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Current outbreak of monkeypox: Essentials for the dermatologist

To the Editor: A rapid increase in global numbers of monkeypox has been noted in the past month. On May 7, 2022, the World Health Organization was alerted after a traveler returning to the United Kingdom from Nigeria tested positive. Since then, 257 confirmed cases have been reported across 23 nations.[1] In the United States, the Centers for Disease Control and Prevention issued an advisory after a traveler returning from Canada tested positive on May 18, 2022.[2] Monkeypox is endemic to western and central Africa. Previous cases in the United States were reported in travelers returning from Africa or due to transmission via animals imported from endemic areas.[3] The current outbreak seems atypical, with an intriguing epidemiology since cases are occurring in non-endemic countries, in the absence of relevant travel, and are being frequently identified in men having sex with men.[1,2]

The cardinal features of monkeypox are fever, rash, and lymphadenopathy (Table I).[3,4] The incubation period ranges from 5 to 21 days. Infection results in prodromal symptoms, quickly followed by an enanthem. The vesiculopustular exanthem develops 1 to 3 days later, first on the face followed by a centrifugal spread, and may involve genitalia and palmoplantar surfaces.[1-3] Lesions could range from a few to thousands in number and are painful, rather than itchy.[2] Patients are considered infectious until all the lesions are crusted over with complete re-epithelization.[5] In view of these prominent cutaneous manifestations, dermatologists might see a spurt in consultations for "fever with rash-suspect monkeypox." Therefore, differentiating monkeypox from other causes of febrile vesiculopustular infectious exanthems becomes imperative (Table I).

The Centers for Disease Control and Prevention and World Health Organization have proposed case definitions for monkeypox (Table II),[1,2] and confirmation requires a positive lesional monkeypox-specific polymerase chain reaction. Samples should be collected by vigorously swabbing the surface of multiple lesions, preferably using dry polyester or Dacron swabs.[1,2] A skin biopsy is typically not indicated since findings can be similar to other differentials (Table I). Complications of monkeypox include sepsis, bronchopneumonia, encephalitis, and ocular infections. Historically, the mortality rate has ranged from 1% to 11% in endemic areas.[3] Fortunately, the majority of cases in the current outbreak are caused by the West African clade, which leads to a milder disease than the Congo Basin clade.[1,2]

In the absence of any specific treatment, monkeypox self-resolves in 2 to 4 weeks.[3] Antiviral therapy may be considered in people presenting with or at risk of severe disease including children <8 years, in pregnant or lactating women and immunocompromised persons, and those with involvement of special sites.[2] Oral antivirals developed for smallpox like tecovirimat and brincidofovir are available to treat monkeypox.[3] Tecovirimat is administered daily for 2 weeks, whereas brincidofovir is given once weekly for 2 doses.[5] Furthermore, 2 smallpox vaccines (ACAM200 and JYNNEOS) have shown 85% efficacy in the prevention of monkeypox.[5] Vaccines can also be used for postexposure prophylaxis, especially if given within 96 hours of exposure.[2]

In conclusion, awareness of these clinicoepidemiological features of monkeypox will enable dermatologists to be better prepared if faced with a suspected case during this international outbreak.

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Table I. Characteristics of monkey pox and its clinical mimickers[3,4]

Exanthem	Virus; family	Route of transmission	Age group affected and distribution	Morphology	Complications and systemic involvement
Monkeypox and other zoonotic orthopox infections* (cow pox, goat pox, horse pox, sheep pox)	ds-DNA; Poxviridae	Respiratory, fomites, direct contact. Primarily a zoonosis; occasional animal-human and human-human transmission can occur	Variable Centrifugal; predominantly face, extremities; can involve trunk as well.	Monomorphic Large (usually around 1 cm, can range up to 2-2.5 cm) and deep vesiculopustular lesions with early central umbilication and a prominent white rim surrounded by erythematous halo (morphology of individual lesions is similar to orf, which is localized to acral areas). Lesions are usually painful.	Rare, usually in immunocompromised hosts Scarring can occur
Smallpox	ds-DNA; Poxviridae	Droplet spread, respiratory route, fomites	Eradicated Numerous lesions, centrifugal, predominantly face, extremities	Monomorphic Vesiculopustular lesions surrounded by erythematous halo (relatively larger than varicella and herpes)	Scarring, bronchopneumonia, secondary infections
Varicella (chicken pox)	HSV III (VZV) ds DNA virus; Herpesviridae	Droplet spread, respiratory; rarely direct contact	Children and adults Centripetal, trunk, proximal limbs, face, scalp for varicella;	Usually polymorphic, lesions at different stages of evolution present at the same time Clear, round 2- to 4-mm vesicles on an erythematous base; followed by evolution to pustules and crusted lesions. Lesions are usually pruritic. Atypical lesions like papules can be seen in breakthrough varicella in vaccinated patients.	Secondary infections, hemorrhagic transformation, hepatitis, pneumonia, and encephalitis

Disseminated HSV and VZV	HSV I and III (VZV) resp., ds DNA viruses; Herpesviridae	Droplet spread, respiratory for zoster; rarely direct contact; direct contact and fomites for herpes simplex, transplacental in neonates	Variable Uniform distribution	Usually, monomorphic Clear, round 2- to 4-mm vesicles on an erythematous base; are painful, and can lead to monomorphic punched-out erosions.	Hepatitis, pneumonia, and encephalitis
Molluscum contagiosum	ds-DNA; Poxviridae	Human-to-human transmission by close contact including sexual route	Children, young adults, and immunocompromised patients Face and genitalia are common sites but can occur any where	Monomorphic Discrete to confluent umbilicated solid papules at the site of inoculation.	Inflammation and secondary infection. No systemic complications
Hand-foot-mouth disease	Coxsackie-A16 and Enterovirus 71; ssRNA enterovirus	Feco-oral route; followed by human-human transmission from droplets, fomites	Usually, children Oral cavity, palms, soles, and buttocks. Atypical manifestations include truncal and proximal limb involvement with large bullae	Usually, monomorphic Gray, elliptical, 2- to 4-mm vesicles surrounded by erythema; large bullae can sometimes form. Hemorrhagic onychomadesis is commonly observed.	Myocarditis, myositis, pneumonitis

ds DNA, Double-stranded DNA; *HSV*, herpes simplex virus; *VZV*, varicella zoster virus; *ss RNA*, single-stranded RNA.
*Histopathological features in monkeypox depend on the stage of the lesion. The findings range from viral cytopathic changes with ballooning degeneration of basal keratinocytes to full-thickness necrosis of a markedly acanthotic epidermis containing few viable keratinocytes. Inflammation surrounding vascular, eccrine, and follicular structures can be present.

Table II. CDC case definitions for the current monkeypox outbreak in nonendemic* countries[2]

Suspected case

New characteristic rash (as explained in text before) **OR** meets 1 of the epidemiologic criteria and has a high clinical suspicion† for monkeypox

Epidemiological criteria

Within 21 days of illness onset:

- Reports having contact with a person or people with a similar appearing rash or who received a diagnosis of confirmed or probable monkeypox **OR**
- Had close or intimate in-person contact with individuals in a social network experiencing monkeypox activity, this includes men who have sex with men (MSM) who meet partners through an online website, digital application (''app''), or social event (eg, a bar or party) **OR**
- Traveled outside the US to a country with confirmed cases of monkeypox or where Monkeypox virus is endemic **OR**
- Had contact with a dead or live wild animal or exotic pet ie an African endemic species or used a product derived from such animals (eg, game meat, creams, lotions, powders, etc.)

Probable case:

No suspicion of other recent *Orthopoxvirus* exposure (eg, *Vaccinia virus* in ACAM2000 vaccination) *AND* demonstration of the presence of‡

- *Orthopoxvirus* DNA by PCR of a clinical specimen *OR*
- *Orthopoxvirus* using immunohistochemical or electron microscopy testing methods *OR*
- Demonstration of detectable levels of anti-orthopoxvirus IgM antibody during the period of 4 to 56 days after rash onset

Confirmed case

- Demonstration of presence of monkeypox virus DNA by PCR or Next-Generation sequencing of a clinical specimen **OR**
- Isolation of monkeypox virus in culture from a clinical specimen

Exclusion criteria

A case may be excluded as a suspect, probable, or confirmed case if:

- An alternative diagnosis can fully explain the illness **OR**
- An individual with symptoms consistent with monkeypox does not develop a rash within 5 days of illness onset **OR**
- A case where high-quality specimens do not demonstrate the presence of orthopoxvirus or monkeypox virus or antibodies to orthopoxvirus

*Monkeypox endemic countries are Benin, Cameroon, the Central African Republic, the Democratic Republic of the Congo, Gabon, Ghana (identified in animals only), Côte d'Ivoire, Liberia, Nigeria, the Republic of the Congo, and Sierra Leone. Benin and South Sudan have documented importations in the past. Countries currently reporting cases of the West African clade are Cameroon and Nigeria.

†Clinical suspicion can exist if initial signs and symptoms are consistent with illnesses confused with monkeypox (eg, secondary syphilis, herpes, and varicella zoster).

‡Antibody and antigen detection methods are not confirmatory since the orthopox viruses show serological cross-reactivity.

Conflicts of interest

None disclosed.

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