

# Clinical and Laboratory Characteristics and Diagnosis of Monkeypox

Subjects: Dermatology

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Monkeypox is a disease caused by Orthopoxvirus, which also includes the smallpox virus. Several endemics have been reported on the African continent, typically in the western and central regions. However, since 13 May 2022, there have been several cases reported from different member states; the number of confirmed cases in 1 month exceeded the total number of cases reported outside the African continent since the first case in 1970. The World Health Organization (WHO) and Centers for Disease Control (CDC) consider monkeypox as an important disease for global public health.

Keywords: monkeypox ; smallpox ; clinical manifestations ; diagnosis

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## 1. Introduction

The COVID-19 pandemic has triggered a global health, economic, and political crisis. As a result, the world has become vigilant and attentive to any outbreak. From early May 2022, hundreds of cases of monkeypox, a zoonotic disease endemic to Africa, have been reported in several non-endemic countries. In one month, 1472 cases from 33 member states were documented <sup>[1]</sup>. The number remains not extremely alarming, despite the spread of the virus outside the African continent, given that, at the beginning of the COVID-19 pandemic, for the same period, the number of cases was much higher (11 March 2020, 7500 cases). However, the World Health Organization (WHO) and Centers for Disease Control (CDC) consider monkeypox as an important disease for global public health. Nevertheless, the risk is moderate, as this is the first time that several cases of monkeypox have been reported in endemic and nonendemic regions <sup>[2][3]</sup>. As the number of confirmed cases in the early months exceeded the total number of cases reported outside the African continent since the first case in 1970, healthcare workers and concerned organizations must remain vigilant about this infectious disease <sup>[4]</sup>. Indeed, to date, on 17 December 2022, the spread is considered much more global, with more than 103 non-endemic countries reached and over 81,500 cases reported <sup>[5]</sup>.

## 2. Clinical and Laboratory Characteristics and Diagnosis of Monkeypox

The clinical manifestations and laboratory findings in patients with monkeypox remain unclear. Several clinical case studies have been performed to gain deeper insight into the pathology of this viral infection <sup>[6][7][8][9][10][11]</sup>.

Based on the (WHO) and (CDC) reports, the national authorities have developed case definition criteria for each outbreak <sup>[12][13][14]</sup>. However, the clinical presentation of monkeypox resembles that of other viral infections (varicella, herpes, and syphilis, among others); therefore, a definition with greater specificity is required for accurate case detection to avoid unnecessary sampling and to prevent patient confinement and the associated isolation-induced stress, before diagnostic confirmation <sup>[15]</sup>.

### 2.1. Prodrome

The most common prodromal symptoms that precede the skin rash within 1 to 3 days <sup>[16]</sup>, and occasionally up to 2 weeks, include fever, headache, chills, myalgia, and back pain <sup>[7]</sup>. However, not all patients will present with these symptoms. Yinka et al. <sup>[13]</sup> observed that fever preceded rash in only 57% of patients. Adler et al. <sup>[6]</sup> 19 observed this finding in 3/7 patients, and Minhaj et al. <sup>[14]</sup> in 7/17 patients. Fever is the main criterion for case definition; however, not all patients will have fever, and this fact should be considered during the current outbreak.

### 2.2. Skin Rash

A monkeypox rash manifests as a progressive maculopapular to vesicular/pustular rash that gradually undergoes crust formation and finally desquamation over a period of 2–4 weeks, with intact skin between lesions <sup>[15][17]</sup>. However, this

clinical presentation closely resembles that of other illnesses, particularly chickenpox, that are commonly encountered in routine medical practice.

Several studies have reported that the monkeypox rash is clinically characterized by monomorphism (all lesions appear to be at the same stage of development at the time of evaluation) <sup>[9][15][16][18]</sup>; however, several other reports have refuted these findings <sup>[6][8][16][19]</sup>.

The centrifugal distribution and palmoplantar or genital localization of lesions is another feature of this rash <sup>[9][13][14][15]</sup>, which has been described by a recent study during this current epidemic. The rash originated in the genital or perianal area before dissemination in eight patients <sup>[14]</sup>. However, this presentation was primarily observed in homosexual men and is attributable to close physical contact <sup>[20]</sup>. Men's genital lesions may have necrotic crusts or paraphimosis, and the rectal lesions can cause pain on defecation or proctitis <sup>[21]</sup>. Palmar-plantar involvement is a characteristic finding associated with this infection <sup>[22]</sup>. Although already been reported, during a suspected monkeypox epidemic, there were several cases of varicella zoster virus (VZV) infection with palmar-plantar involvement <sup>[23][24]</sup>; however, this localization remains uncharacteristic of VZV infections <sup>[15]</sup>.

### 2.3. Associated Signs and Complications

Lymphadenopathy (axillary, inguinal, and/or cervical) is a prominent sign that differentiates MPXV infection from other similar diagnoses <sup>[10][14][15][25]</sup>. Lymphadenopathy may occur before or during the rash, with a prevalence of 35–75% <sup>[8][13][14][16][19]</sup>. Ulcerations may be present in the oral mucosa, tongue, and pharynx, limiting oral intake.

Complications and severe infection, which are known to be associated with the Congo basin clade <sup>[3][7]</sup> may cause encephalitis, pneumonitis, corneal ulceration, keratitis, and secondary bacterial infections <sup>[6][16]</sup>. Mood disturbance, deep tissue abscesses, and conjunctivitis <sup>[6]</sup> are the most common complications observed during the present outbreak; however, a few patients may show no complications <sup>[14]</sup>.

The case fatality rate varies based on the viral clades as follows: Central African 10.6% vs. West African 3.6% <sup>[12]</sup>. To date, 65 deaths have been reported among 82,809 confirmed cases during the current outbreak <sup>[26]</sup>.

Therefore, MPXV infection may present in many forms, and laboratory tests are essential for diagnostic confirmation. However, a study <sup>[15]</sup> reported that detection of 7/8 of the following 12 specific signs or symptoms serve as useful criteria to initiate specific MPXV investigations: fatigue, being bedridden, nausea, uniform size of lesions, genital distribution, deep-seated firm lesions, distribution on the arms, legs, palms, or soles, lymphadenopathy, conjunctivitis, and fever before onset of rash.

### 2.4. Laboratory Tests and Diagnosis

Isolation of the MPXV DNA using a polymerase chain reaction assay (PCR) is the only method for definitive diagnosis in patients who show a high index of clinical suspicion <sup>[18][22][27]</sup>. The WHO recommends performing PCR on swabs from lesions surfaces, exudates, or crusts. It also advises collecting and testing additional specimens (such as blood, semen, urine, and genital and rectal swabs) <sup>[28]</sup>. However, oropharyngeal swabs (OPS) and lesion samples (LS) were evaluated by Ouafi et al., who concluded that OPS might not be helpful for diagnosis <sup>[29]</sup>.

During the current outbreak, researchers performed genomic analysis of MPXV isolates from Portugal and Belgium and compared these with all available MPXV sequences; researchers observed that this particular organism was more closely associated with the virus identified in the West African clade <sup>[30]</sup>. Immunological methods (enzyme-linked immunosorbent assay) may be used for immunoglobulin (Ig)G and IgM antibody detection. In principle, these antibodies are detected in the serum after the onset of the skin eruption, approximately 5 days for IgM, and up to 8 days for IgG <sup>[9]</sup>. MPXV can also be visualized using electron microscopy, although this method is not useful for diagnostic confirmation and only shows that the virus belongs to the Poxviridae family <sup>[31]</sup>. Concomitant sexually transmitted infections (STI) were reported in several studies, in 29% of cases according to Thornhill et al. <sup>[32]</sup>, and in 17% according to Tarin et al. <sup>[33]</sup>, most commonly chlamydia and syphilis in addition to human immunodeficiency virus (HIV). Laboratory tests to look for these STIs are recommended <sup>[32]</sup>.

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