








## Concise Communication

# Antibiotic prescribing patterns for bacterial superinfection of mpox: A retrospective cohort study in an urban center

William F. Simmons MD<sup>1</sup> , Jeannie D. Chan PharmD, MPH<sup>1,2</sup>, Jehan Z. Budak MD<sup>1</sup> , Shireesha Dhanireddy MD<sup>1</sup> , Margaret L. Green MD<sup>1</sup>, Rupali Jain PharmD<sup>1,2</sup> , Santiago Neme MD<sup>1</sup> , Krista Rietberg MPH<sup>3</sup> , Alison C. Roxby MD<sup>1</sup>, John B. Lynch MD, MPH<sup>1</sup>  and Chloe Bryson-Cahn MD<sup>1</sup>

<sup>1</sup>Division of Allergy & Infectious Diseases, Department of Medicine, School of Medicine, University of Washington, Seattle, Washington, <sup>2</sup>Department of Pharmacy and School of Pharmacy, University of Washington Seattle, Washington and <sup>3</sup>Infection Prevention and Control, Harborview Medical Center, Seattle, Washington

## Abstract

Bacterial superinfection and antibiotic prescribing in the setting of the current mpox outbreak are not well described in the literature. This retrospective observational study revealed low prevalence (11%) of outpatient antibiotic prescribing for bacterial superinfection of mpox lesions; at least 3 prescriptions (23%) were unnecessary.

(Received 8 February 2023; accepted 22 March 2023)

Human mpox, a zoonosis caused by the monkeypox virus, previously caused sporadic outbreaks originating in Africa with occasional travel-related spread. In 2022, a global outbreak drove significant spread outside endemic areas, with transmission among sexual partners.

The current outbreak has primarily affected men who have sex with men and people with human immunodeficiency virus (HIV).<sup>1–5</sup> Unlike the classic cutaneous rash, many patients presented with oral or anogenital lesions. Mpox lesions are frequently vesiculopustular in nature, and bacterial skin and soft-tissue infection (SSTI) is often in the differential diagnosis.<sup>3,5</sup>

Several cases of bacterial superinfection of mpox lesions have been reported in this outbreak, but most case series only captured hospitalized patients with SSTI prevalence ranging from 3% to 11%.<sup>1–6</sup> These rates are lower than those reported in previous outbreaks in endemic regions, where bacterial superinfection ranged from 19% to 47%.<sup>7,8</sup> We conducted a retrospective chart review to assess secondary bacterial infection and antibiotic prescribing among patients with mpox.

## Methods

In this retrospective observational study, we reviewed the charts of all patients with mpox (defined as positive polymerase chain reaction [PCR] or tecovirimat prescription) seen at University of Washington Medicine between July 1, 2022, and August 31, 2022. UW Medicine includes a quaternary medical center, an urban safety-net hospital, a secondary inpatient facility, 3 emergency departments, and a network of clinics. Study data were collected

using REDCap electronic data capture.<sup>9</sup> The University of Washington Institutional Review Board approved the study and waived informed consent (no. STUDY00016342).

Clinical data included age, race, ethnicity, sex, microbiologic data, antibiotic prescriptions, and clinical outcomes. Data from other healthcare systems were obtained through linked electronic medical records. Risk factors for severe disease or lesions in anatomical areas constituting a special hazard were categorized based on US Centers for Disease Control and Prevention (CDC) guidance.

Antibiotic prescribing data was collected in the 2 weeks preceding and 4 weeks following mpox diagnosis (or tecovirimat prescription if results unavailable). Bacterial superinfection was defined as SSTI that was possibly associated with mpox lesions and treated with antibiotics. Sexually transmitted infection (STI) test results, location of possible bacterial infection, and infection collocation with mpox lesions were extracted.

The appropriateness of antibiotics for SSTI was determined by independent chart review by 2 investigators (W.S. and C.B.C.); a third investigator (J.B.L.) adjudicated discordant determinations. If the provider indicated clinical suspicion for bacterial superinfection or clinical reasoning was unavailable, the prescription was categorized as appropriate. If the provider indicated clinical findings as most consistent with mpox, or antibiotics were stopped once mpox was diagnosed, antibiotics were deemed inappropriate.

## Results

We identified 184 patients with mpox. However, 63 of these patients were excluded: 21 patients were identified from our center being the regional source for tecovirimat but were not cared for in our health system; 42 patients had insufficient data. Demographic and clinical data for included patients are listed in Table 1. Among

**Corresponding author:** William F. Simmons; Email: [william.simmons@ucsf.edu](mailto:william.simmons@ucsf.edu)

**Cite this article:** Simmons WF, Chan JD, Budak JZ, *et al.* Antibiotic prescribing patterns for bacterial superinfection of mpox: A retrospective cohort study in an urban center. *Antimicrob Steward Healthc Epidemiol* 2023. doi: [10.1017/ash.2023.158](https://doi.org/10.1017/ash.2023.158)

**Table 1.** Demographic and Clinical Characteristics of Participants

| Characteristic   | Participants<br>(n = 121),<br>No. (%) <sup>a</sup> |
|--|--|
| Age, y (range)   | 37 (21–62)   |
| <b>Sex</b>   |  |
| Male   | 120 (99)   |
| Female   | 1 (1)  |
| <b>Race</b>  |  |
| White  | 77 (64)  |
| Black  | 13 (11)  |
| >1 race  | 5 (4)  |
| American Indian/Alaska Native                                  | 4 (3)  |
| Asian  | 3 (2)  |
| Native Hawaiian or Other Pacific Islander                      | 2 (2)  |
| Unavailable or declined  | 17 (14)  |
| <b>Ethnicity</b>   |  |
| Hispanic or Latino   | 37 (31)  |
| Not Hispanic or Latino   | 74 (61)  |
| Unavailable or declined  | 10 (8)   |
| <b>Risk factors for severe disease</b>                         |  |
| Well controlled HIV (CD4>200 and VL<200)                       | 71 (59)  |
| Poorly controlled HIV (CD4<200 or VL>200)                      | 10 (8)   |
| Immunocompromise (non-HIV)                                     | 3 (2)  |
| Atopic dermatitis  | 1 (1)  |
| Other exfoliative skin conditions                              | 5 (4)  |
| <b>Lesions in areas that might constitute a special hazard</b> |  |
| Anal/rectal/genital alone                                      | 74 (61)  |
| Oral alone   | 10 (8)   |
| Ocular alone   | 1 (1)  |
| Oral and anal/rectal/genital                                   | 11 (9)   |
| Ocular and anal/rectal/genital                                 | 1 (1)  |
| Prescribed tecovirimat   | 112 (93)   |
| Required hospitalization                                       | 6 (5)  |

Note. HIV, human immunodeficiency virus; CD4, T-lymphocyte; VL, viral load.  
<sup>a</sup>Units unless otherwise indicated.

the 6 patients who required hospitalization; 3 patients had dysphagia or pharyngitis, 1 patient had knee effusion, 1 patient had significant perineal edema, and 1 patient had facial edema.

Moreover, 13 patients (11%) received antibiotics for presumed bacterial SSTI potentially associated with mpox lesions (Table 2). SSTI antibiotics were deemed inappropriate in 3 patients (23%). Also, 10 patients (77%) were started on SSTI antibiotics at the time of or prior to mpox testing, whereas 2 patients (15%) were prescribed systemic antibiotics and 1 patient (7%) was prescribed topical antibiotics after mpox diagnosis.

Five other patients were initially treated with antibiotics for bacterial pharyngitis: 3 with a positive rapid strep, 1 patient despite a negative rapid strep, and 1 patient empirically. One was tested for mpox at initial presentation, but the mpox diagnoses of the other 4 patients were delayed until new lesions led to re-evaluation.

In total, 26 patients (21%) were prescribed antibiotics for STIs. Overall, 22 patients received ceftriaxone, and 22 patients received doxycycline; 18 of these patients received both antibiotics. In 81% of patients treated for STI testing, either results returned negative after antibiotics were prescribed or testing was never performed.

Other antibiotic prescriptions in 1 patient each were for abscess associated with a site of drug injection, urinary tract infection, antibiotic eye drops after injury, and prophylaxis.

## Discussion

Antibiotic prescribing for bacterial SSTI was uncommon during mpox infection (11%), and at least 23% of prescribed antibiotics were unnecessary using a conservative definition of inappropriateness. Other series have reported similarly low prevalence of bacterial superinfection, though predominantly in hospitalized patients.<sup>2–6</sup> Our data represent the largest comprehensive series of antibiotic prescribing for SSTI in mpox.

Approximately 77% of antibiotic prescriptions for SSTI were initiated for empiric treatment of lesions, before mpox testing results were available. All unnecessary prescriptions were empiric. This phenomenon has not been described previously and may be due to clinical overlap between SSTI and mpox. Conversely, only 2 patients in our cohort were prescribed systemic antibiotics after mpox test results were available, suggesting knowledge of mpox diagnosis helped limit unnecessary antibiotic prescribing. Despite this, only 2 patients had antibiotics discontinued once testing results were available. The rarity of re-presentation with SSTI after mpox diagnosis suggests that bacterial superinfection is rare. Rapidly available testing may reduce unnecessary antibiotic prescribing for this viral infection.

Unusual clinical manifestations likely triggered antibiotic prescription. Several patients were started on antibiotics due to atypical mpox lesions, particularly ulcerated lesions. Also, 2 patients presented with fluid collections that were treated as bacterial (knee effusion and perirectal collection). When the knee was sampled, bacterial cultures were negative, whereas monkeypox PCR was positive.

Atypical symptoms delayed mpox diagnosis, resulting in unnecessary antibiotics. Of 5 patients initially treated for bacterial pharyngitis, only 1 patient was simultaneously tested for mpox. The 4 remaining patients were only diagnosed after development of new lesions. Providers should be aware that oral symptoms in patients with sexual exposure could represent mpox and that a low barrier to testing may reduce delayed diagnosis and unnecessary antibiotics.

The CDC recently warned that widespread use of tecovirimat could promote resistance and that clinicians should reserve treatment for patients with severe presentations.<sup>10</sup> If tecovirimat for mild-to-moderate infections is no longer available, clinicians may prescribe antibiotics as an alternative. Our finding of low prevalence of bacterial infection supports stewardship efforts to withhold unnecessary antibiotics.

Our study also captured antibiotic prescribing around STI. Most STI treatment courses in our study (81%) were empiric. Mpox/STI coinfection rates varied between studies (17%–76%), and knowledge of local trends inform the need for empiric STI courses.<sup>1–3,5</sup>

Our study had several limitations. Antibiotic prescriptions as a proxy for bacterial superinfection may not accurately estimate true prevalence. Also, 63 patients were excluded due to insufficient data, which, along with a low absolute number of prescriptions,

**Table 2.** Clinical Information of Patients Treated With Antibiotics for Suspected Bacterial Skin/Soft-Tissue Infection of Mpox Lesions

| Age, y | Risk Factors for Severe Disease                            | High Risk Lesions | Admitted          | Mpox diagnosis to Antibiotic Treatment, Days | Antibiotic Prescribed             | Location of SSTI   | Clinical Features of Interest                                       | Antibiotic Appropriateness |
|--------|--|-------------------|-------------------|--|-----------------------------------|--------------------|---|----------------------------|
| 40     | None   | AG                |                   | 0  | Amoxicillin-clavulanate           | Genital            | Erythema of penile lesion   | Appropriate                |
| 23     | HIV, controlled; other exfoliative, other immunocompromise | AG                | Y: perineal edema | 0  | Cephalexin                        | Genital            | Soft tissue swelling in groin                                       | Appropriate                |
| 40     | HIV, controlled  | AG                |                   | 0  | Ciprofloxacin + metronidazole     | Perirectal         | Perirectal collection on CT, treated empirically                    | Appropriate                |
| 43     | HIV, controlled  | AG                |                   | -3   | Doxycycline                       | Rectal + Extremity | Empiric treatment prior to mpox diagnosis, limited documentation    | Appropriate                |
| 56     | None   | O                 |                   | 0  | TMP/SMX + cephalexin              | Oral               | Empiric treatment, mpox felt most likely                            | Inappropriate              |
| 22     | None   | O                 |                   | 0  | TMP/SMX + cephalexin              | Face               | Empiric treatment, treating associated thrombophlebitis and lesions | Appropriate                |
| 27     | None   | O                 |                   | 0  | Clindamycin >TMP/SMX + cephalexin | Oral               | Empiric treatment, ABX stopped once mpox diagnosed                  | Inappropriate              |
| 34     | HIV uncontrolled   | O, AG             | Y: facial edema   | 2  | TMP/SMX + cephalexin              | Face               | Honey-crusting of lip lesion  | Appropriate                |
| 32     | HIV uncontrolled   | O, AG             | Y: pharyngitis    | 0  | Amoxicillin-clavulanate           | Face               | Facial swelling   | Appropriate                |
| 36     | HIV, controlled  |                   |                   | 6  | Mupirocin                         | Face               | Facial pustule  | Appropriate                |
| 39     | HIV, controlled  |                   |                   | 8  | TMP/SMX + cephalexin              | Groin              | Groin erythema at mpox lesion                                       | Appropriate                |
| 48     | HIV, controlled  |                   | Y: septic knee    | 0  | TMP/SMX + cephalexin              | Extremity          | Knee effusion: mpox positive, culture negative                      | Appropriate                |
| 38     | HIV, controlled  |                   |                   | 0  | Levofloxacin + doxycycline        | Face               | Empiric treatment, ABX stopped once mpox diagnosed                  | Inappropriate              |

Note. ABX, antibiotics; SSTI, bacterial skin and soft-tissue infection; TM-SMX, trimethoprim/sulfamethoxazole; O, oral lesions; AG, anogenital lesions; HIV, human immunodeficiency virus; CT, computed tomography.

may have introduced systematic bias. Some patients with bacterial superinfection may have presented to outside providers. We mitigated this through linked medical records, which include most systems in the region. Prescriptions without available clinical reasoning were deemed appropriate, potentially overestimating appropriateness. A high proportion of patients were treated with tecovirimat compared to prior case series.<sup>3</sup> Tecovirimat could have accelerated resolution of lesions, limiting bacterial infection, or the availability of tecovirimat may have reduced a provider's impulse to prescribe antibiotics.

In this study, antibiotic treatment for bacterial SSTI in patients with mpox was uncommon. True bacterial superinfection was rare, and antibiotic treatment for bacterial superinfection was inappropriate in some cases. Antibiotics were frequently prescribed empirically due to diagnostic uncertainty, highlighting the importance of available rapid diagnostic testing. Mpox represents another opportunity for antimicrobial stewardship in the setting of viral infection.

#### Acknowledgments.

**Financial support.** This work was supported by the National Institute of Allergy and Infectious Diseases of the National Institutes of Health (grant no. 5T32AI007044 to W.S.). The content is solely the responsibility of the authors

and does not necessarily represent the official views of the National Institute of Health.

**Competing interests.** R.J. serves as a clinical consultant for Wolters-Kluwer for their online content. All other authors report no conflicts related to this article.

#### References

- Català A, Clavo-Escribano P, Riera-Monroig J, *et al.* Monkeypox outbreak in Spain: clinical and epidemiological findings in a prospective cross-sectional study of 185 cases. *Br J Dermatol* 2022;187:765–772.
- Patel A, Bilinska J, Tam JCH, *et al.* Clinical features and novel presentations of human monkeypox in a central London centre during the 2022 outbreak: descriptive case series. *BMJ* 2022;378:e072410.
- Thornhill JP, Barkati S, Walmsley S, *et al.* Monkeypox virus infection in humans across 16 countries—April–June 2022. *N Engl J Med* 2022; 387:679–691.
- Girometti N, Byrne R, Bracchi M, *et al.* Demographic and clinical characteristics of confirmed human monkeypox virus cases in individuals attending a sexual health centre in London, UK: an observational analysis. *Lancet Infect Dis* 2022;22:1321–1328.
- Tarín-Vicente EJ, Alemany A, Agud-Dios M, *et al.* Clinical presentation and virological assessment of confirmed human monkeypox virus cases in Spain: a prospective observational cohort study. *Lancet* 2022;400:661–669.

6. Hammerschlag Y, MacLeod G, Papadakis G, *et al*. Monkeypox infection presenting as genital rash, Australia, May 2022. *Euro Surveill* 2022;27:2200411.
7. Ogoina D, Iroezindu M, James HI, *et al*. Clinical course and outcome of human monkeypox in Nigeria. *Clin Infect Dis* 2020;71:e210–e214.
8. Ježek Z, Szczeniowski M, Paluku KM, Mutombo M. Human monkeypox: clinical features of 282 patients. *J Infect Dis* 1987;156:293–298.
9. Harris PA, Taylor R, Minor BL, *et al*. The REDCap consortium: building an international community of software platform partners. *J Biomed Inform* 2019;95:103208.
10. Guidance for tecovirimat use. Centers for Disease Control and Prevention website. <https://www.cdc.gov/poxvirus/monkeypox/clinicians/Tecovirimat.html>. Published September 15, 2022. Accessed November 6, 2022.