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Letter to editor

When a neglected tropical disease goes global: early estimates from the Monkeypox outbreak, the first 1,054 cases

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To the Editor,

Monkeypox virus (MPXV), genus *Orthopoxvirus,* is a large double-stranded DNA virus (200-250 nm), that is evolutionarily related to human variola virus (VARV) (1), and causes a clinical syndrome quite similar to smallpox, with a generally less severe outcome (1,2).

MPXV has a wide range of hosts and reservoirs in wild animals, and since 1970 has been commonly acknowledged as a human pathogen, endemic to Central and Western African countries through two distinctive clades (2,3). Central African clade (CAC) is responsible of the majority of 20,000 incident cases of the last decade, with a case-fatality-ratio of 7-10%, compared to < 4% for Western African clade (WAC) (4).

In 2003, the importation of infected pests (*Cynomys* spp, i.e. "prairie dogs") to United Stated resulted in the first MPXV-WAC outbreak out of Africa, involving a total of 81 human cases, with no documented deaths (5). In the next decade, the spreading of the MPVX-WAC to Nigeria, has then resulted in multiple travel-related cases in non-endemic countries (4,6).

Since May 7th, 2022, an unprecedented outbreak of MPXV-WAC infections with around 1,051 documented cases (Table 1) is occurring across Europe (89.7% of cases), Americas (10.7%), and Australia (0.6%), mostly occurring in subjects with no established travel link to endemic areas (7–13).

Reported cases are mostly characterized by mild clinical features (Table 2) (7,9,10,12,13), with no deaths and some specificities. First of all, skin lesions are inconsistently pronounced in number, size and density, being possibly confounded with chickenpox (7,13). Similarly, cervical lymphadenopathy, previously acknowledged as a nearly constant clinical sign, has been reported by less than 20% of incident cases (7,9,13), with an increased prevalence of inguinal lymph node involvement (35.3% to 48.1%) (7,9,13), anal and genital ulcers (18.5% to 57%) (9,10,13).

As some cases have been initially reported in men having sex with men (9,14), with a relatively high prevalence of HIV seropositivity (9,10), reporting risky sexual behaviors and multiple sexual partners (9,10,12), and having a documented epidemiologic link with high-risk settings in Madrid and Lisbon areas, and mass gatherings in Antwerp (Belgium), and Gran Canaria (Canary Islands, Spain) (8,9,12,14), such specificities have been initially explained through a presumptive sextually-related transmission. However, labelling the current outbreak as a sort of "gay" disease is not only improper and discriminating, but also scientifically inaccurate (9). First, most of reported cases remain outside a clear and well-defined chain of transmission (9,10,12). Second, the earliest symptom onset clearly ranged between April 20th and April 29th, anticipating all of the aforementioned mass gatherings (9,12). Third, 3 of recent US cases were linked to travel-associated cases from Nigeria reported in 2018 and 2019 (15). In other words, the current MPXV-WAC outbreak has been introduced in Western Hemisphere by several, distinctive episodes that have largely anticipated the initial hypotheses. As its containment of appears, to date, particularly difficult to achieve MPXV-WAC could profit of this outbreak

Table 1. Current estimates of Monkeypox Virus positive cases associated with the international outbreak of 2022 (June 7th, 2022).

Country	No. of cases (/1054, %)
Europe	
United Kingdom	302, 28.7%
Spain	198, 18.8%
Portugal	153, 14.6%
Germany	80, 7.6%
France	66, 6.3%
Netherlands	40, 3.8%
Italy	20, 1.9%
Belgium	17, 1.6%
Switzerland	8, 0.8%
Czech Republic	6, 0.6%
Ireland	6, 0.6%
Slovenia	6, 0.6%
Sweden	5, 0.5%
Denmark	3, 0.3%
Finland	2, 0.2%
Latvia	2, 0.2%
Austria	1, 0.1%
Hungary	1, 0.1%
Malta	1, 0.1%
Norway	1, 0.1%
Gibraltar	1, 0.1%
North America	
Canada	80, 7.6%
USA	30, 2.9%
Central and South America	
Mexico	2, 0.2%
Argentina	2, 0.2%
Middle East and North Africa	
United Arab Emirates	8, 0.8%
Israel	2, 0.2%
Morocco	1, 0.1%
East Asia	
Thailand	1, 0.1%
Oceania	
Australia	6, 0.6%

Note: data were retrieved by June 7th, 2022 from the following data source: CDC Monkeypox summary overview (https://www.cdc.gov/poxvirus/monkeypox/response/2022/index.html); ECDC Situation Update on Monkeypox outbreak (https://www.ecdc.europa.eu/en/monkeypox-outbreak); Robert Koch Institut Situation Update on Monkeypox outbreak in Germany (https://www.rki.de/DE/Content/InfAZ/A/Affenpocken/Ausbruch-2022-Situation-Deutschland.html;jsessionid=092ABC91B05FA416BE0F07EFBA70F572.internet061?nn=2386228); Santé Publique France Situation Update on Monkeypox outbreak in France (https://www.santepubliquefrance.fr/les-actualites/2022/cas-de-monkeypox-point-de-situation-au-7-juin-2022).

Table 2. Summary of main clinical features reported at any point during the course of the clinical syndrome, among the available case series (7,9,10,12,13).

Authors	No. of cases	Hospitalizations	Country	Female Sex	HIV positive	Rash	Lymph node involvement, cervical	Lymph node involvement, inguinal	Genital ulcers	Anal ulcers
Adler et al. (7)	7	7, 100%	United Kingdom	3, 42.9%	0, -	7, 100%	1, 14.3%	-	4, 57.1%	4, 57.1%
Antinori et al. (10)	4	N.A.	Italy	0, -	2, 50%	1, 25.0%	N.A.	N.A.	2, 50.0%	2, 50.0%
Perez Duque et al. (9)	27	3, 11.1%	Portugal	0, -	14, 51.9%	14, 51.9%	4, 14.8%	13, 48.1%	5, 18.5%	5, 18.5%
Minhaj et al. (13)	17	N.A.	United States	N.A.	N.A.	17, 100%	3, 17.6%	6, 35.3%	4, 23.5%	6, 35.3%
Vivancos et al. (12)	89	N.A.	United Kingdom	0, -	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.

to eventually evolve into a global pathogen (3,14), corroborating a decade of disregarded warning from International Health authorities (2,3).

Conflict of Interest: The author declares that he or has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

References

1. McCollum AM, Damon IK. Human monkeypox. Clin Infect Dis 2014; 58: 260–267. doi: 10.1093/cid/cit703
2. Petersen E, Kantele A, Koopmans M, et al. Human Monkeypox: Epidemiologic and Clinical Characteristics, Diagnosis, and Prevention. Infect Dis Clin North Am 2019; 33: 1027–1043. doi: 10.1016/j.idc.2019.03.001
3. Rezza G. Emergence of Human Monkeypox in West Africa. Lancet Infect Dis 2019; 19: 797–799. doi: 10.1016/S1473-3099(19)30281-6
4. Bunge EM, Hoet B, Chen L, et al. The changing epidemiology of human monkeypox—A potential threat? A systematic review. PLoS Neglect Trop Dis 2022; 16: e0010141. doi: 10.1371/journal.pntd.0010141
5. Sejvar JJ, Chowdary Y, Schomogyi M, et al. Human Monkeypox Infection: A Family Cluster in the Midwestern United States. J Infect Dis 2004; 190: 1833–1840. doi: 10.1086/425039
6. Rao AK, Schulte J, Chen TH, et al. Monkeypox in a Traveler Returning from Nigeria — Dallas, Texas, July 2021. MMWR Morb Mortal Wkly Rev 2022; 71: 509–516 doi: 10.15585/mmwr.mm7114a1
7. Adler H, Gould S, Hine P, et al. Clinical features and management of human monkeypox: a retrospective observational study in the UK. Lancet Infect Dis 2022; S1473-3099(22)00228-6 doi: 10.1016/S1473-3099(22)00228-6
8. Hammerschlag Y, MacLeod G, Papadakis G, et al. Monkeypox infection presenting as genital rash, Australia, May 2022. Euro Surveill. 2022; 27: pii=2200411. doi: 10.2807/1560-7917.ES.2022.27.22.2200411
9. Perez Duque M, Ribeiro S, Vieira Martins J, et al. Ongoing monkeypox virus outbreak, Portugal, 29 April to 23 May 2022. Euro Surveill 2022; 27: pii=2200424. doi: 10.2807/1560-7917.ES.2022.27.22.2200424
10. Antinori A, Mazzotta V, Vita S, et al. Epidemiological, clinical and virological characteristics of four cases of monkeypox support transmission through sexual contact, Italy, May 2022. Euro Surveill 2022; 27: pii=2200421. doi: 10.2807/1560-7917.ES.2022.27.22.2200421.
11. Bragazzi NL, Khamisy-Farah R, et al. Attaching a stigma to the LGBTQI+ community should be avoided during the monkeypox epidemic. J Med Virol. 2022; online ahead of print. doi: 10.1002/jmv.27913
12. Vivancos R, Anderson C, Blomquist P, et al. Community transmission of monkeypox in the United Kingdom. Euro Surveill 2022; 27: pii=2200422. doi: 10.2807/1560-7917.ES.2022.27.22.2200422
13. Minhaj FS, Ogale YP, Whitehill F, et al. Monkeypox Outbreak-Nine States, May 2022. MMWR Morb Mortal Wkly Rev 2022;71:epub ahead of print 10.15585/mmwr.mm7123e1.
14. European Centre for Disease Prevention (ECDC). Monkeypox multi-country outbreak Key messages. ECDC Stockholm; 2022 May. Available from: https://www.ecdc.europa.eu/sites/default/files/documents/Monkeypox-multi-country-outbreak.pdf accessed on June 7, 2022

15. O'toole Á, Rambaut A. Update to observations about putative APOBEC3 deaminase editing in the light of new genomes from USA. The Virological. 2022. Available from: https://virological.org/t/update-to-observations-about-putative-apobec3-deaminase-editing-in-the-light-of-new-genomes-from-usa/847/print Accessed on June 7, 2022

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