www.directivepublications.org

The Journal of Virology

ISSN 3064-6812

Review Article

Monkeypox Virus: What Every Biologist Needs to Know.

Ahmed Ibrahim Youssouf [1, 3] *, Marwa Nabil [2,3], Briber Ahmed [2, 3], Aflouch Ayoub [2, 3], Najoua Hnach [2, 3], Yassmine Amor[2, 3], Rachid Abi[1,3], Hicham Elannaz [1, 3], Idriss Lahlou Amine [1, 3], Mohamed Rida Tagajdid [1, 3].

[1] Virology Laboratory, Center for Virology, Infectious and Tropical Diseases, Mohammed V Military Teaching Hospital, Rabat, Morocco.
[2] The Central Virology Laboratory - Specialty Hospital - Ibn Sina University Hospital, Rabat , Morocco.
[3] Mohammed V University, Faculty of Medicine and Pharmacy, Rabat, Morocco.

Abstract

Monkeypox (MPX) is a rare zoonotic viral disease endemic in Central and West Africa caused by Monkeypox virus (MPXV), an orthopoxvirus belonging to the same family as human smallpox.
Until recently, cases reported outside Africa were sporadic and generally associated with travel. However, in May 2022, an unusual global spread of MPOX was observed, with cases reported in several non-endemic countries across various continents.
In 2024, a significant increase in the number of confirmed cases of Mpox and associated deaths was observed worldwide, justifying its classification as a Public Health Emergency of International Concern. The causes of this unusual spread are still under investigation, but may be related to increased international travel and a decrease in herd immunity to orthopoxviruses.
Transmission of the virus currently appears to occur primarily through close, intimate contact, particularly among men who have sex with men. MPOX is generally a self-limited disease, with an incubation period ranging from 7 to 14 days, and sometimes up to 21 days.
In 2022, the following countries recorded the following confirmed cases: United Kingdom: 575 cases; Spain: 497 cases; Germany: 338 cases; Portugal: 276 cases; France: 183 cases; Canada: 167 cases; United States of America: 113 cases; Netherlands: 95 cases; Italy: 71 cases; Israel: 5 cases; and Morocco: 3 cases.
As of 14 December 2023, a total of 91,778 laboratory-confirmed cases of MPXV infection, including 167 deaths, have been reported from 116 countries/territories/areas across the six World Health Organization (WHO) regions.
Faced with a high epidemic risk in Morocco, the Ministry of Health and Social Protection has implemented a national plan for surveillance and response to Mpox.
The implementation of reliable and rapid laboratory tests is crucial for effective disease identification and control. To this end, WHO has issued guidelines for clinical laboratories, including: recommended test types, sample selection and collection criteria, appropriate diagnostic methods, interpretation of results, biosafety requirements, and recommendations for therapeutic management and vaccination.
Molecular tests, particularly PCR-based techniques, are recommended as confirmatory methods. For symptomatic patients, skin lesion samples are most appropriate. In the prodromal or presymptomatic phase, the collection of blood, oropharyngeal swabs, and skin lesion samples is recommended.

Keywords : Monkeypox, Orthopoxvirus, WHO, Molecular tests.

INTRODUCTION

Monkeypox virus (MPXV) is the etiological agent responsible for monkeypox (MPOX), an emerging zoonotic disease. It is a double-stranded DNA (dsDNA) virus belonging to the genus Orthopoxvirus (OPXV), family Poxviridae and subfamily Chordopoxvirinae. This genus also includes several other pathogenic viruses, such as: humanpox virus (VARV), cowpox virus (CPXV), vaccinia virus (VACV), camelpox virus (CMLV), Taterapox virus (TATV), and Ectromelia virus (ECTV) [1].
In 2023, the World Health Organization (WHO) reported a global outbreak of Mpox. Since the outbreak began, a cumulative total of 91,778 laboratory-confirmed cases have been reported in 116 countries, with 167 deaths attributed to the disease as of 14 December 2023 [2]. The rapid spread of this outbreak has raised serious concerns about the potential for a new viral pandemic and the global health threat it poses.
In Morocco, as part of the national epidemiological monitoring and surveillance system, the Ministry of Health and Social Protection announced on June 2, 2022, the detection of the first confirmed case of monkeypox, imported from a European country. Three cases had then been recorded [3].

***Corresponding Author: Ahmed Ibrahim Youssouf**, Virology Laboratory, Center for Virology, Infectious and Tropical Diseases, Mohammed V Military Teaching Hospital, Rabat, Morocco. **Email:** ahmibrahimaiy87@gmail.com.
Received: 12-June-2025, Manuscript No. TJOV-4935 **; Editor Assigned:** 17-June-2025 **; Reviewed:** 16-July-2025, QC No. TJOV-4935 **; Published:** 23-July-2025, **DOI:** 10.52338/tjov.2025.4935.
Citation: Ahmed Ibrahim Youssouf. Monkeypox Virus: What Every Biologist Needs to Know. The Journal of Virology. 2025 July; 12(1). doi: 10.52338/tjov.2025.4935.

MPXV was first isolated in 1958 from laboratory monkeys with a smallpox-like disease at a research center in Copenhagen, Denmark [1].

Two genetic clades of the virus are currently recognized: the first, less virulent, is endemic in West Africa, while the second, more virulent and associated with increased severity, predominates in the Congo Basin.

The current epidemic is linked to the West African clade, which is considered less lethal. However, given the continued growth in the number of cases worldwide, it is essential to strengthen and update knowledge about MPXV [4].

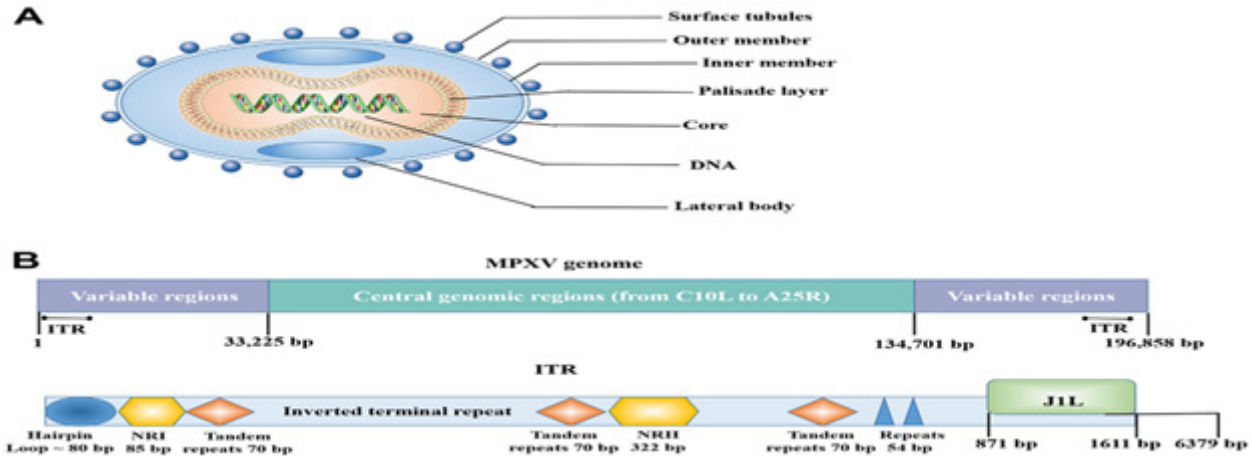
Thus, the present work aims to review the main diagnostic requirements in case of suspicion of Mpox, by addressing: the selection and collection of samples, the types of recommended tests, the available diagnostic methods, the principles of laboratory biosafety, as well as the recommendations for treatment and vaccination.

Finally, it will also be a question of recalling the rules for interpreting biological results in the context of the diagnosis of MPXV.

1.VIRAL CHARACTERISTICS OF MONKEYPOX VIRUS (MPXV)

Monkeypox virus (MPXV) belongs to the Poxviridae family, specifically to the Orthopoxvirus genus, which also includes smallpox, cowpox, and vaccinia viruses [5]. It is a large, enveloped virus, measuring between 200 and 250 nm, with a genome consisting of linear double-stranded DNA. This has covalently closed 5′ and 3′ hairpin ends preceded by inverted terminal repeats (ITRs) (**Figure 1**).

Figure 1. Schematic representation of an MPXV viral particle and its genome [7].



The MPXV genome, measuring 196,858 base pairs, encodes over 200 proteins. This virus shares approximately 90% genomic homology with the smallpox virus. It is currently the largest known virus infecting humans, with a broad host range and extensive tissue tropism. No specific cellular receptors have yet been identified for orthopoxviruses. Viral entry into the host cell relies primarily on interactions with cell surface ligands, followed by membrane fusion. Replication occurs in the cytoplasm of the infected cell and results in the production of two forms of infectious virions: intracellular mature virus (IMV) and extracellular enveloped virus (EEV). IMV is primarily involved in human-to-human transmission, while EEV, surrounded by an additional envelope, contributes to immune evasion and dissemination within the host.

Two distinct clades of MPXV have been identified: clade I (often referred to as the Congo Basin strain) and clade II (West African), with differentiated epidemiological and clinical characteristics (**Table 1**). The viruses responsible for the 2022 outbreak belong to a divergent subclade, termed clade IIb, derived from clade IIa. The latter had been associated with imported cases in 2018 and 2019 in the United Kingdom, Israel, and Singapore, all linked to an outbreak in Nigeria between 2017 and 2018 [6].

The genetic variations observed between clades I and II mainly affect regions coding for virulence genes, which could explain the differences in clinical severity and transmissibility between the two clades.

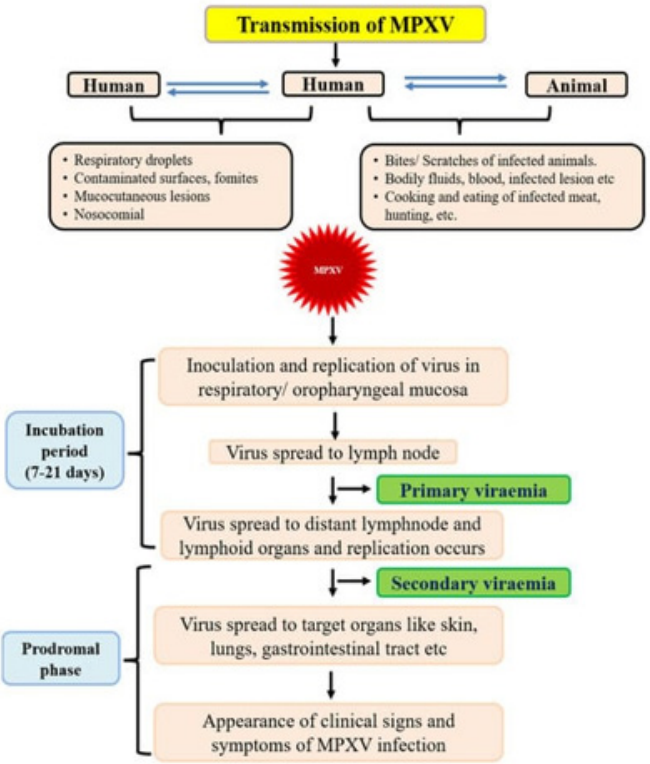
Table 1. Characteristics of infections due to MPXV clades I and II [7].

Features	Clade I	Clade II
Endemicity	Cameroon, Central African Republic, Democratic Republic of Congo, Gabon, Sudan	Benin, Cameroon, Ivory Coast, Liberia, Nigeria, Sierra Leone
Severity	Usually moderate to severe	Usually mild to moderate
Transmission rate within the household	7.5–12.3%	0–3.3%
Mortality	10.6%	1–6%

2.PATHOPHYSIOLOGY

Monkeypox virus (MPXV) is a double-stranded DNA virus belonging to the genus Orthopoxvirus. It is closely related to variola and vaccinia viruses, and is currently the most significant active virus within this genus in the post-smallpox eradication context. Transmission of MPXV infection, or mpox, can occur through direct or indirect contact with an infected animal or human, or with objects or materials contaminated by the virus (**Figure 2**) [8]. Zoonotic transmission occurs, in particular, through handling of wild game, bites, scratches, or contact with bodily fluids or skin lesions of an infected animal, whether alive or dead.

Figure 2. Pathogenesis of Mpox virus [10].



Human-to-human transmission occurs primarily through direct contact with skin lesions or bodily fluids of an infected person, or through contact with contaminated objects (bedding, clothing, etc.). Exposure to respiratory droplets emitted by infected individuals can also lead to contamination. Furthermore, recent data suggest the possibility of airborne transmission via aerosols.

In the recent outbreak, many patients presented with localized genital lesions, particularly among young men who have sex with men, indicating a likely contribution of sexual transmission to the current spread of the virus.

The incubation period is approximately 12 days. During this phase, the virus initially replicates at the site of inoculation before reaching the lymphatic system. Viremia ensues, allowing dissemination of the virus to other organs, leading to the appearance of clinical signs, including fever, myalgia, lymphadenopathy, and flu-like symptoms [9].

3.EPIDEMIOLOGY

Monkeypox has likely been endemic in sub-Saharan Africa for millennia, due to repeated zoonotic transmissions of Monkeypox virus (MPXV) to humans from infected animals. MPXV was first identified in 1958, when a smallpox-like disease was observed in laboratory monkeys. The first confirmed human case was recorded on September 1, 1970 in the Democratic Republic of Congo (DRC), in a 9-month-old infant, with subsequent virus isolation and detection of other cases in the region.

The current emergence of MPXV is a worrying reminder of the long-neglected threat posed by poxviruses since the last natural case of smallpox occurred in Somalia in 1977, followed by the official declaration of its eradication by the WHO on 8 May 1980. MPXV circulates endemically in West and Central Africa, particularly in areas close to tropical forests. In 2018–2019, imported cases were reported in the UK, Israel, and Singapore, following travel from Nigeria [6].

MPXV affects all age groups, although a majority of historical cases have involved children under 16 years of age. Infection can

occur in remote villages where children hunt and consume squirrels, potential animal reservoirs of MPXV. West African strains appear to be less virulent and/or less transmissible than those of the Congo Basin clade. Furthermore, the cessation of smallpox vaccination since the 1980s has increased human susceptibility to MPXV infection.

The first human case of mpox, observed in 1970 in a child in the DRC (formerly Zaire), occurred in an area where smallpox had been eradicated two years earlier. The following year, six more cases were documented in Liberia, Sierra Leone, and Nigeria. Between 1970 and 1979, 47 cases were confirmed, including 38 in the DRC. Between 1981 and 1986, this figure rose to 338 cases, and more than 400 infections were reported between February 1996 and October 1997 [10].

As of 14 December 2023, a total of 91,778 laboratory-confirmed cases of COPD, with 167 deaths, have been reported from 116 countries, territories, or areas, covering all six World Health Organization (WHO) regions [2].

In Morocco, as part of the national epidemiological monitoring and surveillance system, the Ministry of Health and Social Protection announced the detection of the first confirmed case of mpox on Thursday, June 2, 2022, concerning three patients from a European country [3].

4.CLINICAL PRESENTATION,SEVERITY AND COMPLICATIONS

The incubation period for Monkeypox virus (MPXV) infection typically ranges from 5 to 13 days, with a maximum duration of approximately 21 days. In most cases, the disease is self-limiting and presents with a mild form.

Initial clinical symptoms include high fever, chills, severe headache, back pain, dyspnea, asthenia, odynophagia, nasal congestion, and marked lymphadenopathy.

Skin rashesThese lesions typically appear within the first three days following the onset of systemic symptoms. They typically progress through several stages: macules, papules, vesicles, pustules, and finally crusts (**Figure 3**). These lesions are often located on the face, extremities (hands and feet), chest, and genital and anal regions.

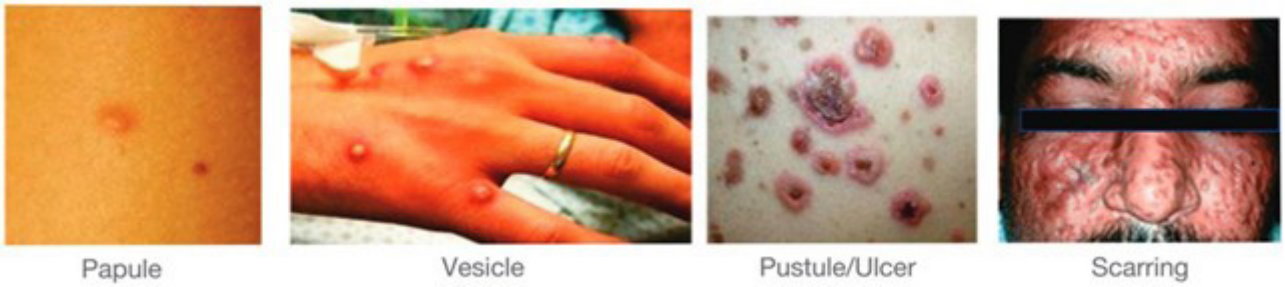
Children have an increased susceptibility to the disease, and severe forms can lead to significant complications such as:

- oral and pharyngeal ulcers , affecting eating;
- enteric disorders , including vomiting and diarrhea ;
- eye damage , which can lead to corneal scarring and vision loss ;
- a marked decrease in T-cell-mediated cytokine response (up to 80%), even in the presence of low viral loads.

Transmission may be associated with an animal bite, although this mode is less common than human-to-human transmission.The clinical presentation varies considerably among individuals:

- Benign forms: Some patients present with a mild form of the disease, resembling a common viral infection, with moderate fever and a localized rash. These cases may go unnoticed or be confused with other dermatological pathologies.
- Severe forms: More serious complications are observed, particularly in immunocompromised individuals. These forms include diffuse skin lesions, multi-organ involvement, and an increased risk of complications. However, children and adolescents generally have less severe forms than adults.

Figure 3. Characteristics of monkeypox lesions.



Although monkeypox is generally considered less severe than human smallpox, it can still cause significant complications, particularly in severe forms of the disease. Some of the main reported complications include:

- Bacterial superinfections: Skin lesions, particularly pustules, can be the site of secondary bacterial infections, which can develop into cellulitis or the formation of abscesses.
- Skin scars: The healing phase of the lesions can leave permanent scars, sometimes disfiguring, particularly when the lesions are located on the face.
- Eye damage: Ocular involvement is possible, manifesting as conjunctivitis or corneal lesions, which can lead to impaired vision or even visual loss in the most serious cases.
- Pneumonias: In severe clinical forms, pneumonia may occur, representing a potentially fatal complication.

5.BIOLOGICAL CONFIRMATION OF MONKEYPOX VIRUS

Laboratory diagnosis of monkeypox virus (MPXV) infection in humans is essential because of the difficulty in clinically distinguishing typical skin lesions from those induced by other viruses, including orthopoxviruses, varicella-zoster virus (VZV), and other similar viral entities (**Table 2**).

Laboratory findings of nonspecific abnormalities commonly observed in patients with Mpox include peripheral leukocytosis, thrombocytopenia, elevated liver transaminases (transaminitis), hypoalbuminemia, and reduced blood urea nitrogen levels.

For virological diagnosis, skin lesions are the specimens of choice, ideally collected at the vesicular or pustular stage of the rash. Samples may include skin scrapings, vesicular or pustular fluid, scabs, and tissue fragments from skin biopsies. These samples should be placed in sterile containers and sent to a virology laboratory, where various diagnostic techniques are used to identify and differentiate MPXV from other viral pathogens [12].

Table 2. Differential diagnosis of skin lesions in human MPXV infections [12].

Gender	Species	Endemicity	Exanthema
Orthopoxvirus	*Smallpox virus*	Eradicated	Centrifugal rash on the face, palms, and soles
	Monkeypox virus	Central and West Africa (rodents)	Centrifugal rash on the face, palms, and soles
	Vaccinia virus	Worldwide (smallpox vaccines)	Local (at the injection site) or generalized
	Vaccinia virus	Europe and Asia (cattle, wild rodents)	Fingers; other sites by autoinoculation
	Camelpox virus	Middle East, Africa, Asia (camels)	Head, neck, limbs, genitals
	Alaskan smallpox virus	Alaska, USA (rodents)	Extremities
Parapoxvirus	*Orf virus*	Worldwide (sheep, goats)	Painful lesions on the fingers, hand, arms and face
	Smallpox virus (milker's nodule)	Worldwide (cattle)	Painful lesions on the hands and face
	Bovine papular stomatitis virus	Worldwide (cattle)	Painful lesions on the hands and arms
	Sealpox virus	Oceanic coastlines of the Northern Hemisphere (seals)	Painful lesions on the hands
Yatapoxvirus	*Tanapox virus*	Equatorial Africa (fauna)	Nodular lesions on the extremities
	Yaba-like disease virusand Yaba monkey tumor virus	Equatorial Africa (fauna)	Palms, extremities, face (professional)
Molluscomycin virus	*Molluscum contagiousum virus*	Worldwide (humans)	Trunk, limbs (except palms and soles), face
Varicellovirus	*Varicella-zoster virus*	Worldwide (humans)	Centripetal rash on the trunk, sometimes the extremities and face

6.WHAT SAMPLES SHOULD BE RECOMMENDED FOR THE DIAGNOSIS OF MONKEYPOX VIRUS?

The diagnosis of monkeypox (MPox) is initially based on a clinical assessment, particularly in the presence of suggestive skin lesions, whether or not associated with general symptoms, in a patient presenting an epidemiological risk factor such as recent travel to an endemic area.

However, several conditions share similar clinical manifestations, making differential diagnosis essential. Conditions to consider include smallpox, chickenpox, herpes simplex virus infections, impetigo, measles, certain bacterial skin infections, scabies, syphilis, and allergic drug reactions.

In this context, biological confirmation is essential to establish a definitive diagnosis, rule out similar pathologies and classify the patient as a suspected or confirmed case.

- Differential diagnosis with other similar conditions

Mpox shares clinical features with a number of other infectious diseases, which can make diagnosis difficult. Key conditions to consider in the differential diagnosis include [11]:

- Smallpox, because of the similarity of skin lesions;
- Chickenpox, especially in the vesicular and pustular stages;
- Herpes infections (HSV-1 and HSV-2), including genital or orofacial lesions;
- Impetigo, in its bullous form;
- Measles, especially during febrile exanthema;
- Bacterial skin infections (e.g : staphylococcus);
- Scabies, which can mimic itchy lesions;
- Syphilitic lesions, including chancres or secondary eruptions;
- Drug reactions, responsible for polymorphic skin rashes.

Table

Smallpox	Varicella	Herpes simplex virus infections	Impetigo	Other viral rashes
Historically, monkeypox was often mistaken for smallpox due to their similar clinical presentations. However, smallpox has been eradicated, so it is extremely rare. PCR and serological tests can distinguish between the two.	Chickenpox also presents with a vesicular rash, fever, and malaise. However, monkeypox typically has a higher fever and more pronounced lymphadenopathy. Laboratory tests can differentiate between the two.	HSV infections can cause painful skin lesions, but they usually do not have serious systemic consequences. Symptoms seen in monkeypox. Laboratory testing for HSV can confirm the diagnosis.	Impetigo is a bacterial skin infection that can cause pustules similar in appearance to monkeypox lesions. Bacterial culture can identify the causative organism.	Other viral infections, such as measles, rubella, and hand, foot, and mouth disease, can cause rashes. Clinical and epidemiological factors, as well as laboratory tests, can help differentiate them from monkeypox.

The recommended biological samples for the initial virological diagnosis of monkeypox virus (MPXV) infection depend on the clinical context and the location of the lesions observed. They include the following types (**Table 3**):

- Cutaneous-mucosal samples: these are swabs or biopsies taken from skin lesions (vesicular roofs, exudates, scabs) as well as from mucosal lesions, particularly genital or anal, excluding mucous membranes of the ENT sphere.
- ENT sphere samples: oropharyngeal swabs are recommended (nasopharyngeal swabs can also be taken depending on the case).
- Deep or semi-deep respiratory samples, in the presence of respiratory symptoms: these include tracheobronchial aspirations, bronchoalveolar fluids, protected distal samples, as well as induced sputum.
- Cerebrospinal fluid (CSF): this type of sample is indicated in cases of suspected neurological damage, in order to look for possible viral dissemination in the central nervous system.

Table 3. Sample, sampling material andstorage temperaturefor the diagnosis and differential of MPXV

Sample type	Collection materials	Storage temperature	Purpose of collection
Skin lesion, including: • Lesion exudate swabs • Roofs of lesions • Crusted lesions	It should be taken with a dry swab or VTM (Dacron or polyester flocked swabs should be used)	Once the samples are collected, they must be kept refrigerated (2–8°C) until they are sent to the laboratory and must be transported in the cold chain.	It is recommended for diagnosis.
Oropharyngeal swab	It should be taken with a dry swab or VTM (Dacron or polyester flocked swabs should be used)	Once the samples are collected, they must be kept refrigerated (2–8°C) until they are sent to the laboratory and must be transported in the cold chain.	Recommended for diagnosis, if possible, in addition to skin lesion material.
Serum	Serum separator tubes	Once the samples are collected, they must be kept refrigerated (2–8°C) until they are sent to the laboratory and must be transported in the cold chain.	Its use in serology should be considered as part of differential diagnosis and to aid research.

7.WHAT DIAGNOSTIC TOOLS FOR THE MONKEYPOX VIRUS?

The gold standard diagnostic methods for rapid and accurate identification of monkeypox virus (MPOX) infection are mainly based on nucleic acid amplification tests (NAATs), including polymerase chain reaction (PCR) and real-time quantitative PCR (RT-

qPCR). These techniques can be used alone or in combination with viral genome sequencing, in accordance with World Health Organization (WHO) recommendations [14].

However, the application of RT-qPCR and genomic sequencing may be limited in low-resource settings, due to constraints related to the necessary equipment, the high cost of reagents, as well as infrastructure requirements, such as reliable access to electricity.

Furthermore, serological tests including viral neutralization, hemagglutination inhibition, immunofluorescence, enzyme-linked immunosorbent assay (ELISA), and Western blotting have diagnostic limitations, particularly due to cross-reactivity between MPXV antigens and those of other members of the Orthopoxvirus genus, making specific confirmation of infection difficult.

Additionally, MPXV can also be detected in clinical samples by electron microscopy or by viral isolation in cell culture, although these methods are less used in routine practice due to their complexity [15].

8.WHAT BIOSECURITY MEASURES AND BIOSECURITY IN THE LABORATORY?

The handling of specimens from suspected, probable, or confirmed cases of monkeypox virus (MPOX) infection should be carried out using a risk-based approach, in accordance with the World Health Organization (WHO) recommendations [14]. Each virology laboratory is required to conduct a local institutional risk assessment to determine appropriate biosafety measures.

Handling procedures must, at a minimum, meet Biosafety Level 2 (BSL-2) standards, with enhanced control measures implemented based on local assessment results. While MPXV can be contracted during sample handling—particularly through contaminated equipment or procedural errors these risks can be significantly reduced by adopting rigorous biosafety protocols.

In the context of clinical diagnosis not requiring virus culture, the following measures are recommended:

- Samples from suspected patients must be handled in a functional Class I or II biological safety cabinet (BSC) before any inactivation step. Once the samples are properly inactivated, they can be handled outside the BSC.
- Laboratory personnel must wear suitable personal protective equipment (PPE), including an FFP2 mask, gloves and safety glasses, particularly during pre-inactivation steps.
- Procedures involving centrifugation should be performed in centrifuges equipped with sealed rotors or safety buckets. Additional control measures should be applied for procedures likely to generate aerosols, depending on the conclusions of the laboratory-specific risk assessment.

The implementation of these precautions constitutes a key element in guaranteeing the protection of personnel and preventing accidental contamination, while ensuring the quality and reliability of virological analyses.

9.INTERPRETATION OF RESULTS

For each test series, the validity of the positive and negative controls is essential. In the event of an invalid control, it is necessary to repeat the entire test, regardless of the target gene or the amplification of the internal control (IC). A negative result can only be interpreted as reliable if the IC is amplified; otherwise, the result is considered invalid, and a new analysis must be performed. Conversely, a positive result can be validated even in the absence of amplification of the internal control.

In multi-target molecular tests, a result can only be confirmed as positive if all target genes are detected. If only a portion of the targets are identified, the result is inconclusive.

In real-time PCR, when the cycle threshold (Ct) value of the target gene is less than or equal to the defined threshold value, the result should be considered positive, regardless of the amplification of the internal control. If no target gene is detected or if the Ct value exceeds the threshold, the result is considered negative, again without taking into account the internal control. However, it is important to note that values close to the detection limit in samples with low viral load can lead to false negatives or false positives. Thus, rigorous verification of the results by the biologist is required, and in case of doubt, a new test should be performed from a residual or newly collected sample.

Due to the variability of the incubation period of monkeypox, a negative result obtained from an isolated blood or oropharyngeal sample does not exclude the diagnosis, especially in a highly suggestive clinical or epidemiological context. In this case, additional samples should be taken at regular intervals.

Even for skin lesion samples, which are the preferred specimens, false-negative results can occur if the sample is inadequate, or taken too early or too late in the course of the disease. It is therefore recommended to repeat the analyses in case of diagnostic doubt, whether for false-negative or false-positive results.

In this regard, it is not sufficient to retest the extracted nucleic acids; it is advisable to re-extract the genetic material directly from the initial clinical samples, or to carry out new samples, especially in cases of high clinical suspicion. However, given that sampling of skin lesions is an invasive procedure, it is often necessary to collect several samples during the initial collection, for possible additional testing [16].

Figure 4. Laboratory testing algorithm for clinical management and surveillance of monkeypox: negative results [17].

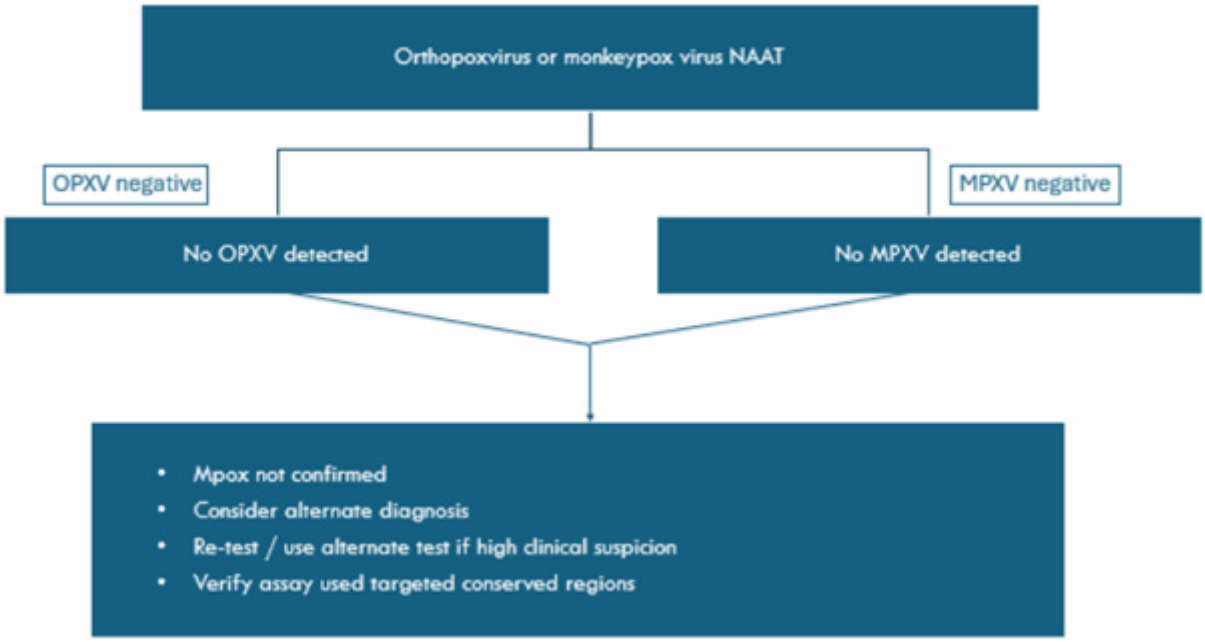
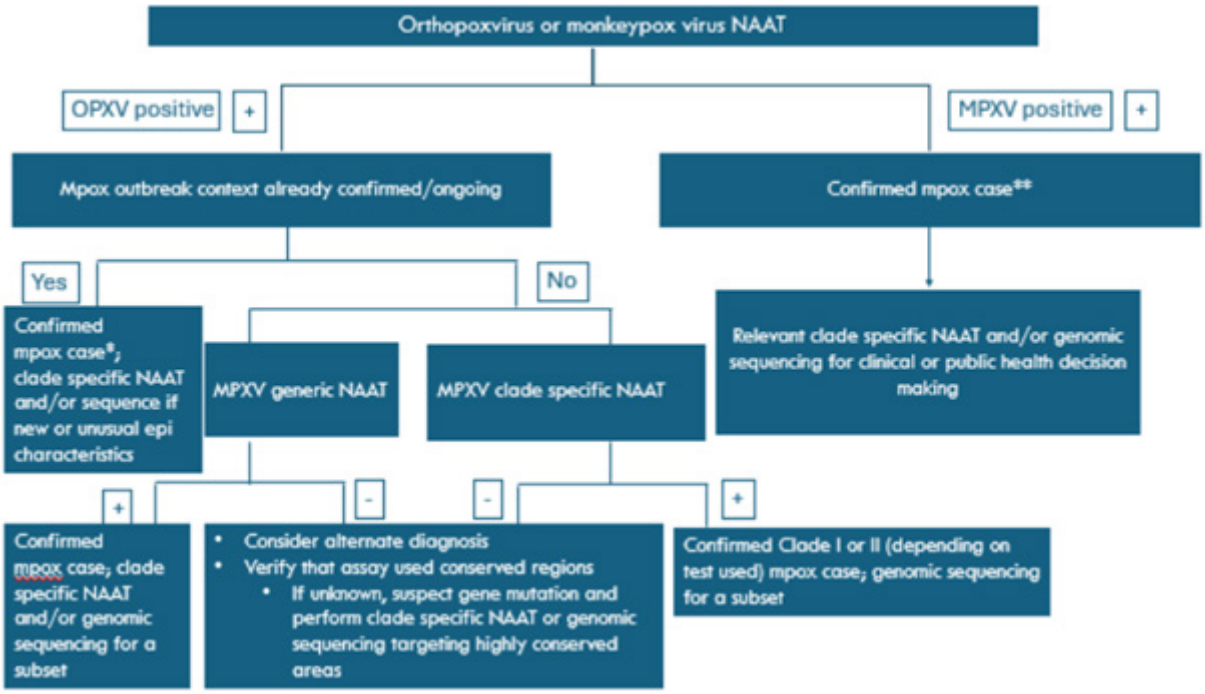


Figure 5. Laboratory testing algorithm for clinical management and surveillance of monkeypox: positive results [17].



10.THERAPEUTIC CARE AND PREVENTIVE MEASURES

To date, no standardized specific treatment is available for monkeypox (MPXV). However, certain antivirals can be administered after diagnostic confirmation of the infection (**Table 4**).

Tecovirimat (also known as ST-246 or TPOXX), a Food and Drug Administration (FDA)-approved antiviral, is currently the standard treatment option for severe MPXV infection. It is an oral, small-molecule antiviral that targets the viral envelope protein VP37, which is essential for extracellular virus formation. Its mechanism of action is based on inhibition of this protein, which prevents viral dissemination, reduces viremia, and promotes rapid recovery without major adverse effects.

Cidofovir, another antiviral agent, is also being considered as a potential therapeutic option for MPXV. It exhibits in vitro activity

against several DNA viruses, including monkeypox virus, by acting through inhibition of viral DNA polymerase.
In addition to antivirals, management includes symptomatic and supportive care, which is essential to promote rapid recovery. This care includes the management of complications such as respiratory distress, bronchopneumonia, sepsis, ulcers, fever, skin lesions, and other associated clinical manifestations.
From a preventative perspective, it is imperative to avoid close contact with infected or at-risk individuals. Forms of contact to avoid include: sharing the same bed or room, sexual intercourse or intimate contact, cohabitation, and sharing dishes or personal items.
Regarding disinfection, orthopoxviruses, once dried, exhibit stability at room temperature. However, they are inactivated by heat (including autoclaving or incineration) as well as by several effective disinfecting agents, including chloroxylenol, 0.5% sodium hypochlorite, glutaraldehyde, formaldehyde, and paraformaldehyde [18].

Table 4. Current antiviral treatments and vaccines to manage and prevent MPOX [19].

Category	Name	Manufacturer's name and location	Use/status	Description
Antiviral agents	Tecovirimate (TPOXX)	SIGA Technologies, New York, New York, USA	Approved/ processing	Tecovirimat is an antiviral drug approved by the US FDA for the treatment of smallpox. It has also been used in compassionate use or experimental protocols for MPOX. It targets the VP37 protein of orthopoxviruses, preventing the formation of enveloped virions and thus inhibiting the spread of the virus.
Antiviral agents	Cidofovir	–	Investigation/ treatment	Broad-spectrum antiviral drug. Although not specifically approved for MPOX, it has been used off-label. Cidofovir works by inhibiting viral DNA polymerase, which is necessary for viral replication. Nephrotoxicity concerns limit its use.
Antiviral agents	Brincidofovir	–	Investigation/ treatment	An antiviral drug that has been shown to be effective against various DNA viruses, including orthopoxviruses. It is an orally administered prodrug of cidofovir, which has a better safety profile, particularly with regard to nephrotoxicity.
Vaccine	JYNNEOSTM (MVA-BN) JYNNEOS (Imvamune or Imvanex)	Bavarian Nordic, Copenhagen, Denmark	Pre-exposure and post-exposure prophylaxis	A new non-replicating vaccinia virus vaccine is approved for the prevention of smallpox and lungpox. It is considered safer than ACAM2000, particularly for immunocompromised individuals, pregnant women, and people with eczema. A third-generation smallpox vaccine is approved by the U.S. FDA for the prevention of smallpox and lungpox in adults.
Vaccine	ACAM2000	–	Pre-exposure and post-exposure prophylaxis/ approved for smallpox	A live vaccinia virus vaccine is traditionally used against smallpox but also offers cross-protection against MPOX. ACAM2000 may be associated with serious adverse effects, particularly in immunocompromised individuals. A second-generation smallpox vaccine that has been used off-label to prevent MPOX.
Immunoglobulin	VIG	–	Considered for severe cases or high-risk populations in experimental protocols	Although there is no specific anti-MPOX immunoglobulin, VIG immunoglobulin, derived from individuals vaccinated against smallpox, may provide passive immunity. It is primarily considered for severe cases or for specific high-risk populations. Its efficacy against MPOX needs to be better established.

11.VACCINATION AGAINST THEIR MONKEYPOX VIRUS

Vaccination using vaccinia virus, a live attenuated vaccine, provides an estimated protection of approximately 85% against monkeypox virus (MPXV) infection.
Smallpox vaccines (Table 4) may be effective for post-exposure prophylaxis, provided they are administered within 4 days of contact with a confirmed case of Mpox. They can be administered up to 14 days after exposure, provided the exposed person does not yet have clinical symptoms.

The global reduction in smallpox vaccination coverage, following the cessation of mass vaccination after the eradication of human smallpox, is considered a major factor contributing to the current global resurgence of MPOX cases. In response to this threat, the World Health Organization (WHO) recommends targeted pre-exposure vaccination for certain high-risk groups, including:

- healthcare professionals exposed to confirmed or suspected cases,
- laboratory personnel handling infectious samples,
- epidemic response teams, and
- people with multiple sexual partners [17].

CONCLUSION

Monkeypox (MPox) is a neglected viral zoonotic disease whose spread has been documented in more than 116 countries worldwide. A thorough understanding of the causative agent, clinical manifestations, transmission patterns, and prevention, control, biosafety, and biosecurity measures is essential for effective management of this disease.

The laboratory plays a central role in the fight against MPOX. Close collaboration between clinicians and biologists is essential to integrate relevant epidemiological and clinical data, guide the choice of appropriate diagnostic methods, and rigorously interpret biological results. It is crucial to maintain constant vigilance regarding compliance with the requirements of the pre-analytical phase, as well as recognizing the methodological limitations of the tests used.

This review provides an updated overview of MPOX. Epidemiological surveillance, targeted vaccination, and rational use of antivirals are complementary tools that can help reduce the incidence of the disease.

Accordingly, national health authorities are encouraged to conduct a contextual risk assessment and consider vaccination of at-risk groups, taking into account the following factors: clinical vulnerability, likelihood of exposure, and vaccine availability.

Populations eligible for preventive vaccination may include:

- exposed healthcare professionals,
- laboratory personnel handling risky samples,
- individuals working in contact with wildlife, whether in the field or in a veterinary laboratory,
- as well as any other person who may be exposed to the MPXV virus.

REFERENCES

1. Alakunle, E., Moens, U., Nchinda, G., Okeke, MI (2020). Monkeypox virus in Nigeria: infection biology, epidemiology, and evolution. Viruses 12, 1–29. doi: 10.3390/v12111257.

2. WHO. 2022–23 Mpox (Monkeypox) Available from: https://worldhealthorg.shinyapps.io/mpx_global/.

3. https://www.sante.gov.ma/Pages/communiqu%C3%A9s.aspx?communiqueID=438.

4. L.Vandenbergen, G.Vandercam, E.Hoornaert, A.Sluijters, JC.Yombi (2022). Monkeypox virus (MPXV). Louvain Med 2022 Juin-Juillet-August; 141:301-306.

5. Goia AR, Muntean D, Musta V, Herlo A, Vulpie S, Izmendi O, Jumanca R, Licke M (2024). Understanding the pathogenesis, clinical, laboratory diagnosis and treatment of the recent monkeypox virus outbreak. Revista Română de Medicină de Laborator 2024;32(1):97-106 DOI:10.2478/rrlm-2024-0005

6. Isidro J., Borges V., Pinto M., et al. Phylogenomic characterization and signs of microevolution in the 2022 multi-country outbreak of monkeypox virus. Nat Med. 2022; 28(8):1569–1572. doi:10.1038/s41591-022-01907-y.

7. S Hantz,S Mafi,P Pinet,C Deback.From monkeypox to Mpox or the re-emergence of an ancient zoonosis (2023). 2023(553):25–37. doi:10.1016/S1773-035X(23)00132-6

8. Hutson, CL · Carroll, DS · Gallardo-Romero. (2015). Comparison of the kinetics and pathology of monkeypox virus clades in the prairie dog animal model using a serial sacrifice study. BioMed Res Int. 2015; 2015 doi:965710-965711

9. Bunge, EM · Hoet, B. · Chen, L. ...(2022). The changing epidemiology of monkeypox in humans: a potential threat. A systematic review. PLOS Negl Trop Dis. 2022; 16 doi:e0010141-e0010142

10. R Ranjan, JK Biswal (2022). Monkeypox: A Re-Emerging Zoonotic Threat.Zoonotic Dis. 2022, 2 (4), 234-246;https://doi.org/10.3390/zoonoticdis2040019

11. SM Raza, MB Dawood, M Sajid, O Nasir, S Husain.... (2023). Monkeypox Virus: From Origins to On-going Challenges - A Comprehensive Review. Journal

homepage: www.ijrpr.com ISSN 2582-7421. DOI:https://doi.org/10.55248/gengpi.4.1023.102704

12. Laura Hughes,Victoria A. Olson,Inger K. Damon(2015). Poxvirus. Wiley Online Library.https://doi.org/10.1128/9781555817381.ch107

13. M Altindis, E Puca, L Shapo (2022).Monkeypox Virus Diagnosis – OverviewVolume 50, November-December 2022, 102459. https://doi.org/10.1016/j.tmaid.2022.102459

14. World Health Organization. Laboratory Biosafety Manual, 4th edition.2020. Available from:https://www.who.int/publications/i/item/9789240011311

15. Blacksell SD, Dhawan S, Kusumoto M, Le KK (2023).The Biosafety Research Road Map: The Search for Evidence to Support Practices in the Laboratory—Mpox/Monkeypox Virus. Published by Mary Ann Liebert, Inc. https://doi.org/10.1089/apb.2022.0045

16. Hong, Ki Ho, Kim, Gab Jung...(2023). Guidelines for laboratory diagnosis of monkeypox in Korea. Ann Lab Med 2023; 43(2): 137-144https://doi.org/10.3343/alm.2023.43.2.137

17. WHO reference number: WHO/MPX/Laboratory/2024.1

18. Roess, AA; Monroe, BP; Kinzoni, EA; Gallagher, S.; Ibata, SR; Badinga, N.; Molouanie, TM; Mabola, FS; Mombouli, JV; Carroll, DS; et al. Evaluation of the effectiveness of a community-based intervention for the prevention of monkeypox in the Congo Basin. PLoS Negl. Trop. Dis. 2011, 5, e1356.

19. S Anil,B Joseph,....(2024). Monkeypox: A viral zoonotic disease of increasing global concern. Infectious Diseases and Immunity (2024) 4:3 http://dx.doi.org/10.1097/ID9.0000000000000124