### ORIGINAL ARTICLE

# Clinical characteristics of monkeypox virus infections among men with and without HIV: A large outbreak cohort in Germany

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#### **Abstract**

Background: Since May 2022, increasing numbers of monkeypox virus (MPXV) infections have been reported from across Europe and North America. Studies, mainly from Africa, have suggested a higher risk for severe MPXV cases in people living with HIV.

Methods: This was a retrospective study of all confirmed MPXV infections observed in the participating centres since 19 May 2022. We conducted a chart review to evaluate clinical characteristics, comorbidities, and coinfections, including HIV, viral hepatitis, and sexually transmitted infections (STIs).

Results: By 30 June 2022, a total of 546 MPXV infections were reported from 42 German centres. All patients were men who have sex with men (MSM), of whom 256 (46.9%) were living with HIV, mostly with a preserved immune system and with viral suppression. In total, 232 (42.5%) MSM were also taking HIV pre-exposure prophylaxis (PrEP) and 58 (10.6%) MSM had no known HIV infection or PrEP use. The median age was 39 years (range 20-67), and comorbidities were rare. However, 52.4% and 29.4% of all patients had been diagnosed with at least one STI within the last 6 months or within the last 4 weeks, respectively. The most frequent localizations of MPXV infection were

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genital (49.9%) and anal (47.9%), whereas fever (53.2%) and lymphadenopathy (42.6%) were the most frequent general symptoms. The hospitalization rate was low (4.0%), and no fatal course was observed. The clinical picture showed no apparent differences between MSM with or without HIV.

**Conclusions:** In this preliminary cohort analysis from a current large outbreak among MSM in Germany, the clinical picture of MPXV infection did not differ between MSM with and without HIV infection. Severe courses were rare and hospitalization rates were low. However, most patients were relatively healthy, and only a few people living with HIV were viremic or severely immunosuppressed.

#### **KEYWORDS**

lymphadenopathy, monkeypox, MPXV infection

### INTRODUCTION

Monkeypox virus (MPXV) belongs to the orthopoxvirus genus, which also includes variola virus (which causes smallpox), vaccinia virus (used in the smallpox vaccine), and cowpox virus. The first human case of MPXV infection was observed in 1970 in a 9-year-old boy in the Democratic Republic of Congo [1]. Since then, sporadic outbreaks outside Central and West African countries have been limited to a few cases in recent years and were based on zoonotic transmission or exported cases from endemic countries [2]. In 2022, this changed dramatically. Since 7 May 2022, when the UK Department of Health reported an initial case in a traveller returning from Nigeria, unusually high and increasing numbers of cases are now being reported across Europe and other regions. Initial publications suggest that, to date, the disease has almost exclusively affected men who have sex with men (MSM) [3-5]. In Munich, Germany, the first case was published on 20 May 2022 [6]. By 17 June 2022, 338 confirmed cases were known to the Robert Koch Institute; 1 week later, the number had doubled to 676, making Germany one of the most affected countries worldwide [7].

Person-to-person transmission of MPXV mainly occurs through close physical contact. The reasons for the current increase in case numbers are still unclear, and questions remain about the dynamics of transmission. Preliminary genome sequence data suggest a close relationship with the MPXV clade circulating in West Africa [8, 9]. It has been suggested that this clade may cause milder disease and have a lower mortality than the clade first described in Central Africa [10, 11]. However, a 2017–2018 Nigerian outbreak was associated with a case fatality rate of 6%. Four of the seven patients who died had concomitant HIV/AIDS, suggesting a need to further explore the potential connection between the two diseases [12]. Little is known about other

risk factors for severe courses, but children and pregnant women are probably at increased risk [13, 14]. The aim of the present work was to compare the clinical picture in patients with MPXV with or without HIV.

### **METHODS**

The German AIDS Society and the German Association of Outpatient Physicians for Infectious Diseases and HIV Medicine invited registered centres to take part and sent an anonymized questionnaire to all care centres that expressed interest in participating. Centres were asked to, if possible, retrospectively document all confirmed cases from 19 May 2022 to 30 June 2022. The questionnaire included demographics (age, sex, nation, ethnicity) and comorbidities, including HIV infection (with current CD4 cell counts and HIV RNA copies/ml) or current use of HIV pre-exposure prophylaxis (PrEP). Previous or current viral hepatitis B and C were also documented, as were sexually transmitted infections (STIs) in the past 6 months. Data collected were as follows: date of confirmed diagnosis of MPXV infection, probable country of infection, symptom onset, location and number of lesions, previous smallpox vaccinations, and severity of monkeypox disease, including the number of lesions (categorized) and possible general symptoms such as fever, head/limb pain, night sweats, and lymph node swelling. Possible specific therapies and any current hospitalizations (with the main reason) were also evaluated. All diagnostic procedures, including MPXV polymerase chain reaction (PCR) were performed in the local laboratories of the participating centres and/or in the reference laboratory of the German national Robert Koch Institute, Berlin, Germany. The study was submitted to the Ethics Committee of the Technical University of Munich for

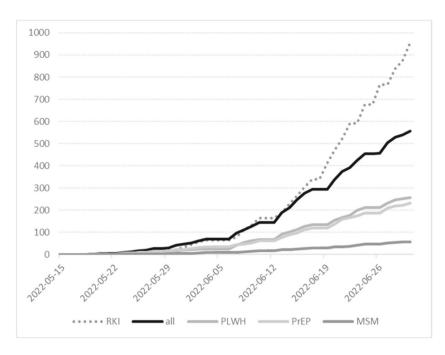


FIGURE 1 Cumulative monkeypox virus case numbers. The dashed line represents total cases in Germany as reported by the Robert Koch Institute (RKI). The solid black line represents all patients included in this cohort. Grey lines represent people living with HIV (PLWH), pre-exposure prophylaxis (PrEP) users, and men who have sex with men (MSM) without HIV or PrEP, time of diagnosis (first positive swab)

consultation prior to initiation, in accordance with Section 67 [6] AMG (reference number 2022-338-S-NP).

This preliminary investigation used only descriptive statistics, including frequency distribution for categorical variables, 95% binomial confidence intervals (CIs) for binary variables, and median, minimum, and maximum values for continuous variables.

### RESULTS

By 30 June 2022, 42 centres from 17 German cities had reported a total of 546 PCR-confirmed MPXV cases. More than half of them were from Berlin, the capital city (303 [55.5%] cases from 14 centres), followed by Cologne (64 [11.7%] cases) and Hamburg (60 [11.0%] cases from two centres each). The vast majority (410 [75.1%]) of cases probably acquired the MPXV infection in Germany. A total of 39 patients (7.1%) acquired the infection in Spain, most of them in Gran Canaria. Many of these cases were observed at the beginning of the outbreak; 14 of the 35 (40%) cases diagnosed by 30 May 2022 reported Spain as the probable country of infection. Other countries reporting multiple infections were Belgium and Portugal, with four cases each, and the UK, with three cases.

All patients were MSM, among them, 256 (46.9%) were living with HIV (including one subject who reported having only sexual contact with an unknown

female sex worker). The vast majority of the people living with HIV had a normal immune status, with a median CD4 T-cell count of 691/ $\mu$ l (range 185–1603). Only 17.2% (42/244) and 2.9% (7/244) had a CD4 T-cell count of <500 and <350/ $\mu$ l, respectively. In total, 4.2% (10/236) of the patients were viremic for HIV at last measurement, with an HIV RNA >50 copies/ml, including only four of ten with HIV RNA >200 copies/ml. In the patient with the highest viral load, HIV infection was diagnosed at the time of the current MPXV infection.

The second largest affected group was MSM without HIV infection currently using PrEP (232 [42.5%]). The remaining 58 cases (10.6%) were MSM without known HIV infection or PrEP use. The increase in total numbers is depicted in Figure 1, and Table 1 shows the main clinical characteristics and coinfections among these three patient populations.

The overall median age of this MPXV cohort was 39 years (youngest, 20; oldest, 67). People living with HIV were slightly older than PrEP users and MSM without HIV or PrEP. Only 5.7% of the patients were either aged <25 years (n=20) or >60 years (n=11). A total of 12.8% had been vaccinated against smallpox at least once, with somewhat higher rates in people living with HIV. Most patients were of German nationality and Caucasian ethnicity. Very few patients (n=25) had non-infectious and somatic comorbidities; the most frequent was

TABLE 1 Demographic characteristics and existing coinfections

Characteristics	All	PLWH	PrEP user	MSM without HIV or PrEP
n	546	256	232	58
Age, years	39 (20–69)	41 (23-64)	37 (20–67)	37 (23–67)
Caucasian ethnicity	89.4 (440/492)	87.7 (207/236)	90.0 (190/211)	95.6 (43/45)
Nationality German	71.3 (313/439)	68.5 (148/216)	73.5 (136/185)	76.3 (29/38)
Documented prior smallpox vaccination	12.8 (49/382)	20.3 (35/172)	5.9 (10/170)	10.0 (4/40)
Hepatitis B infection				
Anti-HBc negative	89.3 (419/469)	83.6 (189/226)	95.3 (203/213)	90.0 (27/30)
Anti-HBc positive, HBsAG negative	9.8 (46/469)	15.0 (34/226)	4.2 (9/213)	10.0 (3/30)
HBsAG positive	0.9 (4/469)	1.3 (3/226)	0.5 (1/213)	0 (0/30)
Hepatitis C infection				
Anti-HCV negative	86.3 (415/481)	75.1 (175/233)	96.3 (208/216)	100 (32/32)
Anti-HCV positive, PCR negative	13.3 (64/481)	24.5 (57/233)	3.2 (7/216)	0 (0/32)
Anti-HCV positive, PCR positive	0.4 (2/481)	0.4 (1/233)	0.5 (1/216)	0 (0/32)

Note: denominators vary because not all information was available from all patients. Data are presented as % (n/N) or median (range) unless otherwise indicated.

Abbreviations: HBc, hepatitis B core antibody; HBsAG, hepatitis B surface antigen; HCV, hepatitis C virus; MSM, men who have sex with men; PCR, polymerase chain reaction; PLWH, people living with HIV; PrEP, pre-exposure prophylaxis.

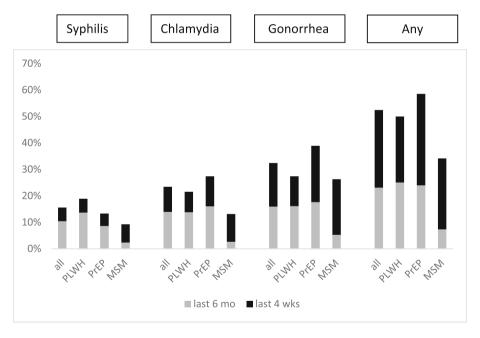


FIGURE 2 Percentage of frequent sexually transmitted infections in the past 6 months (but not during the last month [grey]) or within the past 4 weeks (black) prior to monkeypox virus infection. mo, months; MSM, men who have sex with men; PLWH, people living with HIV; PrEP, pre-exposure prophylaxis; wks, weeks.

psoriatic arthritis in seven cases, arterial hypertension in five cases, bronchial asthma in four cases, and diabetes mellitus and chronic obstructive pulmonary disease in two cases each. A relatively large proportion (13.7%) of patients, mainly people living with HIV, had a history of hepatitis C virus infection. The proportion of patients who had contracted another STI within the previous

6 months or within the last 4 weeks is shown in Figure 2. The most frequent STI diagnosed during the last 6 months was gonorrhoea, which was found in 32.4% of all patients, reaching 38.9% in PrEP users. Only 47.6% of all patients had not experienced any STI in the past 6 months. MSM without HIV or PrEP had lower STI rates than did the other two groups.

TABLE 2 Monkeypox virus infection manifestations (only cases with available information)

Characteristics	All	PLWH	PrEP User	MSM without HIV or PrEP
n	546	256	232	58
Hospitalization <sup>a</sup>	4.0 (22/546)	2.7 (7/256)	5.2 (12/232)	5.2 (3/58)
Localization				
Genital	49.9 (267/535)	43.8 (110/251)	49.8 (114/229)	78.2 (43/55)
Anal	47.9 (257/536)	50.4 (127/252)	50.7 (116/229)	25.5 (14/55)
Oral, perioral, head and neck	23.5 (123/523)	25.9 (64/247)	21.0 (47/224)	23.1 (12/52)
Extremities and/or trunk	37.5 (196/522)	37.4 (92/246)	40.2 (90/224)	26.9 (14/52)
Number of lesions				
None <sup>b</sup>	0.8 (4/493)	0.9 (2/235)	1.0 (2/208)	0 (0/50)
1–3	45.2 (223/493)	43.0 (101/235)	46.6 (97/208)	50.0 (25/50)
4–10	36.7 (181/493)	39.1 (92/235)	35.1 (73/208)	32.0 (16/50)
11–50	15.0 (74/493)	14.5 (34/235)	15.4 (32/208)	16.0 (8/50)
>50	2.2 (11/493)	2.6 (6/235)	1.9 (4/208)	2.0 (1/50)
General symptoms				
Fever	53.2 (272/511)	53.2 (126/237)	53.2 (118/222)	53.8 (28/52)
Headache and pain in the limbs	41.0 (208/507)	41.7 (98/235)	41.4 (91/220)	36.5 (19/52)
Night sweats	14.5 (73/503)	17.2 (40/233)	13.7 (30/219)	5.9 (3/51)
Lymph node swelling	42.6 (213/500)	40.9 (95/232)	44.2 (95/215)	43.4 (23/53)

Note: Data are presented as % (n/N) unless otherwise indicated.

Abbreviations: MSM, men who have sex with men; PLWH, people living with HIV; PrEP, pre-exposure prophylaxis.

## Clinical appearance

Since a large proportion of infections was diagnosed only a few days before this analysis, the observation period was very short, with a median of 3 days since diagnosis (range 0–35). The median duration between symptom onset and MPXV diagnosis was 4 days (range 0–21). A total of 298 patients had a follow-up of at least 7 days since symptom onset. Thus, we expect some of the patients to present with more severe symptoms over subsequent days. Nevertheless, the disease characteristics are briefly outlined here.

Most of the illnesses so far have been relatively mild. No fatal courses have been observed. A total of 26 patients were hospitalized, at least four of whom were clearly for quarantine reasons or diagnostic purposes rather than severity of illness or (impending) complications. Thus, 22 hospitalizations were due to the severity of the clinical picture or complications, mainly massive swelling of lymph nodes and genitals, extensive involvement of the entire integument, haemorrhage, or refractory pain that could not be managed on an outpatient basis, especially in patients with anal or oral involvement. The total hospitalization rate was 4.0% (95% CI 2.5–6.0). The

hospitalization rate was 5.7% (95% CI 3.4–9.0) in patients with an observation period of at least 7 days and 2.0% (95% CI 0.7–4.6) in those with an observation time of <7 days. The average duration of hospitalization was 4 days (range 3–6); however, 9/22 patients remained hospitalized at the end of the observation period. One hospitalized patient received antiviral therapy with tecovirimat.

The disease manifestations are listed in Table 2. The vast majority of smallpox lesions manifested anally or genitally. Neither genital nor anal involvement was present in 68 (12.4%) patients, 40 of whom had head and neck (including oral and perioral areas) involvement. In only 24 (4.4%) patients, lesions were limited to trunk and extremities. Of note, in four asymptomatic patients, MPVX infection was found in the context of STI screening or environmental screening (contact with an infected person). While there were no differences between MSM with or without HIV, MSM without HIV or PrEP had higher rates of genital lesions and lower rates of anal lesions.

In 82.7% of patients, the disease was localized, with a maximum of 10 lesions. Only a few patients had extensive findings, with  $\geq$ 50 lesions. These rates did not

<sup>&</sup>lt;sup>a</sup>Four hospitalizations for quarantine reasons or diagnostic purposes and not due to severity of illness or (impending) complications were excluded.

<sup>&</sup>lt;sup>b</sup>Positive smears only, throat swabs in all four cases.

change significantly when the analysis was restricted to patients with at least 7 days of follow-up after symptom onset (data not shown). Common general symptoms included fever, headache, and limb pain, as well as often painful lymph node swelling. There were no differences between MSM with or without HIV.

### DISCUSSION

In this large retrospective study, a total of 546 patients with PCR-confirmed MPXV infections from 42 participating centres were evaluated by 30 June 2022, corresponding to more than 50% of all 2022 cases reported to the German health institutions by that day. The vast majority of cases was reported from the three largest cities: Berlin, Cologne, and Hamburg. Cases were almost exclusively found among MSM, most of them living with HIV or taking PrEP. Of note, most centres focused on HIV infection and/or PrEP, meaning that most, if not all, of their patients were MSM with or without HIV infection. It seems therefore possible that people outside the affected groups have either not yet been diagnosed or were diagnosed in centres that did not participate in this survey. However, Figure 1 illustrates that, at least until mid-June, almost all cases reported to German health officials were included in the present cohort.

The disease course was predominantly mild to moderate, with no fatal courses. The total hospitalization rate was 4.0% and did not differ between MSM with or without HIV. However, most patients were predominantly young and otherwise healthy. In addition, most people living with HIV had a good immune status and viral suppression and were on antiretroviral therapy. Only four patients had viral loads >200 copies/ml. In particular, the observation period was very short, and it is possible that hospitalization rates will increase with longer follow-up. However, limiting the analysis to patients with longer observation periods did not change rates dramatically.

Whether the currently circulating West African clade is associated with low severity remains to be seen. Among 122 Nigerian patients infected with this clade, overall mortality was 6%, and patients with HIV and AIDS were predominantly affected [12]. The present analysis indicates that the clinical picture of MPXV infection does not differ between MSM with and without HIV infection. Little is known to date about other risk factors for severe courses; it has been reported that children and pregnant women may be at increased risk [13, 14]. To date, these populations are yet to present in the current outbreak.

The high number of other STIs diagnosed either in parallel with or shortly before MPXV infection was

striking. Almost two-thirds of patients had been diagnosed with at least one STI within the last 6 months, and almost one-third had been diagnosed within the last month or even at the same time. This high coincidence suggests that, in the current situation, an acutely diagnosed STI should definitely prompt MPXV diagnostics (and vice versa). In one case, HIV infection was diagnosed at the same time as MPXV infection, suggesting that offering HIV testing to patients without HIV but with MPXV infection also seems advisable, similar to processes for other STIs. Two recent cohort studies from Madrid and London found similarly high rates of STIs among MSM with MPXV infections [4, 5].

In the present cohort, a total of 13% were known to have been vaccinated against smallpox, probably at least 40 years previously as compulsory vaccination ended in 1976 in West Germany and in 1982 in East Germany. Laboratory studies and clinical observations suggest that smallpox vaccination provides some but by no means complete protection against MPXV [15-17]. Epidemiological studies from the 1980s in Zaire found 85% protection [18], and a large study from the Democratic Republic of Congo reported that vaccinated people had a 5.2-fold lower risk than non-vaccinated people [19]. Clinical courses appear to be milder in vaccinated individuals [20]. The present analysis also shows that smallpox vaccination does not provide sterilizing protection, although some protection against severe infection cannot be excluded. Of note, at least 4/22 patients (18.2%) who were hospitalized for severe illness or complications had been vaccinated against smallpox. It remains to be seen whether the smallpox vaccinations will indeed confer a substantial level of protection against severe infections in this affected group.

Interestingly, the disease localization observed in this cohort appeared to differ in part from those of the larger outbreaks from Africa. In the 2017/2018 outbreak in Nigeria described earlier [12], the main manifestation of MPVX infection was on the face (96%), followed by the legs (91%), trunk (80%), arms (79%), and palms (69%). Although genitalia (68%) were also commonly affected in the Nigerian patients, overall, manifestations in the cohort described here appear to affect the face and trunk and extremities significantly less. Anogenital manifestations, on the other hand, were much more common, in line with recent observations from Madrid and London [4, 5].

Since specific therapies have only been used in individual cases, statements on effectiveness are not possible. The synthetic substance tecovirimat, developed specifically for poxviruses, is a tetracyclic acylhydrazide that targets the VP37 protein. By inhibiting VP37, tecovirimat blocks the final steps of viral maturation and release from

the infected cell. In a large study of 449 healthy volunteers, "no pattern of worrisome adverse events" was observed [21]. In the monkey model, tecovirimat was shown to be effective against MPXV [22, 23].

Our study had several limitations. First, this was an observational study with limited follow-up and with incomplete data collection during the outbreak. In view of the study design, we could not explore all possible risk factors for disease transmission. In addition, the number of severe cases (defined by hospitalization) was low. Given the small number of cases with comorbidities, severe immunodeficiency, and/or severe courses, we could not determine risk factors such as comorbidities.

In conclusion, all 546 patients with MPXV in this German cohort were MSM. The Joint United Nations Programme on HIV/AIDS has already expressed concern that the high prevalence of affected MSM could lead to homophobic and racist stereotypes and reinforce stigmatization [24]. There were no clinical differences in MPXV infections between MSM with or without HIV. Most cases were mild. However, some cases were severe, and current outbreak kinetics suggest that MPXV will become established as a new and serious STI. A rapid and comprehensive education campaign in at-risk populations is urgently needed. Skin lesions in sexually active MSM, especially those with anogenital localization and with a history of other STIs, should prompt MPXV diagnostic procedures.

### **AUTHOR CONTRIBUTIONS**

The authors confirm contributions to the paper as follows: study conception and design, Christian Hoffmann, Christoph Boesecke; data collection, Christian Hoffmann, Christoph Boesecke, Malte Benedikt Monin; analysis and interpretation of results, Christian Hoffmann, Christoph Boesecke, Eva Wolf; and draft manuscript preparation, Christian Hoffmann, Christoph Boesecke. All authors reviewed the results and approved the final version of the manuscript.

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### CONFLICT OF INTEREST

CB has received honoraria for lectures and/or consultancies from AbbVie, Gilead Sciences, Janssen-Cilag, MSD, and ViiV Healthcare. BJ has received honoraria for presentations from Gilead Sciences, GSK, Falk, Janssen-Cilag, ViiV Healthcare, Fresenius Medical Care (outside the submitted work); has received travel support from Gilead; and has served on advisory boards for ViiV Healthcare, Gilead Sciences, and Theratechnologies (outside the submitted work). CH has received honoraria for presentations and/or travel support from Gilead Sciences, Janssen-Cilag, MSD, ViiV Healthcare, and Eusa Pharm (outside the submitted work), and has served on advisory boards for Eusa Pharm, MSD, ViiV Healthcare, Gilead Sciences, and Theratechnologies (outside the submitted work). CW has received honoraria for lectures and/or consultancies from AbbVie, Gilead Sciences, Janssen-Cilag, MSD, Roche, and ViiV Healthcare. CDS has received grants and personal fees from AbbVie, Janssen-Cilag, MSD, and Viiv Healthcare; grants, fees, and non-financial support from Gilead Sciences; grants from Cepheid, and personal fees from GSK during the conduct of the study. CDS has also received fees from AstraZeneca; other from Apeiron; grants, personal fees, and non-financial support from B. Braun Melsungen; grants and personal fees from BioNtech and Eli Lilly; and personal fees from Formycon, Molecular Partners, Roche, and SOBI. EW has received honoraria for lectures and/or consultancies from AbbVie, Biogen, Gilead Sciences, Janssen-Cilag, MSD Sharp & Dohme, Theratechnologies, and ViiV Healthcare.

#### DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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### REFERENCES

- 1. Ladnyj ID, Ziegler P, Kima E. A human infection caused by monkeypox virus in Basankusu territory, Democratic Republic of the Congo. *Bull World Health Organ*. 1972;46:593-597.
- Simpson K, Heymann D, Brown CS, et al. Human monkeypoxafter 40 years, an unintended consequence of smallpox eradication. *Vaccine*. 2020;38:5077-5081.

 Minhaj FS, Ogale YP, Whitehill F, et al. Monkeypox outbreak nine states, may 2022. MMWR Morb Mortal Wkly Rep. 2022;71: 764-769.

- Martínez JI, Montalbán EG, Bueno SJ, et al. Monkeypox outbreak predominantly affecting men who have sex with men, Madrid, Spain, 26 April to 16 June 2022. Eurosurveillance 27, 07/Jul/2022 Article.
- 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:S1473-3099 (22)00411-X. doi:10.1016/S1473-3099(22)00411-X.
- Noe S, Zange S, Seilmaier M, et al. Clinical and virological features of first human monkeypox cases in Germany. *Infection*. 2022:1-6. Published only 11 July.
- Robert Koch Institute. International monkeypox outbreak: case numbers and assessment of the situation in Germany. Status 17.6.2022. https://www.rki.de/DE/Content/InfAZ/A/Affenpocken/Ausbruch-2022-Situation-Deutschland.html
- Giorgi FM, Pozzobon D, Di Meglio A, Mercatelli D. Genomic analysis of the recent monkeypox outbreak. *bioRxiv*. 2022. doi: 10.1101/2022.06.01.494368.
- Gigante CM, Korber B, Seabolt MH, et al. Multiple lineages of monkeypox virus detected in the United States, 2021–2022. bioRxiv. 2022. doi:10.1101/2022.06.10.495526.
- Likos AM, Sammons SA, Olson VA, et al. A tale of two clades: monkeypox viruses. J Gen Virol. 2005;86:2661-2672.
- 11. Chen N, Li G, Liszewski MK, et al. Virulence differences between monkeypox virus isolates from West Africa and The Congo basin. *Virology*. 2005;340:46-63.
- 12. Yinka-Ogunleye A, Aruna O, Dalhat M, et al. Outbreak of human monkeypox in Nigeria in 2017-18: a clinical and epidemiological report. *Lancet Infect Dis*. 2019;19:872-879.
- Huhn GD, Bauer AM, Yorita K, et al. Clinical characteristics of human monkeypox, and risk factors for severe disease. Clin Infect Dis. 2005;41:1742-1751.
- Mbala PK, Huggins JW, Riu-Rovira T, et al. Maternal and fetal outcomes among pregnant women with human Monkeypox infection in the Democratic Republic of Congo. *J Infect Dis*. 2017;216:824-828.
- Hammarlund E, Lewis MW, Carter SV, et al. Multiple diagnostic techniques identify previously vaccinated individuals with protective immunity against monkeypox. *Nat Med.* 2005;11:1005-1011.
- Karem KL, Reynolds M, Hughes C, et al. Monkeypox-induced immunity and failure of childhood smallpox vaccination to provide complete protection. Clin Vaccine Immunol. 2007;14:1318-1327.
- 17. Gilchuk I, Gilchuk P, Sapparapu G, et al. Cross-neutralizing and protective human antibody specificities to poxvirus infections. *Cell*. 2016;167:684-694.e9.
- Fine PE, Zezek Z, Grab B, Dixon H. The transmission potential of monkeypox virus in human populations. *Int J Epidemiol*. 1988;17:643-650.
- Rimoin AW, Mulembakani PM, Johnston SC, Lloyd Smith JO, Kisalu NK, Kinkela TL. Major increase in human monkeypox incidence 30 years after smallpox vaccination campaigns cease in the Democratic Republic of Congo. *Proc Natl Acad Sci U S A*. 2010;107:16262-16267.
- 20. Petersen E, Abubakar I, Ihekweazu C, Heymann D, Ntoumi F, Blumberg L. Monkeypox-enhancing public health

preparedness for an emerging lethal human zoonotic epidemic threat in the wake of the smallpox post-eradication era. Int J Infect Dis. 2019;78:78-84.

- 21. Grosenbach DW, Honeychurch K, Rose EA, et al. Oral tecovirimat for the treatment of smallpox. *N Engl J Med.* 2018;379:44-53.
- 22. Huggins J, Goff A, Hensley L, et al. Nonhuman primates are protected from smallpox virus or monkeypox virus challenges by the antiviral drug ST-246. *Antimicrob Agents Chemother*. 2009;53:2620-2625.
- 23. Russo AT, Grosenbach DW, Chinsangaram J, et al. An overview of tecovirimat for smallpox treatment and expanded anti-orthopoxvirus applications. *Expert Rev Anti Infect Ther.* 2021; 19:331-344.

24. UNAIDS. UNAIDS warns that stigmatizing language on monkeypox jeopardizes public health. https://www.unaids.org/en/ resources/presscentre/pressreleaseandstatementarchive/2022/ may/20220522\_PR\_MONKEYPOX. Accessed: June 17, 2022.

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