(1), 57-64. https://doi.org/10.1016/s1473-3099
3. Ulaeto, D., Agafonov, A., Burchfield, J., Carter, L., Happi, C., Jakob, R., ... & Lewis, R. F. (2023). New nomenclature for mpox (monkeypox) and monkeypox virus clades. *The Lancet Infectious Diseases*, *23*(3), 273-275. https://doi.org/10.1016/s1473-3099
4. Dries, D. J. (2022). Monkeypox. *Air Medical Journal*, *41*(6), 510. https://doi.org/10.1016/j.amj.2022.09.007
5. Lu, J., Xing, H., Wang, C., Tang, M., Wu, C., Ye, F., ... & Shen, L. (2023). Mpox (formerly monkeypox): pathogenesis, prevention, and treatment. *Signal Transduction and Targeted Therapy*, *8*(1), 458. https://doi.org/10.1038/s41392-023-01675-2
6. Ghosh, N., Chacko, L., Vallamkondu, J., Banerjee, T., Sarkar, C., Singh, B., ... & Dewanjee, S. (2023). Clinical strategies and therapeutics for human monkeypox virus: a revised perspective on recent outbreaks. *Viruses*, *15*(7), 1533. https://doi.org/10.3390/v15071533
7. Thornhill, J. P., Gandhi, M., & Orkin, C. (2024). Mpox: The Reemergence of an Old Disease and Inequities. *Annual Review of Medicine*, *75*, 159-175. https://doi.org/10.1146/annurev-med-080122-030714
8. Karagoz, A., Tombuloglu, H., Alsaeed, M., Tombuloglu, G., AlRubaish, A. A., Mahmoud, A., ... & Alsuhaimi, E. (2023). Monkeypox (mpox) virus: Classification, origin, transmission, genome organization, antiviral drugs, and molecular diagnosis. *Journal of infection and public health*, *16*(4), 531-541. https://doi.org/10.1016/j.jiph.2023.02.003
9. Peterson, H., Adler, B. L., & Ochoa, M. T. (2023). Mpox (Monkeypox) Clinical Pearls. *Cutis*, *111*(4), 170-171. https://doi.org/10.12788/cutis.0746.

10. Ahmed, S. K., Mohamed, M. G., Dabou, E. A., Abuijlan, I., Chandran, D., Nahed, A., ... & Dhama, K. (2023). Monkeypox (mpox) in immunosuppressed patients. *F1000Research*, *12*. https://doi.org/10.12688/f1000research.130272.1
11. Rodríguez, T. (2022). Ángela. *No title.* (Photos taken in the place) 2022
12. Saavedra, J., Faviero, G. F., Baruch, R., & Pinzon, A. (2023). MPOX vaccines needed in Mexico. *The Lancet Regional Health–Americas*, *20*. https://doi.org/10.1016/j.lana.2023
13. Szilagyi, P. G., Humiston, S. G., & Coyne-Beasley, T. (2023). Addressing Vaccine Hesitancy for Child and Adolescent Vaccines: The Next Big Challenge. *Pediatric Clinics*, *70*(2), xvii-xix. https://doi.org/10.1016/j.pcl.2022.12.002
14. Lim, C. K. (2022). Mpox Diagnostics: Review of Current and Emerging Technologies. *Journal of Medical Virology*. https://doi.org/10.1002/jmv.28429
15. Deputy, N. P., Deckert, J., Chard, A. N., Sandberg, N., Moulia, D. L., Barkley, E., ... & Feldstein, L. R. (2023). Vaccine effectiveness of JYNNEOS against mpox disease in the United States. *New England Journal of Medicine*, *388*(26), 2434-2443. https://doi.org/10.1056/nejmoa2215201.