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A Practical Clinical Review of Recognition, Diagnosis, Initial Management, and Referral of MPOX

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Abstract **Review Article**

Mpox can present to primary care with a wide spectrum of skin and mucosal disease, ranging from a few localized lesions to disseminated or complicated infection. Contemporary presentations may lack the classical generalized rash or prominent systemic prodrome, creating diagnostic overlap with herpes simplex, varicella-zoster, syphilis, molluscum contagiosum, bacterial skin disease, and other causes of vesicular, pustular, or ulcerative lesions. Primary-care clinicians therefore have a key role in recognition before laboratory confirmation. This practical clinical review provides a frontline approach to suspicion, immediate infection-prevention measures, lesion-based PCR testing, assessment for important coinfections, severity stratification, supportive management, and timely referral. The central sequence is: suspect mpox, protect patients and staff, test appropriately, assess severity and risk, and determine safe outpatient management versus escalation of care.

Keywords: Mpox; monkeypox virus; primary care; vesiculopustular rash; PCR; differential diagnosis; infection prevention; referral.

1. When to suspect Mpox

Consider mpox in a patient with an otherwise unexplained vesicular, pustular, umbilicated, or ulcerative eruption, especially when lesions are firm, deep-seated, painful, well-circumscribed, genital or perianal, oral, or associated with lymphadenopathy or a compatible exposure. Some patients have only a few lesions and systemic symptoms may be mild or absent. A known exposure increases suspicion, but its absence should not automatically exclude the diagnosis [1-3].

Clinical pearl:

Do not wait for a classic generalized rash. Contemporary mpox may be localized and may resemble common sexually transmitted or dermatologic conditions.

2. Focused clinical assessment

Ask about lesion onset and progression, pain or pruritus, fever and constitutional symptoms, lymphadenopathy, rectal pain or proctitis, dysuria, oral symptoms, ocular symptoms, close skin-to-skin or intimate contact, contact with a suspected or confirmed case, relevant travel, pregnancy, immunosuppression, and known HIV status. Take sensitive exposure and sexual histories without assumptions or stigmatizing language [1,2].

3. First 5 minutes: practical actions

Step	Action
Suspect	Recognize a compatible lesion pattern and obtain a focused exposure and symptom history.
Protect	Separate the patient from others and apply locally recommended infection-prevention precautions before prolonged examination.
Examine	Assess skin and mucosa as clinically appropriate; ask specifically about oral, genital, anorectal, ocular, and neurologic symptoms.
Test	Collect lesion material for MPXV nucleic-acid amplification/PCR according to local laboratory instructions.
Triage	Identify severe disease, high-risk host factors, uncontrolled pain, dehydration, ocular disease, neurologic involvement, or other complications.

4. Differential diagnosis at the bedside

Condition	Typical clues
Mpox	Firm/deep-seated, well-circumscribed lesions; often painful; may umbilicate; localized genital/perianal or disseminated disease possible.
HSV	Grouped superficial painful vesicles or ulcers; recurrent episodes common.
Varicella	Superficial pruritic lesions commonly present in different stages of evolution.
Herpes zoster	Painful unilateral dermatomal vesicles; neuropathic pain may precede rash.
Syphilis	Primary chancre often painless; secondary disease is polymorphic and requires serology.
Molluscum contagiosum	Chronic small umbilicated papules, usually with little systemic illness.
Hand-foot-mouth disease	Oral plus acral lesions, particularly in children; epidemiologic context helps.
Bacterial infection	Impetigo, folliculitis, cellulitis or abscess morphology; culture when indicated.

Important:

Coinfection can occur. Identification of another STI or skin infection does not automatically exclude mpox when clinical suspicion remains [1,2].

5. Diagnostic testing

Laboratory confirmation is based on detection of MPXV DNA by nucleic-acid amplification testing, usually real-time PCR. Lesion material is the key diagnostic specimen. Follow the receiving laboratory's instructions for lesion selection, swab number, labeling, and transport. CDC guidance emphasizes vigorous swabbing of lesion surfaces and advises against routine use of sharp instruments to unroof or aspirate lesions [4]. Additional testing may include HSV/VZV testing, syphilis serology, HIV testing, other STI testing, or bacterial culture according to presentation [1,2].

6. Infection prevention in primary care

Infection-prevention measures should begin when mpox is reasonably suspected, not after PCR confirmation. Separate the patient from other patients where feasible, minimize unnecessary contact, cover lesions when practical, perform meticulous hand hygiene, and use PPE according to local institutional and national guidance. WHO's current living guideline explicitly includes primary-care clinics among intended care settings [1].

7. Initial management

Most patients without severe disease or severe immunocompromise recover with supportive care. Priorities include hydration, appropriate analgesia, skin and wound care, treatment of pruritus during healing, and management of secondary bacterial infection when present. Pain can be substantial, especially with anorectal or mucosal disease. Antiviral therapy is not routine primary-care treatment for uncomplicated disease and should be guided by specialist/public-health pathways in patients with severe disease or high-risk features [1,5].

8. Referral and escalation

Urgent specialist or hospital assessment should be considered for ocular involvement, neurologic manifestations, rapidly progressive or extensive disease, severe mucosal or anorectal disease, inability to maintain hydration, severe uncontrolled pain, significant secondary bacterial infection, respiratory compromise, or substantial immunocompromise. Pregnancy and other vulnerable clinical contexts warrant early specialist discussion [1,2].

9. Red flags

Red flag	Concern
Eye pain, redness, visual symptoms, periocular lesions	Potential ocular disease and threat to vision.
Severe anorectal or mucosal disease	May require stronger analgesia, hydration support, specialist assessment.
Unable to drink / dehydration	May require IV fluids or hospital care.
Rapidly progressive or extensive disease	Possible severe mpox.
Altered mental status, seizures, major neurologic symptoms	Potential neurologic complication.
Respiratory deterioration	Potential systemic or pulmonary complication.
Severe immunocompromise	Higher risk of progressive or severe disease.
Severe uncontrolled pain	May require escalation beyond routine outpatient care.

10. Practical clinical algorithm

Unexplained compatible lesion

SUSPECT - morphology + distribution + symptoms + exposure

PROTECT - separate patient, use appropriate IPC/PPE

TEST - lesion PCR/NAAT; consider HSV/VZV, syphilis, HIV and other tests as indicated

ASSESS SEVERITY - ocular, neurologic, mucosal, hydration, pain, progression, immunocompromise

DISPOSITION - Stable/uncomplicated: supportive care + isolation/public-health advice + follow-up.

Severe/high-risk/complicated: urgent specialist or hospital assessment.

11. Take-home messages

1. Mpox may be localized; a generalized rash is not required.
2. Firm, deep-seated, painful or umbilicated lesions should increase suspicion.
3. Genital, perianal, oral and mucosal disease can dominate the presentation.
4. Begin infection-prevention precautions before PCR confirmation when suspicion is reasonable.
5. Use lesion material for PCR/NAAT and follow local specimen instructions.
6. Do not routinely unroof or aspirate lesions with sharps for sampling.
7. Consider HSV, VZV, syphilis, molluscum, HFMD and bacterial infection.
8. Coinfection is possible; another diagnosis does not always exclude mpox.
9. Supportive care and pain control are sufficient for most uncomplicated patients.
10. Ocular, neurologic, progressive, dehydrating or severely immunocompromised disease requires escalation.

12. CONCLUSION

Primary care is a critical point for early mpox recognition. The practical objective is not to make an immediate visual diagnosis with certainty, but to recognize a compatible presentation early enough to protect others, obtain the correct diagnostic specimen, assess severity, and arrange appropriate management or referral. A simple frontline sequence - SUSPECT, PROTECT, TEST, ASSESS SEVERITY, MANAGE/REFER - provides a clinically useful framework.

Declarations

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