Elsevier has created a Monkeypox Information Center in response to the declared public health emergency of international concern, with free information in English on the monkeypox virus. The Monkeypox Information Center is hosted on Elsevier Connect, the company's public news and information website.

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**Conflicts of interest**

Reid A. Waldman, MD, has served as a subinvestigator on clinical trials sponsored by AbbVie, Eli Lily, Janssen, Regeneron/Sanofi, and Galderma. He has also served as a subinvestigator on the CorEvitas Registry. He received no direct compensation for participation in these trials/registries. He has received direct compensation for participation on an advisory board for Argenx and for participation in marketing materials for Almirall. He is also a shareholder and board member of VeraDermics Inc, a preclinical stage dermatology-focused startup. Kelley L. Sharp, Jonas A. Adalsteinsson, and Jane M. Grant-Kels have no conflicts of interest to declare.

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## Monkeypox: Cutaneous clues to clinical diagnosis

*To the Editor:* Monkeypox, until recently, was considered a rare zoonotic infection of the sub-Saharan West Africa, associated with contact with infected animals such as squirrels, rats, and primates.[1] The monekypox virus belongs to the genus *Orthopox* of the family Poxviridae, alongside other cutaneous viruses including smallpox and cowpox.[1,2] Whilst occasional cases outside of Central and West Africa have been historically reported, it has been a condition largely ignored by the wider medical community.[1,3] The 2022 monkeypox outbreak has led to an increasing awareness of the condition, and a desire amongst clinicians to know when to clinically suspect the disease. Despite increasing concern regarding reports of human-to-human (including sexual) transmission across more than 40 countries globally,[1,3] the risk of monkeypox developing into a new global pandemic is less than the situation with SARS-CoV2 (COVID-19) given the obvious cutaneous manifestations of the disease and the lack of presymptomatic contagious spread.[3]

As dermatologists, we are uniquely skilled to provide expertise in the evaluation of suspected cases of monkeypox through evaluation of cutaneous morphology and clinical exclusion of other differential diagnoses such as varicella and syphilis[4,5] (Table I). This is particularly prudent given that the global monkeypox outbreak remains an evolving situation, with unresolved questions regarding the relative frequency of droplet transmission,[1,3] and limited information regarding mortality rates in high-risk groups such as children, the elderly, and the immunocompromised.[1,3]

A major barrier to clinician education regarding monkeypox, is the current messaging comparing the features of monkeypox to smallpox and primary varicella. Given that it has been over 40 years since

**Table I.** A comparative table of the disease and clinical characteristics of monkeypox, cowpox, varicella, and secondary syphilis. The varied clinical characteristics of the various stages of the monkeypox associated eruption include the papular eruption on an erythematous (almost morbilliform) base with central umbilication, followed by a painful pustular eruption, and resolving through the development of eschar formation. This is in contrast to the clinical features of other differential diagnoses including cowpox, varicella, and secondary syphilis

| Condition | Monkeypox | Cowpox | Primary varicella | Secondary syphilis |
|---|---|---|---|---|
| Causative agent *(Genus)* | Monkeypox virus *(Orthopoxvirus)* | Cowpox virus *(Orthopoxvirus)* | Varicella zoster virus *(Varicellovirus)* | Treponema pallidum *(Treponema)* |
| Incubation period | 5-21 d | 7 d | 14-16 d | 2-8 wk post primary chancre |
| Transmission | Direct contact, droplet, fomites, transplacental | Direct contact | Direct contact, droplet, transplacental | Direct contact, transplacental |
| Contagious period | Symptomatic period only | Symptomatic period only | 2-5 d prior to lesions until 6 d post last crop | Symptomatic period only |
| Morphology | Sequential evolution: macules, papules, vesicles, pustules, eschar. (<10 lesions in 64% cases) | Solitary or limited 5-20 mm diameter. Sequential evolution: macule, papule, haemorrhagic pustule, eschar. | 1-3 mm vesicles on an erythematous background. (presence of lesions in various stages) | Widespread papulosquamous eruption, mucous patches, alopecia, condyloma lata. |
| Lymphadenopathy | Yes (during prodrome) | Yes (with rash) | Yes (with rash) | Yes (with rash) |
| Fever | Yes | Yes | Yes | Yes (with chancre and rash) |
| Myalgia | Yes | Yes | Yes | Yes |
| Lethargy | Yes | Yes | Yes | Yes |
| Complications | Secondary bacterial infection, pneumonia, encephalitis | Disseminated disease in atopic dermatitis, Darier's disease | Secondary bacterial infection, respiratory distress syndrome (Adults) | Multisystem disease, (cardiac, neurological, ophthalmological etc) |
| Mortality | 3.6% (West African clade) | 1%-3% | 1/100,000-21/100,000 cases per y | 5%-58% (Untreated) |

the global eradication of smallpox, the number of practicing clinicians who have seen smallpox (as opposed to rare cases of limited variolation) is rapidly declining. Additionally, routine varicella vaccinations have drastically reduced cases of primary varicella,[5] making this a rarity to younger dermatologists and trainees. Revisiting the commonalities and differentiating features of these conditions (Supplementary Fig 1, available via Mendeley at https://doi.org/10.17632/ypy5f6d8r9.1) is important in raising awareness and encouraging accurate clinical diagnosis in cases of suspected monkeypox.

Monkeypox virus can be spread through direct contact as well as possibly through droplet transmission.[1,3] The prodromal stage may involve fever, malaise, and lymphadenopathy prior to the development of cutaneous lesions. (Table I, Supplementary Fig 1). Along with cowpox[2] and varicella,[5] cutaneous lesions of monkeypox present as erythematous macules, progressing to umbilicated papules, painful vesicles, and pustules, followed by firm indurated eschar during the period of resolution (Supplementary Fig 1).[1,3] Initial lesions occur at sites of direct contact, however, more disseminated lesions can occur during the course of the illness.

The main differentiating features of monkeypox as opposed to other viral infections under consideration, is the monomorphic progression of lesions in distinct anatomical areas. In acral sites, all lesions will progress through papular, pustular, or eschar stages in synchrony, as opposed to primary varicella where various stages of lesion are interspersed[1,3] and molluscum contagiosum in which morphological progression of lesions will not occur. Monkeypox often presents with less than 10 distinct umbilicated lesions (in 64% cases)[2] which may aid in diagnosis when combined with history and lesion evolution. An additional differentiating feature is the presence of lymphadenopathy in the prodromal stage of the disease. This may be a useful feature for evaluation of close contacts; however, lymphadenopathy is present during the eruptive stages of a number of differential

conditions which is why such a feature should not be relied upon in isolation. Secondary syphilis,[4] when rapidly following the initial chancre, may present in a similar fashion to monkeypox and should be a differential diagnosis under consideration.

The current monkeypox outbreak is an evolving situation; however, a deeper understanding of the comparative morphological and temporal order of features should allow for a degree of clinical diagnosis to be undertaken by the astute dermatologist.

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**Conflicts of interest**

JWF has conducted advisory work for Janssen, Boehringer-Ingelheim, Pfizer, Kyowa Kirin, LEO Pharma, Regeneron, Chemocentryx, Abbvie, Azora, Novartis and UCB, participated in trials for Pfizer, UCB, Boehringer-Ingelheim, Eli Lilly, CSL, Azora and received research support from Ortho Dermatologics, Sun Pharma, LEO Pharma, UCB and La Roche Posay.

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## Treatment of dermatofibrosarcoma protuberans with Mohs micrographic surgery is associated with lower odds of postoperative radiotherapy compared to wide local excision

*To the Editor:* Dermatofibrosarcoma protuberans (DFSP) is a locally aggressive cutaneous sarcoma that is principally treated with Mohs micrographic surgery (MMS) or wide local excision (WLE). For recurrent or persistent disease that becomes unresectable, radiotherapy (RT) or chemotherapy is recommended.[1] However, there is significant morbidity, including pain, fibrosis, lymphedema, and secondary malignancies, associated with RT.[2] This study sought to investigate the likelihood of receiving RT after the treatment of DFSP with MMS versus that of receiving RT after treatment with WLE.

We identified DFSP cases using the International Classification of Diseases for Oncology, Third Edition (ICD-O-3) 0-3 codes 8832 and 8833 in the National Cancer Database, the largest oncology database worldwide, which comprises >70% of all reported cancer diagnoses in the United States.[3] Patients with prior or multiple cancer diagnoses were excluded. Clinicodemographic information was extracted for primary cases diagnosed between 2004 and 2017 that received treatment at the reporting facility, were diagnosed after the facility's reference date, and reported at a follow-up time of >0 months. Missing data were imputed using multiple imputation by chained equations with 30 imputations. In each imputed dataset, MMS and WLE cases were matched using 1:1 nearest neighbor propensity score matching to account for baseline covariate differences, with propensity scores estimating the probability of treatment with MMS. The odds ratio (OR) of RT comparing MMS and WLE was calculated using logistic regression in each imputed dataset, and the estimates were combined using Rubin rules.

Seven hundred sixteen DFSP cases were treated with MMS, and 3242 cases were treated with WLE (Supplementary Table I, available via Mendeley at https://data.mendeley.com/datasets/6jwcsr2s2j/2). The MMS and WLE cohorts received postoperative RT in 2.9% and 7.3% of the cases, respectively