Guidance on Clinical Suspicion and Differential Diagnosis of Monkeypox

Provisional technical note, June 2022

PAHO Pan American Health Organization
World Health Organization Regional Office for the Americas

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Background

In light of the monkeypox outbreaks currently being reported in non-endemic countries of the Region of the Americas and other regions, the Pan American Health Organization is publishing graphic information to facilitate clinical suspicion and diagnostic guidance for health professionals. The objective is to support proper patient management and the application of infection control practices.

This publication is aimed at health professionals, especially in primary health care services, sexually transmitted infection clinics, specialized units providing care for people living with HIV, and emergency services.

What is monkeypox?

Monkeypox is a zoonotic viral disease that is endemic in some regions of Africa. It usually presents with fever, an extensive characteristic rash, and adenopathies (Box 1). It is important to differentiate monkeypox from diseases such as chickenpox, measles, and syphilis, as well as bacterial skin infections and drug allergies.

BOX 1 Critical points for clinical practice

Incubation period: 7 to 14 days, although it can range from 5 to 21 days.

Prodromes: fever, weakness, headache, sometimes cough and pharyngeal pain, and adenopathies.

Clinical manifestations: In the cases described so far in this outbreak, the usual presenting symptoms include oral lesions, fever, adenopathies and pain when swallowing, and skin and anogenital lesions.

Mucocutaneous manifestations: These are characteristic of the disease. Pharyngeal exudate and skin lesions that evolve from macules to papules, vesicles, pustules, and crusts in 3 to 7 days are observed. These lesions are infective until the detachment of the crust, which happens at 7 to 14 days. During this outbreak, the sequence is similar, but lesions of different stages have been observed at the same time.

Transmission: from person to person, by symptomatic people through close contact with lesions, respiratory secretions, and bodily fluids, and through objects that have had contact with crusts or bodily fluids.

Treatment: symptomatic and supportive. Appropriate measures for the care of skin lesions to prevent secondary bacterial infections. Assess treatment for sexually transmitted co-infections (e.g., syphilis), in particular if there are related risk factors.

Infection prevention and control measures: In health facilities, patients with suspected monkeypox infection should be isolated with contact and droplet measures. Hand hygiene and use of personal protective equipment should be strengthened.

WHO has developed a rapid response guideline for clinical management and infection prevention that is available online.*

Note: World Health Organization. Clinical management and infection prevention and control for monkeypox: Interim rapid response guidance, 10 June 2022. Geneva: WHO; 2022. Available from: https://www.who.int/publications/i/item/WHO-MPX-Clinical-and-IPC-2022.1.

Why is monkeypox of concern for Latin America and the Caribbean?

Since mid-May 2022, cases of monkeypox have been identified and reported in people with no travel history to Africa. Most cases have been reported in countries in Europe, as well as in Canada and the United States of America, with sporadic cases confirmed in Latin American and Caribbean countries, even among people with no history of travel abroad.[1]

The cases in the current outbreak have been primarily mild and have followed a positive evolution. Monkeypox is a self-limiting infection that does not require antiviral treatment. However, the monkeypox virus could cause severe illness in immunosuppressed or vulnerable populations.

What is known about this outbreak? What makes it different from endemic cases in Africa?

In this outbreak, the majority of people affected are men who have sex with men and people seeking care for suspected sexually transmitted infections at sexual health care clinics or centers. The initial symptoms, in the form of a rash (macules, vesicles, pustules, or ulcers), usually occur in the genital and anal areas. They are often accompanied by proctitis, oral ulcers, and lesions around the mouth.

Clinical diagnosis

Skin lesions

Skin lesions usually appear 1 to 3 days after fever, pharyngeal pain, and adenopathies and follow the sequence presented in Figure 1. However, in this outbreak, cases were observed with rash (with vesicular, pustular, or ulcerated lesions) limited to the anogenital zone as the first manifestation, without systematically spreading to other parts of the body. Cases have also been described in which pustules appear prior to constitutional symptoms (e.g., fever) and in which the lesions are at different stages of development. Both are atypical of the classic form of the disease. For more information, see the figures below.

1 For more information, see Pan American Health Organization. Epidemiological alerts and updates. Washington, DC: PAHO; 2022. Available from: https://www.paho.org/en/epidemiological-alerts-and-updates.

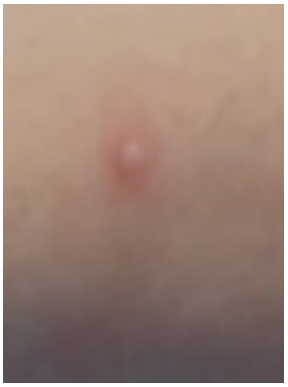
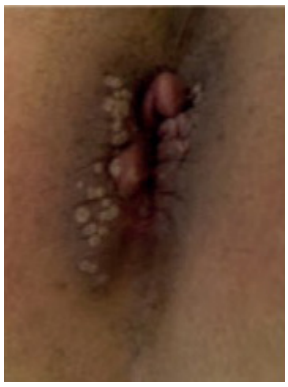
FIGURE 1. **Classic skin manifestations**

Note: Images courtesy of www.gov.uk/guidance/monkeypox.

Genital lesions

Genital and anal lesions are of relevance in this outbreak because of their frequency. Lesions typically appeared 1 to 3 days after systemic symptoms, clustered in the anal region, and simulating a herpetic lesion (Figure 2).

FIGURE 2. **Anal, genital, and skin lesions and their temporal evolution**

Days since symptom onset	Anal lesions	Genital lesions	Skin lesions
Sixth day			
Seventh day			
Ninth day			
Eleventh day			

Note: Images courtesy of Antinori A, Mazzotta V, Vita S, Carletti F, Tacconi D, Lapini LE, et al. Epidemiological, clinical and virological characteristics of four cases of monkeypox support transmission through sexual contact, Italy, May 2022. Eurosurveillance. 2022;27(22):p ii. Available from: https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2022.27.22.2200421.

Differential diagnosis

Various infections and skin diseases should be considered. Both clinical and epidemiological data and specific laboratory studies can lead to different diagnoses. In the current outbreak, cases of both monkeypox and other sexually transmitted infections have been reported. Therefore, diagnosis of an infection such as syphilis or lymphogranuloma venereum should not rule out infection with the monkeypox virus (Figure 3).

FIGURE 3. Lesions of the various differential diagnoses

Disease	Images		Comments
Herpes simplex			Very painful polycyclic lesions that evolve to crust, usually in people with a history of herpes.
Primary or secondary syphilis		 © Portal del Sur	**Primary:** firm, painless chancre with a clean base. **Secondary:** roseola or disseminated papules that affect the palms and the soles of the feet.
Chickenpox		 © Wikimedia/Noj Han	Starts on the upper back as asynchronous papules that evolve into vesicles and scabs.
Impetigo			Meliceric (yellowish) crusts, sometimes with blisters, caused by bacterial infection.
Hand-mouth-foot disease		 © O. Sued	Although it is common in childhood, it can occur in adults. Caused by various enteroviruses. Fever, and lesions on the mucosa, mouth, palms, and buttocks.

Note: Unless otherwise indicated, images courtesy of the Federation of Spanish Medical Scientific Associations. Diagnóstico diferencial de las lesiones cutáneas de viruela del mono. Madrid: FACME; 2022. Available from: https://seorl.net/wp-content/uploads/2022/06/01.06.2022-DIAGNOSTICO-DIFERENCIAL-LESIONES-CUTANEAS-.pdf.

Bibliography

Adler H, Gould S, Hine P, Snell LB, Wong W, Houlihan CF, et al. Clinical features and management of human monkeypox: A retrospective observational study in the UK. Lancet Infectious Diseases 2022:S1473-3099(22)00228-6. Available from: https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(22)00228-6/fulltext.

Antinori A, Mazzotta V, Vita S, Carletti F, Tacconi D, Lapini LE, et al. Epidemiological, clinical and virological characteristics of four cases of monkeypox support transmission through sexual contact, Italy, May 2022. Eurosurveillance. 2022;27(22):p ii. Available from: https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2022.27.22.2200421.

Bížová B, Veselý D, Trojánek M, Rob F. Coinfection of syphilis and monkeypox in HIV positive man in Prague, Czech Republic. Travel Medicine and Infectious Disease 2022;49:102368. Available from: https://doi.org/10.1016/j.tmaid.2022.102368.

Dhawan M, Emran TB, Islam F. The resurgence of monkeypox cases: Reasons, threat assessment, and possible preventive measures. Travel Medicine and Infectious Disease 2022;49:102367. Available from: https://doi.org/10.1016/j.tmaid.2022.102367.

Hammerschlag Y, MacLeod G, Papadakis G, Adan Sanchez A, Druce J, Taiaroa G, et al. Monkeypox infection presenting as genital rash, Australia, May 2022. Eurosurveillance 2022;27(22):2200411. Available from: https://doi.org/10.2807/1560-7917.ES.2022.27.22.2200411.

Heskin J, Belfield A, Milne C, Brown N, Walters Y, Scott C, et al. Transmission of monkeypox virus through sexual contact - A novel route of infection. Journal of Infection 2022:S0163-4453(22)00335-8. Available from: https://doi.org/10.1016/j.jinf.2022.05.028.

Harris E. What to know about monkeypox. Journal of the American Medical Association 2022;327(23):2278-2279. Available from: https://doi.org/10.1001/jama.2022.9499.

Perez Duque M, Ribeiro S, Martins JV, Casaca P, Leite PP, Tavares M, et al. Ongoing monkeypox virus outbreak, Portugal, 29 April to 23 May 2022. Eurosurveillance 2022;27(22):2200424. Available from: https://doi.org/10.2807/1560-7917.ES.2022.27.22.2200424.

Vivancos R, Anderson C, Blomquist P, Balasegaram S, Bell A, Bishop L, et al. Community transmission of monkeypox in the United Kingdom, April to May 2022. Eurosurveillance 2022;27(22):2200422. Available from: https://doi.org/10.2807/1560-7917.ES.2022.27.22.2200422.

Zumla A, Valdoleiros SR, Haider N, Asogun D, Ntoumi F, Petersen E, et al. Monkeypox outbreaks outside endemic regions: Scientific and social priorities. Lancet Infectious Diseases 2022:22(7):929-931. Available from: https://doi.org/10.1016/S1473-3099(22)00354-1.

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The purpose of this publication is to present guidelines for the clinical diagnosis of monkeypox to assist in the proper management of patients and the application of infection control practices. In addition, given that the appearance and evolution of the typical skin lesions of this viral disease are variable, a selection of photographs of different cases is included that will help in the differential diagnosis.

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