Medical Science Journal for Advance Research

Vol. 6, No. 2, June 2025
e-ISSN: 2774-4892

Mpox Disease Transmission, Clinical Presentation and Prevention: Article Review

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ABSTRACT

Background: *Mpox one of zoonotic disease (WHO), in 1958 are first discovered in monkeys; the virus that is responsible of these disease belongs to the genus Orthopoxvirus, a member of the Poxviridae family. It gained significant attention in the 1970s when the first cases for human were recorded, particularly in Central, West Africa. spread of recent outside these endemic areas has raised global concerns. This article discusses monkeypox, its clinical features, and prevention strategies. Direct contact with infected animals causes transmission to humans. transmitted of the virus from person to person by respiratory droplets, skin attached, and sexually. The fever, swollen lymph nodes considered most common symptoms in monkeypox patients, also rash that progresses through many stages before recovery. The immunocompromised individuals experience complications like secondary bacterial infection and severe systemic problems. Although there is no specific cure, antivirals like (tecovirimat), supportive care have shown promising results. Vaccination remains a critical preventive measure, especially for the most vulnerable groups. Understanding the epidemiology, pathogenesis, and effective control strategies is essential to mitigate the global impact of viral infection.*

Keywords: Mpox Disease Transmission, Antivirals,Clinical Presentation and Prevention.

Article Information

Received: April 27, 2025; Revised: May 30, 2025; Online: June, 2025

INTRODUCTION

Monkey pox is a contagious disease caused by monkey pox viruses, virus may be transmitted to human. 1 In 1958, monkeypox appeared as skin lesions on monkeys utilized in laboratory experiments in Denmark, where the virus was first isolated, hence the name "monkeypox." 2 Monkeypox is classified as memmber of poxviruses family ,belongs to the Orthopoxvirus[3] genus. Its scientific classification is: • Family: Poxviridae, • Genus: Orthopoxvirus [3], Monkeypox virus , smallpox virus (variola virus), smallpox vaccine virus (variola virus), and cowpox virus (cowpox virus) belong to one family. [4] In 1970, during smallpox vaccination campaigns, in Congo was first case of human that. Afterward, This virus is considered an epidemic in West and Central Africa. [5].

Cases have been reported outside Africa, raising global concerns in recent years about the spread of this disease. [6]. On August 17, 2024, the African Union health agency reported 18,737(Africa CDC, 2024) suspected or confirmed cases of monkeypox across Africa since the beginning of the year, with 1,200 cases recorded in a single week. The Africa Centers of Disease Prevention and Control also released data a report confirming , presence 3,101 confirmed cases and 15,636 probable cases. It also stated that 541 deaths had occurred in 12

https://doi.org/10.46966/msjar.v6i2.270

African countries, and that several variants of the virus had been detected [8]. Also, at the beginning of 2024, reports emerged confirming that all cases reported at 2023 are 14,838, with the Congo which formerly Zaire, considered epicenter to outbreak, with a total of approximately 16,800 reported cases and 500 deaths. Since the beginning of 2024 [9,10].

Burundi, which borders in Congo, also reported a 75% increase one week of cases, with 173 cases (39 unconfirmed and 134 confirmed). [11] "Clade 1b," a novel strain of monkeypox, was found in the Democratic Republic of the Congo in September 2023. Africa continues to face this hardship. [12] This strain is thought to be more deadly and contagious than earlier varieties. It is also important to note that the World Health Organization issued the highest possible warning level, a worldwide emergency, in response to reports of monkeypox cases in Sweden and Pakistan. A similar alert was issued in 2022 during the global spread of monkeypox strain 2, which was later lifted in May 2023[13,14]. It is also worth noting that the "Clade 1B" strain was discovered in countries that have never reported any cases of monkeypox, including (Burundi, Uganda, and Kenya)[16].

Figure 1: Shows the spread of mpox disease around the world.[1]

Transmission

1. Human infection with this virus is transmitted through direct interactions with animals (have infect) , such as eating raw (undercooked) meat (or) contac body fluids, tissues, and, mucous membranes , the nature reservior of monkeypox are (monkeys and rodent). [17]

2. Another mode of transmission is Scratches, and bites, by animals are (have infect), the direct contact of droplet , respiratory secretion of infected person to other consider one of important mod of transmission.[18] In addition, the vertically transmitted (mothers to their newborns).[19]

3. The current monkeypox outbreak is the largest documented pandemic outside Africa. This is in contrast to previous outbreaks, where monkeypox infection was primarily related of contact with animals (have infect) and travel into endemic areas. However, the major cases of current outbreak are related with person-to-person transmission,

may particularly through sexualy c, rather than animal exposure or travel. [20] , 21a .

Affected Populations

Studies indicate that gay and bisexual men were the most prominent victims of the monkeypox outbreak, with 41 percent of patients infected with HIV and 98 percent of cases involving gay men.[22]

Incubation and symptoms

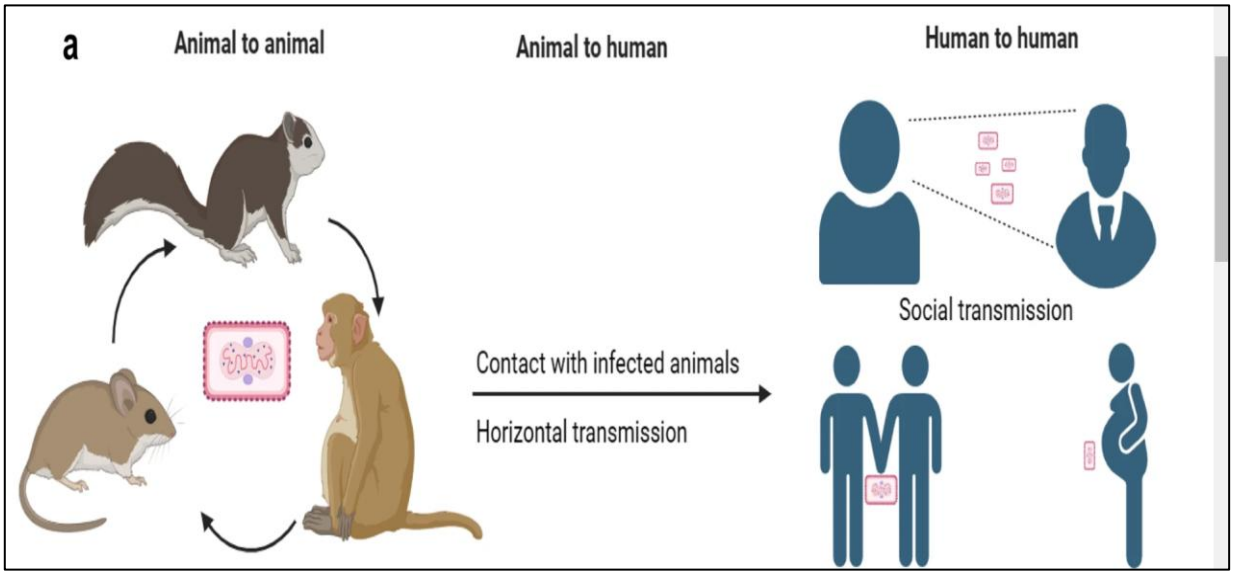
The incubation period for monkeypox ranges from 7 to 14 days, with symptoms typically appearing within 14 to 21 days after exposure. The extended incubation period complicates timely diagnosis, often leading to delayed medical care, worsening of the disease, and increased transmission.[23],[24b]

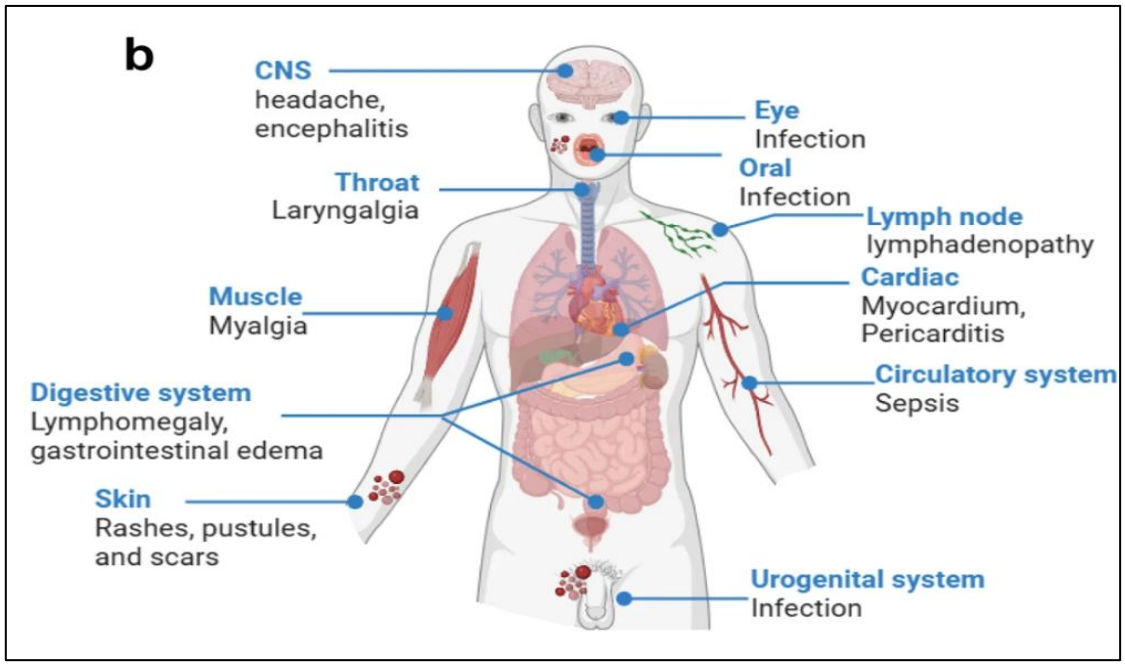
Symptoms

According to (Thornhill 2022), Initial symptoms include (swollen lymph nodes, headache, backache, fever, muscle pain, chills, and fatigue). rash typically develops after onset of fever, starting from face and hands then feet, before ,spreading, to other parts of body.[25] The rash also affect on eyes, genitals, and inside of mouth. In severe cases, large areas of skin may peel off as the rash progresses, eventually forming scabs that fall off. Symptoms usually appear (5 to 13) days after, infection but take up to (21 days) for manifest .[26]

Pathogenesis

Exposure to infected people, animals, or artifacts can lead to the natural acquisition of human mpox infection through respiratory tract , skin , and mucous membranes .[28] The pathological progression and clinical presentation of monkeypox determine its course as an infectious disease.[29] Exposure, host immune system, virus dose, and strain. Challenge experiments in nonhuman animals provide the majority of information on the pathophysiology of mpox in humans. The disease typically takes 5–21 days to complete its incubation, with a median of 12 days, although it can take 1–30 days [30]





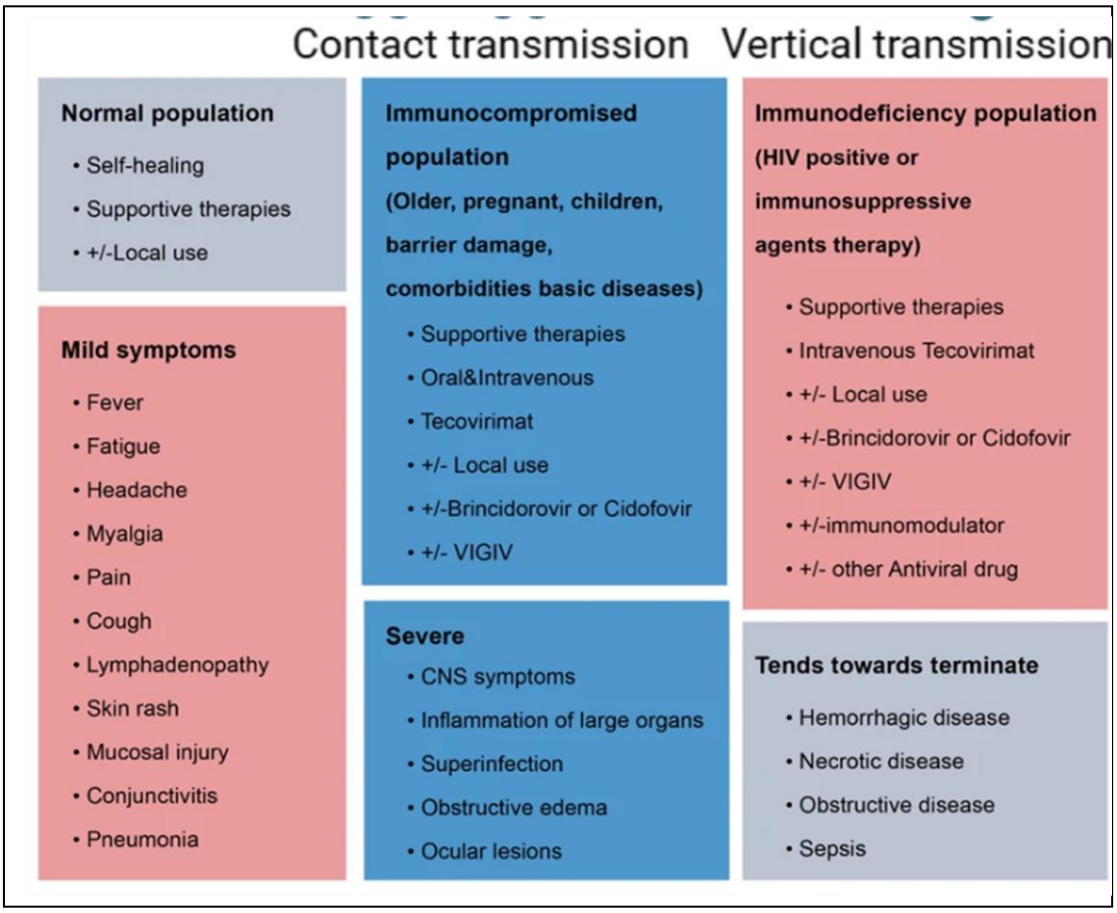


Fig. 2 Mpox's pathophysiology, clinical diagnosis, epidemiological characteristics, and management. a) Mpox can spread from animal to animal, from animal to human, and from human to human. b) Following a Mpox infection, clinical signs usually appear c) .

The symptoms of a Mpox infection might change according on the patient's immunological state and the available therapeutic treatments.[27] Since inoculation-related mpox is not linked to an initial viral multiplication in the respiratory tract, its incubation time (average of 7–9) is frequently shorter than that of respiratory , related ,infections (average of 12 days). pathogenesis are summarized in Fig. 3[31]

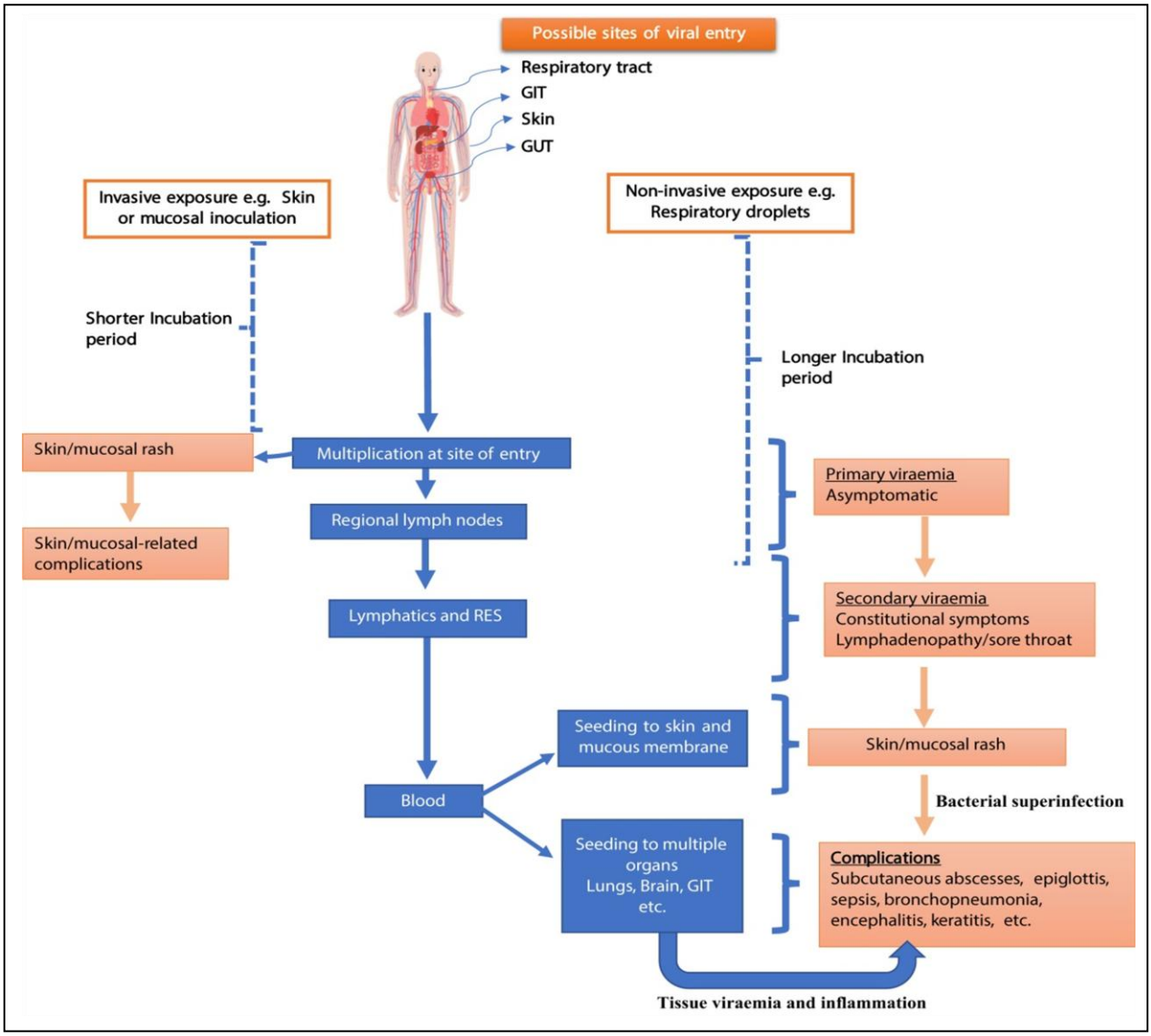


Figure 3 This figure illustrates the pathophysiology of human viral meningitis virus (mPOX) in relation to the point of viral entry. Following exposure, the virus penetrates the skin and mucosal surfaces, followed by the presence of virus in the blood and lymph without initial symptoms, as well as in the oropharynx and peripheral lymph nodes in non-invasive cases of the respiratory tract.[32]

Clinical presentation

The severity of mpox ,vary widely, ranging from a minor , short -lived illness to sever case, potentially grave condition, particularly of individuals with immunocompromised. During Clade IIb outbreak, which was primarily driven by sexual transmission, the average incubation period was 7 to 10 days , may range from (2 to 21 days).[33] After an asymptomatic incubation phase, the patients experience prodromal period lasting 1 to 5 days. Common prodromal symptoms , (62%-72%) of fever, (56%-86%) of swollen lymph nodes, (31%-55%) of muscle pain, (23%-57%) malaise, and (25%-55%)

headache . In 2022, with the outbreak of (Clade IIb), it was found that symptoms appear during or after the rash, and may also be accompanied by other symptoms such as proctitis. [34]

The characteristic clinical presentation of mpox is the evolution of painful skin lesions that go through four stages over the course of 2 to 4 weeks: macules, papules, vesicles, and pustules, and then crust and heal. The individuals are infectious from the moment they show symptoms until the point when all the skin lesions have healed, which is up to four weeks.[35]

Rash distribution and complications

The mpox rash typically follows a centrifugal distribution, appearing on the face, torso, and limbs. However, in the recent global outbreak, cases linked to sexual transmission often presented with fewer lesions (median of 10), non-uniform progression (e.g., lesions at different stages simultaneously), and localized lesions in the oral (14%-25%) and anogenital regions (36%-73%). Other complications associated with mpox include urethritis, pharyngitis, proctitis (14%-36%), and ocular involvement.[36] In rare cases (less than 5%), they can have one cutaneous lesion but neither mucosal nor systemic symptom (for example, proctitis or pharyngitis) without any lesions on their skin. Further, healthcare personnel also have been documented to develop localized lesions at the site where the needlestick injury was sustained.[37]

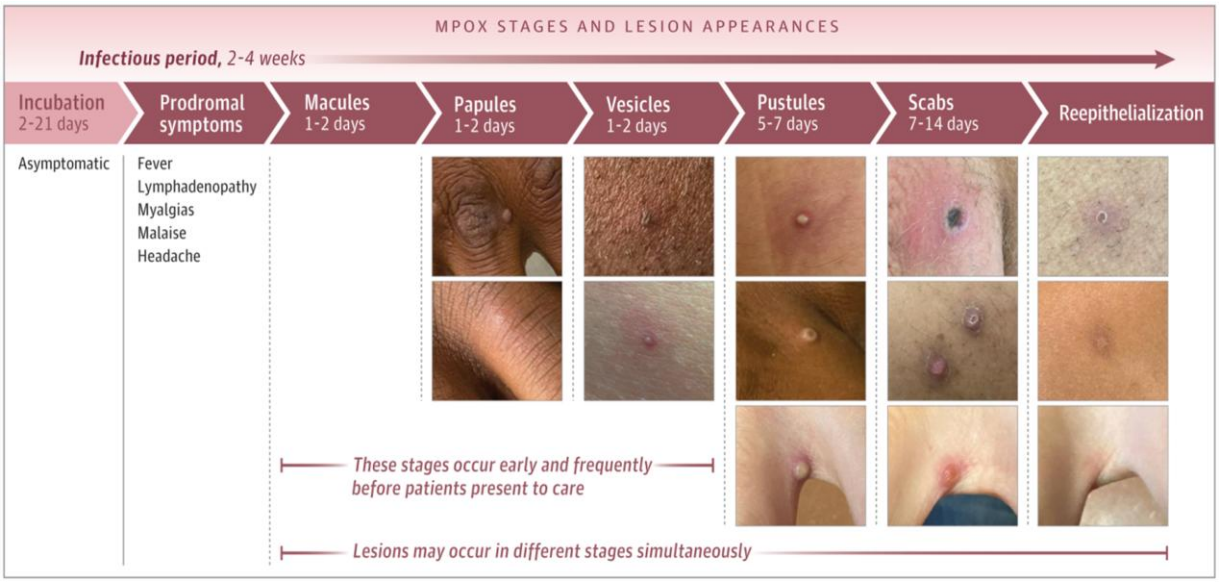


Figure 4. Stages of Mpox and Lesion Examples[38]

Complications, severity, and sequelae

Complications

Figure 5 lists the many systemic and local consequences linked to mpox , Necrotizing ulcers can occasionally result from secondary bacterial skin infections, particularly in people with , HIV infection .[39] Additionally, individuals with HIV might have larger lesions and more frequent consequences that result in death .[40] Rarely, late in the course of the illness, sepsis and bronchopneumonia may develop due to bacterial infections that have been superimposed .[41] Seizures and altered awareness are symptoms of encephalitis, an uncommon but serious consequence. The atypical host reaction is ascribed to either the central nervous system direct infected of viral or (viral antigens) and complexes (antigen-antibody) that localized in neural tissue[42] .

Severity and prognosis

Clinical severity of mpox and prognosis are based on the viral clade, history of previous smallpox vaccination, underlying general health of the patient, acute co-morbid illness (such as chickenpox, measles, malaria, or diarrheal disease), chronic illness (such as chronic kidney disease), and immunosuppression (such as post-transplants or HIV infection). The majority of mpox infections are mild to moderate, and the disease may resolve by itself without the necessity for admission..[43] However, approximately 35% of diagnosed cases may require hospitalization, with a 4% mortality rate. Hospitalizations are typically necessary to manage extreme pain especially (oropharyngeal also anogenital discomfort) , (anogenital ulcers) , and other complications. Mild cases are sometimes hospitalized to prevent further transmission.[44] The leading of death include (bronchopneumonia, encephalitis, and sepsis), with fatalities occurring among unvaccinated individuals, children under five, and young adults with advanced HIV and significant immunosuppression.[45]

Mpox cases are categorized based on severity:

- Mild: Less than 25 skin lesions; no special care or disability.
- Moderate: 25–99 skin lesions; activity is limited but not necessitating nursing.
- Severe (non-fatal): 100 or more skin lesions; complete incapacitation necessitating medical attention.[46,47]

The clinical course and presentation can be influenced by the viral clade, exposure route, and host immunity. The clinical disease has three phases: prodromal, eruptive, and recovery phases. In typical clade I infection, skin rashes evolve from macules, papules, vesicles, to pustules and form crusts and scabs before healing. The eruptive phase may be complicated by eruptive stage-associated complications of diverse systems. Absence of definite febrile prodrome pleomorphic evolution of cutaneous lesions and fulminant mucosal complications are more frequent in clade IIb infections compared to clade I and IIa infections. In the aftermath of recovery, sequelae occur in a minority of cases. Mpox reinfection is described but the actual burden of clinical relapse and repeated infections warrants additional investigation.[48]

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e-ISSN: 2774-4892

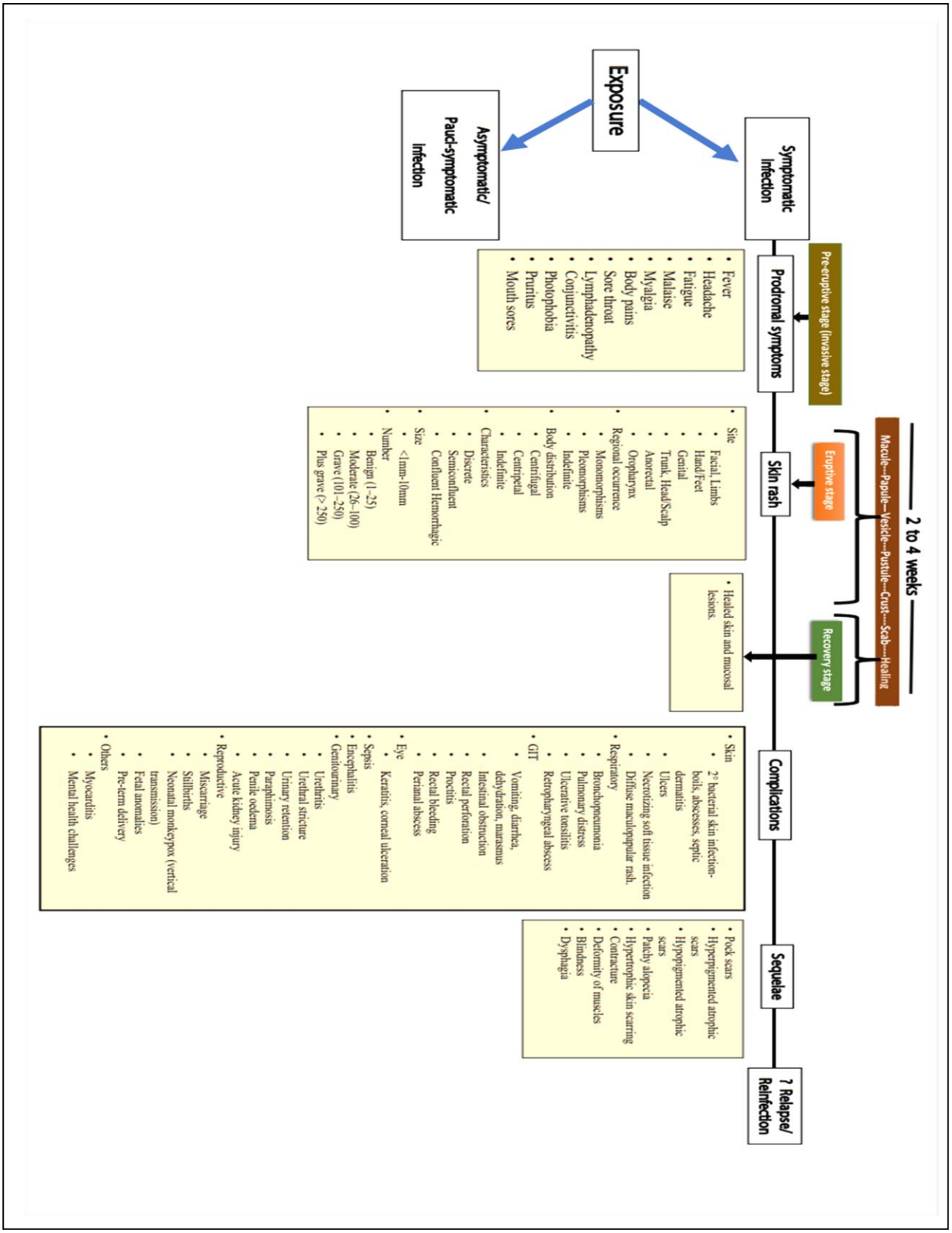

Figure 5. Clinical presentation and natural history of human monkeypox following MPXV exposure. Human mpox can occur as an asymptomatic/sub-clinical or symptomatic/clinical disease.

https://doi.org/10.46966/msjar.v6i2.270

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Diagnosis

Tests for MPXV identification are always being improved because to the frequent development of new cases in non-endemic locations. There are now three different types of testing for MPXV infection: nucleic acid, antigen, and antibody tests. The identification and assessment of environmental materials by the removal of various orthopoxvirus types is also crucial for pathological diagnosis, among other laboratory procedures (Figure 6)[49].

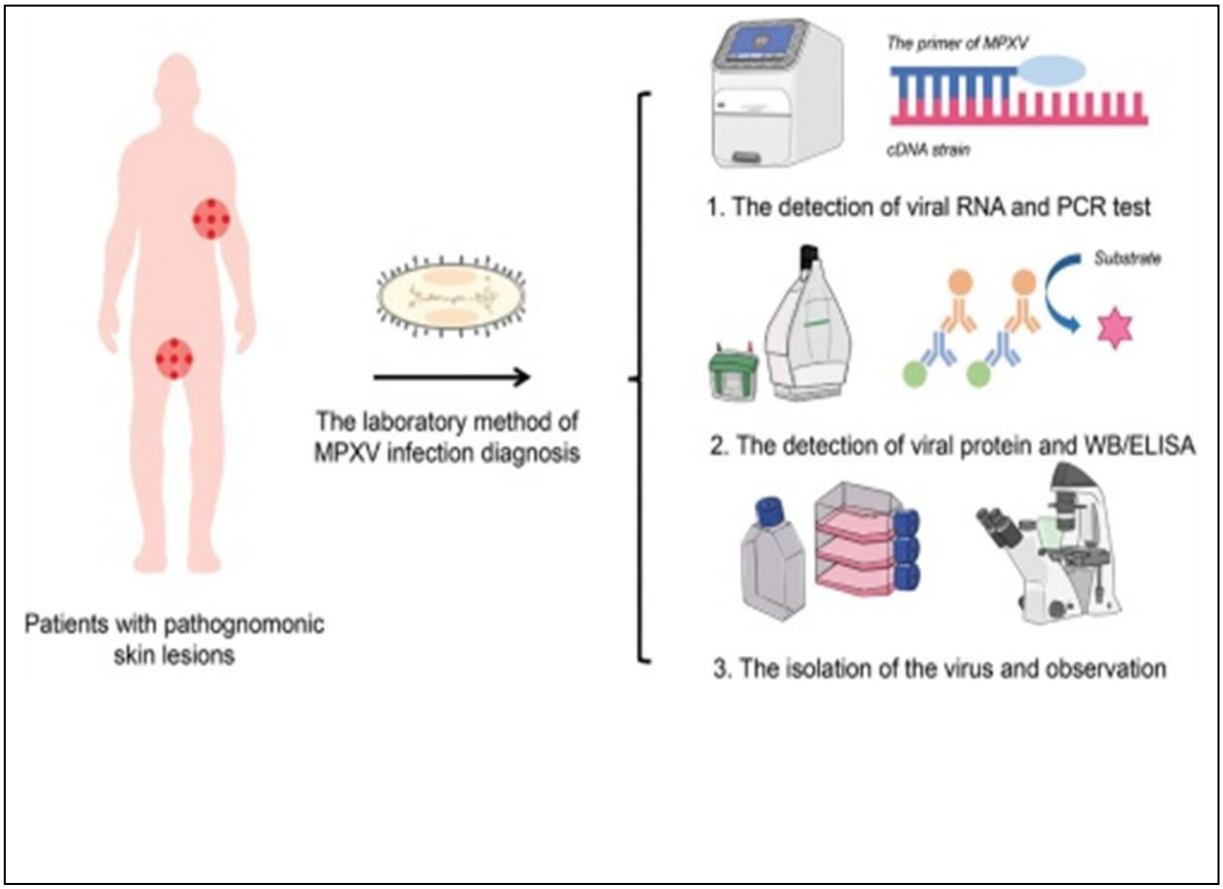

Figure 6. Main assays for the diagnosis of Mpox. The primary assays include nucleic acid detection, antigen and antibody detection, and pathological diagnosis. PCR has become a widely used and early tracing technique in diagnosing Mpox. Immunologic diagnosis depends on antigen specificity. Microscopic examination reveals simple pathogenic morphological differences.[50]

- ***Nucleic acid assay***

As per the US Centers for Disease Control and Prevention (CDC) and WHO, PCR is the main laboratory diagnostic method owing to its validity and high sensitivity [51] and is utilized in the confirmation of Mpox cases.[52] The test can be done in two steps: Mpox-specific PCR and pan-orthopox PCR, Clinical specimens are scabs/lesion crusts, blood, pustule swabs, vesicle swabs, and saliva[53] Certain MPXV genes, such as the orthopoxvirus DNA polymerase gene (E9L-NVAR), envelope protein gene (B6R), DNA polymerase gene, dependent RNA polymerase subunit 18 (Rpo18), F3L gene, and the A-type inclusion body gene (ATI gene), are typically identified by their conserved sequence.[54] Orthopoxviruses may be selectively detected

using LC-qPCR that targets the gene producing the haemagglutinin (HA) protein. Melting curve analysis can then be used to distinguish between distinct orthopoxvirus members[55].

- ***Antigen–antibody assays***

The laboratory diagnosis of Mpox also heavily relies on antigen and antibody tests. A novel technique for diagnosing poxvirus-related illnesses was developed in the late 20th century when researchers employed radioimmunoassay (RIA) to find antibodies in patient samples for smallpox, cowpox, and MPXV infections.[56] During the same century, orthopoxviruses were often identified using electrophoretic methods. The structural proteins of the cowpox, High-resolution sodium dodecyl sulfate (SDS)-polyacrylamide gel electrophoresis (SDS-PAGE) technique was used to separate and compare MPXV and variola virus, enabling their successful identification.[57] During the 2003 Mpox outbreak in the USA, the popular serological test known as enzyme-linked immunosorbent assay (ELISA) was used to identify IgM and IgG in patients. It produced results that were similar to those of PCR and viral cultures, suggesting a high diagnostic performance for Mpox but it was not used to confirm the infection.[58]

However, the independent use of antigen and antibody tests to establish MPXV infection is hindered by used serological cross-reactivity amongst orthopox viruses and potential for (false-positive) findings following smallpox vaccinations.[59] An antigen capture ELISA against the viral surface protein A27 was developed by Stern et al. in 2016 and is capable of detecting all human pathogenic orthopoxviruses, including MPXV.[60] When it comes to protein detection, monoclonal antibodies (mAbs) are crucial. To diagnose Mpox species-specifically, researchers have created an enzyme immunoassay (EIA) technique based on mAbs The ELISA's overall sensitivity was increased by combining polyclonal detection antibodies with monoclonal capture antibodies that respond with viral envelope epitopes.[61] In 2022, Mpox was quickly diagnosed using a lateral flow test based on four distinct MAbs.[62]

Differential Diagnosis

A number of additional illnesses involving skin and mucosal sores are included in the differential diagnosis for mpox. Although mucocutaneous lesions and a widespread rash are possible symptoms of secondary syphilis, they are often painless in contrast to mpox. Especially in the anogenital region, the herpes simplex virus can cause painful vesicular lesions that mimic mpox. Other soft tissue and skin diseases, such as cellulitis or impetigo, can also cause vesicular or pustular lesions that resemble mpox.The differential diagnosis of mpox in children and, less commonly, adults would be enteroviral infection, molluscum contagiosum, varicella-zoster virus, and other orthopoxviruses.[63]

Prognosis

The majority of mpox patients have a self-limiting sickness and usually get well in two to four weeks after symptoms start. After healing, 5%–40% of mpox skin lesions might leave scars, which can have a stigmatizing cosmetic appearance and are more prevalent in patients with advanced HIV.[64] Long-term issues including scarring and strictures in anogenital regions can arise from mpox-related genital lesions, which can as it has an impact on the quality of life and sexual functions..[65] Because eye damage is one of the main consequences of Ampoules, it is recommended to undergo an early ophthalmological examination so that the condition does not develop into partial loss of vision or even blindness.[66] Rectal perforations, fistulas, and strictures are less frequent consequences, as are urethral strictures and paraphimosis , In these situations, urology's

participation also colorectal , surgery _ specialists may be , beneficial.[67]

Treatment and prevention

Currently no authorized therapy of (MPXV) infections; Additionally, the US Strategic National Stockpile (SNS) advises physicians to treat Mpox with Tecovirimat, Brincidofovir, and Cidofovir (which were created for use in smallpox patients.[68]

- ***Tecovirimat***

By blocking the VP37 protein on the surface of orthopoxviruses, Tecovirimat (4-trifluoromethylphenol derivative), commonly known as Tecovirimat or TPOXX, is a core protein cysteine protease inhibitor that has an antiviral effect.[53] Tecovirimat inhibits the maturation and release of viral particles from infected cells, thereby preventing viral transmission between cells. It does this by binding to MPXV F13 (poxvirus phospholipase D), which is essential for the formation and infectivity of EVs. (According Rao 2022) [69.] Preclinical trials have shown that Tecovirimat is efficacious; four important investigations in nonhuman primates showed that the drug provided 95% protection against death compared to a placebo. Phases 1 and 2 trials have investigated Tecovirimat's safety and adverse impact profile in human subject, After rash start, tecovirimat has been used to treat systemic orthopoxvirus infection. It has been demonstrated to be very successful in avoiding illness and lowering mortality based on changes in viral load, number of lesions, and survival in animal models.[70] Clinical studies on humans have also demonstrated the drug's safety and tolerability.[71]

- ***Cidofovir***

Cidofovir ({CDV, (S)1-(3-hydroxy-2-phosphono-methoxypropyl) cytosin}) is a cyclic phosphonate nucleoside, a family of anti-DNA viral medications that disrupt DNA virus replication by acting as pyrimidine and purine analogs for DNA synthesis , With notable suppression of poxviruses, cidofovir has broad-spectrum action against the majority of DNA viruses ,By preventing viral DNA replication via Cidofovir's phosphonic acid moiety, the medication combats MPXV, However, the medication is susceptible to nephrotoxicity and may potentially result in irreparable kidney damage due to the phosphonic acid moiety's greater negative ionic group.[72] Cidofovir is a promising antiviral for short-term prophylaxis against orthopoxviruses. In SCID mice, cidofovir is a very successful treatment for VACV infections , Based on existing evidence, topical 5% Cidofovir reduces viral titers in the kidneys, spleen, lungs, and skin while providing modest protection against systemic infections ,To lessen nephrotoxicity with IV delivery, probenecid therapy and hydration should be coupled.[73]

- ***Brincidofovir***

In 2021, the US (FDA) Food and Drug Administration authorized brincidofovir (CMX001; BCV) as the second medication to cure smallpox , A more potent therapy for poxvirus is brincidofovir, a lipid-doped derivative of cidofovir , By blocking viral DNA polymerase, brincidofovir prevents DNA synthesis and viral replication , Brincidofovir's greater effectiveness is also attributed to its enhanced cellular absorption, which facilitates better conversion to its active form via intracellular enzymes.[74] Both mice and rabbits have shown that this medication is beneficial in increasing survival after infection , Clinical studies for CMV illness in recipients of hematopoietic stem-cell transplantation assessed its safety in human subjects. Brincidofovir has a worse safety profile than Tecovirimat with adverse effects on the hepatic and gastrointestinal systems , To prevent negative effects, liver function tests should be

carried out both before and during therapy for MPXV infection because brincidofovir is known to affect serum transaminase and bilirubin levels.[75]

- ***Vaccination***

Although there is no specific vaccine for mpox, the CDC recommends smallpox vaccination as a preventive measure to curb MPXV transmission.[76] Vaccination is particularly important for high-risk groups, such as men who have sex with men (MSM), healthcare workers, and individuals with occupational exposure (e.g., veterinarians).[78] . The ACAM2000 vaccine is recommended for laboratory workers and healthcare professionals at risk of exposure.[79] Smallpox vaccines induce a robust cross-protective immune response against MPXV and variola virus, primarily through T- and B-cell activation. However, their effectiveness may be reduced in immunocompromised individuals.[80]

CONCLUSION

Mpox poses a significant public health threat due to its expanding geographic range and severe complications, particularly in vulnerable populations. Early diagnosis, public awareness, and preventive measures such as vaccination and hygiene practices are crucial for outbreak control. Advances in antiviral therapies and diagnostic tools offer hope for better management. However, addressing the socio-environmental factors driving zoonotic spillover and ensuring equitable access to healthcare resources are essential for a comprehensive response. Continued research and international collaboration are vital to prevent mpox from becoming a persistent global threat.

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