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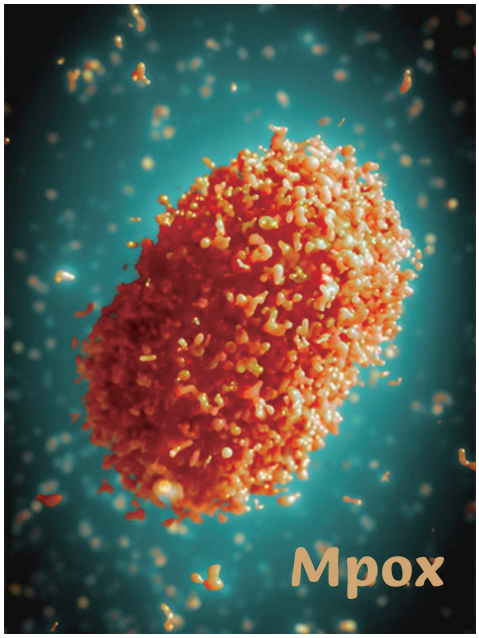

MPOX ISSUE

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Cover Image: adapted from the World Health Organization, https://www.who.int/health-topics/monkeypox/#tab=tab_1.
This week's issue was organized by Guest Editor Lei Zhou.

Preplanned Studies

Knowledge, Attitude, and Practice Towards Mpox and Associated Factors Among HIV-Infected Individuals — Beijing Municipality, China, 2023

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Summary

What is already known about this topic?

Approximately 50% of patients with mpox are human immunodeficiency virus (HIV)-infected globally. Studies have shown that individuals with advanced HIV infection tend to have more severe clinical manifestations and higher mortality rates after mpox infection.

What is added by this report?

The study revealed that individuals living with HIV have a low level of Knowledge, Attitude, and Practice (KAP) towards mpox. Several factors, including age, registered residence, sexual orientation, education level, viral load, and co-occurrence of other sexually transmitted diseases, were found to influence the KAP towards mpox.

What are the implications for public health practice?

This study is the first to investigate the KAP of mpox among individuals living with HIV. The findings suggest that mpox health education should prioritize individuals with co-existing sexually transmitted diseases (STDs) and a high viral load.

The global mpox outbreak, starting in May 2022, has spread rapidly across non-endemic regions (*1*). In this wave of the epidemic, 38% to 50% of mpox patients are also human immunodeficiency virus (HIV)-infected individuals, which face a higher risk of mpox infection, more severe clinical symptoms, and higher mortality rates due to their compromised immune system (*2*). The spread of mpox is particularly insidious (*3*), and the absence of smallpox vaccination among individuals born after 1980 has resulted in their lack of resistance to mpox (*4*). Furthermore, there is currently a lack of effective treatment measures for mpox, with symptomatic supportive therapy being the primary approach in clinical practice. Consequently, preventing and controlling mpox heavily relies on individuals' self-regulation and responsible behavior. The Knowledge, Attitude, and Practice (KAP) theory, frequently used in health education for HIV-infected individuals and men who have sex with men (MSMs), addresses this need. Establishing beliefs in individuals requires both knowledge and a strong sense of responsibility. Behavior changes positively only when knowledge transforms into belief. Given these circumstances, the objective of this study is to evaluate the current level of mpox KAP among HIV-infected individuals and identify potential influencing factors.

This cross-sectional study was conducted at the Beijing Ditan Hospital of Capital Medical University from July 18 to August 9, 2023, using convenience sampling through a combination of online and field surveys. The study included participants who were 18 years or older, without any gender restrictions, while those who had previously experienced mpox infection or participated in mpox-related programs were excluded. The field survey involved on-site data verification, while the online survey utilized the Questionnaire Star platform to implement logical jumps and limit responses to one per WeChat account, thus ensuring the questionnaire's data quality.

The questionnaire surveyed sociodemographic characteristics, HIV infection status, and mpox KAP. The 25-question knowledge section, based on the study by Jairoun AA et al. (*5*), scored 1 point per correct answer, with ≥16 points (≥60% accuracy) indicating mpox awareness. The attitude section included 16 questions and utilized a 5-point Likert scale. Higher scores indicated a more favorable attitude, with 5 points for strongly agree and 1 point for strongly disagree (and vice versa for negative statements). The total attitude score ranged from 16 to 80. Participants scoring ≥48 points (representing more than 60% of the total score) were considered to have a positive attitude towards mpox. To obtain the standardized attitude score, the dimension score was divided by the number of dimension entries. The

practice section consisted of 7 questions. The highest score for each question was 3 points, while the lowest score was 1 point. The total practice score ranged from 7 to 21. Participants scoring ≥17 points (representing more than 80% of the total score) were considered to have a positive practice towards mpox. A collinearity test was conducted on the independent variables (Supplementary Table S1, available at https://weekly.chinacdc.cn/). The mpox knowledge, attitude, practice, and KAP scores were converted into binary variables for binary logistic regression analysis.

Subject duplication was prevented by cross-verifying paper and electronic questionnaires using a unique identification code referred to as the ART (antiretroviral therapy) number. Statistical analysis was performed using SPSS software (web version 26.0; IBM, New York, USA) and RStudio software (version 4.2.1; R Foundation for Statistical Computing, Vienna, Austria). A significance level of $P<0.05$ (two-tailed) was employed to determine statistical significance. The Ethics Committee of Ditan Hospital granted approval.

A total of 1,235 individuals with HIV infection were included, with 486 from field surveys and 749 from online surveys. Among the participants, 48.3% (597/1,235) were aged between 35 and 55, 91.5% (1,130/1,235) were male, 61.5% (760/1,235) identified as homosexual, and 61.7% (762/1,235) reported a monthly income over 5,000 Chinese Yuan (CNY). The majority of participants had not received influenza vaccination (72.5%, 895/1,235), had not experienced other sexually transmitted diseases (85.9%, 1,061/1,235), and did not have any chronic diseases (68.9%, 851/1,235). In addition, most respondents reported being infected with HIV for more than 3 years (75.7%, 935/1,235), had a latest CD4 cell count greater than 500/mm^3 (55.3%, 683/1,235), and had a latest viral load test result of less than 20 copies/mL (76.2%, 941/1,235) (Table 1).

The mean knowledge score for mpox was 14 (interquartile range: 8–18, range: 0–25), with an awareness rate of 46.0%. Out of the 25 questions, two had a correct answer rate of over 80% (Q1 and Q8), while the other three questions had a correct answer rate over 70% but not exceeding 80% (Q7, Q18, and Q19). The lowest correct answer rate was observed for the two questions related to "rash" (Q12 and Q20). The dimension of epidemiologic characteristics had a relatively high correct answer rate (mean: 62.8%), while the treatment dimension had a low correct answer rate (mean: 37.4%). Three questions in the treatment dimension had a correct answer rate of less than 30.0% (Q22, Q23, and Q24) (Supplementary Table S3, available at https://weekly.chinacdc.cn/). The results of the binary logistic regression analysis indicated that residing in an urban area, homosexual orientation, having a master's degree or above, and having undetectable viral copies (<20 cps/mL) were all positively associated with knowledge of mpox (Figure 1).

After accounting for standardization, the total score for mpox attitude was 3.81 (interquartile range: 3.50, 4.12). The barrier dimension had the lowest score, 3.25 (interquartile range: 2.50, 4.00) points (Supplementary Table S4, available at https://weekly.chinacdc.cn/). The results of the binary logistic regression analysis showed that having a master's degree or higher education and not having any other sexually transmitted diseases (STDs) were positively associated with a favorable attitude towards mpox (Figure 1).

The score for mpox practice was 20 (interquartile range: 19, 21). Among the 1,235 individuals infected with HIV, a majority of them (87.3%, 1,078/1,235) sought medical advice upon experiencing unexplained lymphadenopathy and voluntarily disclosed recent exposure to mpox. Furthermore, 78.9% (975/1,235) of individuals expressed willingness to receive the mpox vaccine. With the exception of 27 individuals who had not initiated ART, the majority (87.0% 1,075/1,235) demonstrated good adherence to their daily ART medication. In the past six months, almost 30% (325/1,235) reported having two or more sexual partners, with 107 individuals engaging in male-to-male group sex. When experiencing mpox-related symptoms, the most common actions taken were seeking medical treatment at an infectious disease hospital (96.8%, 1,195/1,235), practicing home quarantine (30.8%, 380/1,235), and notifying the local CDC in their community of residence (29.4%, 363/1,235) (Table 2). The results of the binary logistic regression analysis indicated that not suffering from other STDs was a positive factor associated with the practice of mpox (Figure 1).

The total KAP score is calculated by summing the scores of mpox KAP. The score range is from 23 to 126, with the highest score being 124 points and the lowest score being 30 points. The majority of research subjects fall within the range of 90 to 106 points. Binary logistic regression analysis revealed that individuals below the age of 35, with homosexual orientation, holding a master's degree or higher, and

TABLE 1. Sociodemographic characteristics and infection status of HIV-infected individuals (*N*=1,235).

Variable	*n*	Constituent ratio (%)	Awareness rate (%)	Knowledge score*	Mann-Whitney U test/Kruskal-Wallis test		Attitude score*	Mann-Whitney U test/Kruskal-Wallis test		Practice score*	Mann-Whitney U test/Kruskal-Wallis test		KAP score*	Mann-Whitney U test/Kruskal-Wallis test	
					U value/H value	*P* value		U value/H value	*P* value		U value/H value	*P* value		U value/H value	*P* value
Age, years															
<35	551	44.6	52.3	15 (10, 19)			62 (57, 68)			20 (19, 21)			97 (88, 105)		
35–55	597	48.3	43.0	14 (8, 18)	43.8	<0.001	60 (55, 65)	31.4	<0.001	20 (19, 21)	1.8	0.398	93 (83, 101)	43.6	<0.001
>55	87	7.1	26.4	9 (0, 15)			59 (52, 64)			20 (19, 21)			85 (77, 98)		
Gender															
Male	1,130	91.5	48.6	14 (9, 18)			61 (56, 67)			20 (19, 21)			95 (85, 103)		
Female	103	8.3	16.5	7 (0, 13)	64.0	<0.001	59 (53, 64)	10.9	0.004	21 (19, 21)	9.1	0.011	86 (76, 96)	37.1	<0.001
Transgender	2	0.2	100.0	22 (22, 22)			65 (57, 72)			21 (21, 21)			108 (100, 115)		
Registered residence															
Urban area	645	52.2	55.0	15 (11, 19)	142,773.5†	<0.001	62 (57, 67)	165,406.5†	<0.001	20 (19, 21)	142,449.0†	0.191	97 (88, 104)	149,673.5†	<0.001
Rural area	590	47.8	36.1	12 (6, 17)			60 (54, 65)			20 (19, 21)			92 (80, 100)		
Sexual orientation															
Homosexual	760	61.5	54.7	15 (10, 19)			62 (57, 67)			20 (19, 21)			97 (88, 104)		
Heterosexual	188	15.2	23.4	9 (2, 14)	109.6	<0.001	58 (53, 64)	40.6	<0.001	21 (19, 21)	11.2	0.011	87 (76, 97)	78.1	<0.001
Bisexual	208	16.9	41.8	13 (9, 17)			60 (55, 66)			20 (19, 21)			93 (85, 102)		
Uncertain	79	6.4	26.6	11 (1, 15)			57 (52, 64)			20 (18, 21)			83 (74, 99)		
Marital status															
Unmarried	774	62.7	54.5	15 (10, 19)			62 (57, 68)			20 (19, 21)			97 (89, 104)		
Married	291	23.6	28.9	11 (3, 15)	97.6	<0.001	59 (53, 64)	46.4	<0.001	20 (19, 21)	6.0	0.114	89 (79, 98)	83.4	<0.001
Divorced /widowed	144	11.6	34.0	13 (5, 17)			59 (54, 64)			20 (19, 21)			91 (81, 99)		
Cohabitation	26	2.1	50.0	15 (6, 18)			60 (57, 65)			20 (19, 21)			93 (80, 99)		
Education															
Master's degree or above	96	7.8	78.1	18 (15, 20)			63 (58,69)			20 (19, 21)			100 (95, 107)		
University or technical college	678	54.9	55.0	15 (11, 19)	209.9	<0.001	63 (57, 68)	82.6	<0.001	20 (19, 21)	3.7	0.299	97 (90, 104)	179.2	<0.001
High school or technical secondary	293	23.7	30.4	11 (6, 15)			60 (54, 64)			20 (19, 21)			90 (80, 98)		

Continued

Variable	*n*	Constituent ratio (%)	Awareness rate (%)	Knowledge score*	Mann-Whitney U test/Kruskal-Wallis test		Attitude score*	Mann-Whitney U test/Kruskal-Wallis test		Practice score*	Mann-Whitney U test/Kruskal-Wallis test		KAP score*	Mann-Whitney U test/Kruskal-Wallis test	
					U value/H value	*P* value		U value/H value	*P* value		U value/H value	*P* value		U value/H value	*P* value
Junior high school or below	168	13.6	18.5	6 (0, 13)			56 (52, 62)			20 (18, 21)			82 (73, 94)		
Occupation															
Students	22	1.8	63.6	16 (12, 19)			65 (60, 69)			20 (20, 21)			101 (93, 108)		
Official staffs/Personnel of enterprises and institutions	144	11.7	55.6	16 (9, 19)			62 (58, 67)			20 (19, 21)			98 (88, 103)		
Commercial service providers	321	26.0	43.9	14 (9, 17)	52.86	<0.001	60 (56, 66)	39.4	<0.001	20 (18, 21)	4.1	0.664	94 (84, 101)	58.5	<0.001
Workers/Farmers	207	16.8	28.5	11 (3, 15)			58 (52, 64)			20 (19, 21)			88 (79, 97)		
Retired people	109	8.8	45.9	13 (9, 18)			61 (56, 66)			20 (19, 21)			93 (85, 103)		
Housekeeping and unemployment	14	1.1	57.1	18 (12, 21)			62 (57, 64)			21 (19, 21)			98 (91, 105)		
Others	418	33.8	51.7	15 (9, 19)			62 (56, 68)			20 (19, 21)			96 (87, 104)		
Monthly income															
<2,000 CNY	199	16.1	34.2	10 (3, 16)			59 (53, 65)			20 (19, 21)			88 (78, 101)		
2,000–4,999 CNY	274	22.2	34.3	12 (6, 17)	69.6	<0.001	59 (54, 64)	35.2	<0.001	20 (19, 21)	4.0	0.259	91 (80, 98)	70.3	<0.001
5,000–9,999 CNY	449	36.4	45.4	14 (9, 18)			62 (56, 68)			20 (19, 21)			95 (87, 103)		
>10,000 CNY	313	25.3	64.5	17 (13, 19)			62 (57, 67)			20 (19, 21)			98 (91, 105)		
Have you been vaccinated against flu?															
Yes	340	27.5	47.1	14 (8, 18)	154,652.0†	0.654	60 (54, 65)	137,693.0†	0.010	20 (19, 21)	147,120.0†	0.348	94 (84, 102)	143,029†	0.103
No	895	72.5	45.6	14 (9, 18)			61 (56, 67)			20 (19, 21)			95 (85, 103)		
Have any other sexually transmitted diseases?															
Yes	174	14.1	37.9	13 (7, 17)	85,787.5†	0.134	60 (53, 65)	82,192.0†	0.020	20 (18, 21)	76,434.5†	<0.001	92 (81, 100)	860,817.5†	0.008
No	1061	85.9	47.3	14 (9, 18)			61 (56, 67)			20 (19, 21)			95 (85, 103)		

Continued

Variable	*n*	Constituent ratio (%)	Awareness rate (%)	Knowledge score*	Mann-Whitney U test/Kruskal-Wallis test		Attitude score*	Mann-Whitney U test/Kruskal-Wallis test		Practice score*	Mann-Whitney U test/Kruskal-Wallis test		KAP score*	Mann-Whitney U test/Kruskal-Wallis test	
					U value/H value	*P* value		U value/H value	*P* value		U value/H value	*P* value		U value/H value	*P* value
Have any other chronic diseases?															
Yes	215	17.4	46.0	14 (10, 18)			61 (55, 66)			20 (19, 21)			94 (85, 102)		
No	851	68.9	48.4	14 (9, 19)	29.5	<0.001	61 (56, 67)	16.0	<0.001	20 (19, 21)	9.2	0.010	95 (86, 103)	27.9	<0.001
Uncertain	169	13.7	33.7	10 (5, 16)			58 (53, 64)			20 (18, 21)			88 (78, 99)		
Time of confirmed HIV infection															
<1 year	90	7.3	38.9	13 (5, 17)			61 (56, 66)			20 (19, 21)			94 (83, 101)		
1–3 years	210	17.0	48.1	14 (9, 18)	4.0	0.137	62 (56, 67)	2.9	0.231	20 (19, 21)	4.6	0.101	95 (87, 104)	4.2	0.120
>3 years	935	75.7	46.2	14 (8, 18)			61 (55, 66)			20 (19, 21)			94 (84, 102)		
Latest CD4 test results															
<350/mm^3	181	14.6	45.3	14 (9, 17)			60 (55, 65)			20 (19, 21)			95 (84, 102)		
350–500/mm^3	280	22.7	39.6	13 (7, 17)	48.9	<0.001	62 (57, 67)	25.1	<0.001	20 (19, 21)	5.9	0.052	94 (83, 102)	46.2	<0.001
>500/mm^3	683	55.3	52.1	15 (10, 19)			61 (56, 67)			20 (19, 21)			96 (87, 104)		
Uncertain	91	7.4	20.9	8 (1, 13)			57 (52, 63)			20 (18, 21)			83 (74, 97)		
Latest varial copies test results															
<20 cps/mL (undetectable)	941	76.2	52.7	15 (10, 19)			62 (57, 67)			20 (19, 21)			96 (88, 104)		
<10^5 cps/mL	107	8.6	31.8	11 (4, 15)	127.6	<0.001	58 (53, 64)	58.0	<0.001	20 (19, 21)	2.2	0.329	89 (80, 98)	119.5	<0.001
>10^5 cps/mL	17	1.4	29.4	10 (4, 15)			59 (52, 64)			21 (17, 21)			90 (78, 97)		
Uncertain	170	13.8	19.4	8 (0, 13)			57 (52, 63)			20 (18, 21)			83 (73, 95)		

Abbreviation: HIV=human immunodeficiency virus; CNY=Chinese Yuan; KPA=Knowledge, Attitude, and Practice.

* The normality test results for mpox knowledge, attitude, practice, and KAP scores and scores in all dimensions indicated that the data did not follow a normal distribution (P<0.05) (Supplementary Table S2, available at https://weekly.chinacdc.cn/). Consequently, the median and interquartile intervals were utilized to describe the scores.

† Calculations were conducted using the Mann-Whitney U test.

Variable	Eligible	Ineligible	*OR* (95% *CI*)
Knowledge			
Registered residence			
Urban area	355	290	Ref.
Rural area	213	377	0.71 (0.54−0.92)
Sexual orientation			
Homosexual	416	344	Ref.
Heterosexual	44	144	0.36 (0.24−0.53)
Bisexual	87	121	0.68 (0.49−0.96)
Uncertain	21	58	0.47 (0.27−0.84)
Education			
Master's degree or above	75	21	Ref.
University or technical college	373	305	0.41 (0.24−0.68)
High school or technical secondary	89	204	0.19 (0.11−0.33)
Junior high school or below	31	137	0.13 (0.07−0.25)
Viral copies			
<20 cps/mL (undetectable)	496	445	Ref.
⩽100,000 cps/mL	34	73	0.59 (0.38−0.94)
>100,000 cps/mL	5	12	0.47 (0.15−1.45)
Uncertain	33	137	0.40 (0.25−0.66)
Attitude			
Education			
Master's degree or above	95	1	Ref.
University or technical college	672	6	1.33 (0.16−11.3)
High school or technical secondary	282	11	0.35 (0.04−2.74)
Junior high school or below	146	22	0.10 (0.01−0.73)
Other sexually transmitted diseases			
No	1,033	28	Ref.
Yes	162	12	0.37 (0.18−0.77)
Practice			
Other sexually transmitted diseases			
No	999	62	Ref.
Yes	153	21	0.45 (0.27−0.76)
KAP			
Age, years			
<35	442	109	Ref.
35−55	424	173	0.86 (0.63−1.18)
>55	43	44	0.40 (0.22−0.72)
Sexual orientation			
Homosexual	610	150	Ref.
Heterosexual	99	89	0.46 (0.32−0.68)
Bisexual	158	50	1.04 (0.70−1.56)
Uncertain	42	37	0.66 (0.38−1.17)
Education			
Master's degree or above	89	7	Ref.
University or technical college	565	113	0.46 (0.21−1.04)
High school or technical secondary	187	106	0.20 (0.09−0.47)
Junior high school or below	68	100	0.10 (0.04−0.23)
Other chronic diseases			
Yes	162	53	Ref.
No	650	201	0.67 (0.44−1.02)
Uncertain	97	72	0.35 (0.21−0.58)
Viral copies			
<20 cps/mL (undetectable)	761	180	Ref.
⩽100,000 cps/mL	63	44	0.49 (0.31−0.77)
>100,000 cps/mL	10	7	0.45 (0.16−1.28)
Uncertain	75	95	0.30 (0.21−0.44)

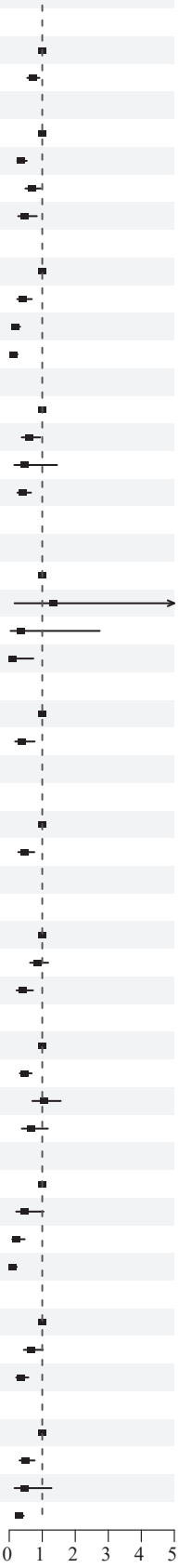

FIGURE 1. Binary logistic regression analysis of Knowledge, Attitude, and Practice of mpox.
Abbreviation: *OR*=odds ratio; *CI*=confidence interval; KAP=Knowledge, Attitude, and Practice.

TABLE 2. Behavioral characteristics of mpox in HIV-infected individuals.

Variable	*n*	Constituent ratio/percent (%)
When you have unexplained lymphadenopathy, will you seek medical advice and inform yourself of mpox-related exposure voluntarily?		
Yes, I will seek medical advice and inform myself of mpox-related exposure voluntarily.	1,078	87.3
No, I will not seek medical advice and inform myself of mpox-related exposure voluntarily.	96	7.8
Yes, I will seek medical advice, but not inform myself of mpox-related exposure voluntarily.	30	2.4
Not seek medical advice	31	2.5
If the mpox vaccine is available, would you like to get it?		
Yes	975	78.9
Normal	202	16.4
No	58	4.7
What would you do if you had mpox-related symptoms? (Multiple choices)		
Go to an infectious disease hospital	1,195	96.8
Informing the CDC in the community of residence	363	29.4
Seek help from social organizations	238	19.3
Ask friends for help	76	6.2
Buy medicine by yourself	57	4.6
Home quarantine	380	30.8
Nothing was done	4	0.3
Whether you can take ART drugs regularly every day?		
Yes	1,075	87.0
Forget to take it occasionally every month (1 or 2 times)	126	10.2
No, I often forget.	7	0.6
ART is not initiated.	27	2.2
Number of sexual partners engaged in anal sex between men in the past six months.		
One	325	26.3
Two	173	14.0
Three and above	179	14.5
No same-sex sexual activity has occurred	558	45.2
Has there been any male-to-male group sexual activity in the past six months?		
Yes	107	8.7
No	1,128	91.3

Abbreviation: HIV=human immunodeficiency virus; ART=antiretroviral therapy.

having undetectable viral copies (<20 cps/mL) were all positive factors associated with higher mpox KAP scores. The relationship between suffering from chronic diseases and mpox KAP remains uncertain (Figure 1).

DISCUSSION

The survey revealed that the level of knowledge regarding mpox among 1,235 investigated HIV-infected individuals was low (46.0%). This aligns with the awareness rate (47.2%, 1,781/3,563) of mpox among MSM reported by Zheng Min et al. in July 2022 (*6*) and is significantly lower than the knowledge of other infectious diseases such as acquired immunodeficiency syndrome (AIDS, 91.0%) (*7*) and syphilis (70.9%) (*8*). A low level of awareness regarding typical features of mpox, like rash, among HIV-infected individuals was found. It suggests that individuals with HIV do not associate rash with prevention measures or seek medical advice, which hinders self-monitoring of symptoms in key

populations. The attitude score towards mpox among HIV-infected individuals was moderate, similar to the findings of an analysis of AIDS health beliefs in newly infected individuals conducted by Yang Rongrong et al. (7.27/10) (*9*). A lower score in the dimension of the barrier indicates that HIV-infected individuals perceive more obstacles in preventing mpox.The practice scores for mpox were high, as most HIV-infected individuals proactively sought medical advice when experiencing mpox-related symptoms. However, more than 20% of respondents displayed hesitancy towards receiving the mpox vaccine, which was lower than in other studies (78.9% *vs.* 90.2%) (*10*).

Approximately 10% of participants engaged in male-to-male group sex in the past six months, increasing mpox infection risks. Despite higher mpox awareness in the homosexual population, behavior changes remain limited, indicating that high awareness rates do not necessarily translate into positives attitudes or behavioral changes. Studies have shown significant knowledge-behavior separation in MSM groups (*11*). Factors such as social discrimination and traditional culture contribute to the challenge of changing behaviors, with having multiple sexual partners being a common and difficult-to-change behavior in the community.

The absence of other STDs in the past six months positively influenced attitudes and practices related to mpox prevention measures among HIV-infected individuals. HIV-infected individuals with STDs were more likely to engage in sexual activity with multiple partners compared to those without STDs (39.5% *vs.* 26.6%). This indicates that individuals who are HIV-infected but do not have other STDs are more knowledgeable about safe sexual behavior and are more concerned about their own health in relation to diseases, prompting them to actively seek information about mpox prevention measures. Therefore, implementing interventions targeting HIV-infected individuals with STDs is essential for enhancing their KAP towards mpox.

Viral load significantly influences mpox KAP among individuals living with HIV. Those with undetectable viral load exhibited better medication adherence (89.4% *vs.* 79.2%). Improving ART effectiveness can enhance mpox KAP, subsequently reducing mpox infection risk. Therefore, targeted interventions and improved adherence to medication should be implemented for HIV-infected individuals with high viral load in order to enhance mpox prevention and control efforts.

This study has certain limitations. First, a convenience sampling method was used, which may affect the representativeness of the results. However, the large size of the cohort helps to mitigate this potential selection bias. Future research should aim to include studies from different regions to obtain a more comprehensive understanding. Second, the inclusion of sensitive questions, such as the number of sexual partners, might introduce information bias. To minimize this issue, questions were placed at the end of the questionnaire, and participants were provided with a private and quiet environment during the survey to encourage honest responses.

This study is the first to investigate mpox KAP among individuals living with HIV. The findings serve as a reference for preventing and managing mpox in this population. The survey results indicate that the level of mpox KAP among HIV-infected individuals is suboptimal. Age, registered residence, sexual orientation, education level, viral load, and co-infection with other STDs are factors that influence mpox KAP. Therefore, targeted mpox health education programs should be prioritized for HIV-infected individuals who have STDs and high viral load.

Conflicts of interest: No conflicts of interest.

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SUPPLEMENTARY MATERIAL

SUPPLEMENTARY TABLE S1. Collinearity test of independent variables.

Variables	Non standardized coefficients		Standardized coefficients	t	*P*	Tolerance	*VIF*
	β	SE	β				
Age	−0.020	0.026	−0.024	−0.757	0.449	0.679	1.472
Gender	−0.129	0.048	−0.074	−2.684	0.007	0.888	1.126
Registered residence	−0.073	0.029	−0.073	−2.540	0.011	0.821	1.218
Sexual orientation	−0.037	0.014	−0.072	−2.561	0.011	0.868	1.152
Marital status	−0.028	0.019	−0.045	−1.496	0.135	0.769	1.300
Education	−0.125	0.020	−0.206	−6.377	<0.001	0.655	1.526
Occupation	<0.001	0.007	<0.001	−0.015	0.988	0.967	1.034
Monthly income	0.019	0.015	0.038	1.248	0.212	0.735	1.360
Have you been vaccinated against flu?	0.001	0.030	0.001	0.021	0.983	0.974	1.026
Have any other sexually transmitted diseases?	−0.063	0.038	−0.044	−1.671	0.095	0.972	1.029
Have any other chronic diseases?	−0.048	0.024	−0.053	−1.973	0.049	0.937	1.067
Time of confirmed HIV infection	−0.019	0.023	−0.023	−0.818	0.414	0.858	1.165
Latest CD4 test results	0.011	0.016	0.018	0.688	0.492	0.963	1.038
Latest varial copies test results	−0.071	0.014	−0.149	−5.069	<0.001	0.793	1.261

Abbreviation: SE=standard error; VIF=variance inflation factor.

SUPPLEMENTARY TABLE S2. Normality test of total score and scores in various dimensions of mpox.

Variables and dimensions	Shapiro-Wilk test	
	Z value	*P* value
Mpox knowledge score	0.937	<0.001
Basic cognition	0.874	<0.001
Epidemiological characteristics	0.876	<0.001
Clinical manifestation	0.890	<0.001
Prevention	0.866	<0.001
Treatment	0.912	<0.001
Mpox attitude score	0.986	<0.001
Susceptibility	0.949	<0.001
Seriousness	0.897	<0.001
Benefits	0.908	<0.001
Barrier	0.967	<0.001
Self-efficacy	0.807	<0.001
Mpox practice score	0.803	<0.001
Mpox KAP score	0.980	<0.001

Abbreviation: KAP=Knowledge, Attitude, and Practice.

SUPPLEMENTARY TABLE S3. List of mpox knowledge among subjects.

Knowledge dimension	Serial number	Items	Correct No.	Rate of correct answer (%)
Basic cognition	Q1	Mpox is a viral infectious disease.	994	80.5
	Q2	Mpox is a bacterial infectious disease.	519	42.0
	Q3	The current worldwide epidemic of mpox occurs mainly in tropical rainforest areas and occasionally in other areas.	488	39.5
Epidemiological characteristics	Q4	Do you know what are the sources of infection for mpox?	862	69.8
	Q5	Do you know the time interval between mpox infection and the onset of symptoms?	625	50.6
	Q6	Mpox can be transmitted from animals to humans through direct contact with the blood, body fluids, and consumption of undercooked meat of infected animals.	724	58.6
	Q7	Mpox can be transmitted from person to person through contact with respiratory secretions, blood, and body fluids of infected person.	953	77.2
	Q8	Mpox can be transmitted sexually.	1,007	81.5
	Q9	People are generally susceptible to mpox.	480	38.9
Clinical manifestation	Q10	Mpox and smallpox have similar signs and symptoms.	661	53.5
	Q11	Will people experience fever, runny nose, sore throat, and other cold symptoms in the early stages after being infected with mpox?	805	65.2
	Q12	How long does mpox rash usually appear after onset?	134	10.9
	Q13	After infection with mpox, will there be lymphadenopathy?	659	53.4
	Q14	After infection with mpox, will muscle pain and severe headache occur?	647	52.4
	Q15	Mpox is a self-limited disease with symptoms usually lasting 2-4 weeks.	581	47.0
Prevention	Q16	Can 20 seconds of regular hand washing with soap or alcohol-based hand sanitizer prevent mpox transmission?	550	44.5
	Q17	Can mpox transmission be prevented by avoiding contact with wild animals (live or dead) or by adequately cooking wild animal products?	661	53.5
	Q18	Can mpox transmission be prevented by avoiding any object that has been in contact with a mpox patient/sick animal?	866	70.1
	Q19	Can reducing the number of sexual partners reduce the risk of mpox transmission?	930	75.3
	Q20	Can transmission of mpox be prevented by avoiding contact with anyone with rash?	196	15.9
Treatment	Q21	The treatment of mpox should be based on symptomatic and supportive treatment.	824	66.7
	Q22	Can Paracetamol be used to treat patients with mpox fever?	313	25.3
	Q23	Are antibiotics effective in the treatment of mpox?	212	17.2
	Q24	For AIDS patients co-infected with mpox, can effective ART improve the treatment effect of mpox?	308	24.9
	Q25	So far, there is no effective cure for mpox. Is that correct?	653	52.9

Abbreviation: AIDS=acquired immunodeficiency syndrome; ART=antiretroviral therapy.

SUPPLEMENTARY TABLE S4. Mpox attitude total and dimensional scores.

Variables	Range of scores	Score M (Q25, Q75)*	Standardized score M (Q25, Q75)*	Explanation
Mpox attitude score	16.00–80.00	61.00 (56.00, 66.00)	3.81 (3.50, 4.12)	
Susceptibility	3.00–15.00	12.00 (10.00, 13.00)	4.00 (3.33, 4.33)	Individual's subjective feelings about the possibility of suffering from mpox.
Seriousness	3.00–15.00	12.00 (10.00, 14.00)	4.00 (3.33, 4.67)	Individual's subjective perceptions and feelings about the severity of mpox.
Benefits	4.00–20.00	16.00 (14.00, 20.00)	4.00 (3.50, 5.00)	Individual's subjective perceptions and feelings about the benefits obtained by taking healthy behaviors.
Barrier	4.00–20.00	13.00 (10.00, 16.00)	3.25 (2.50, 4.00)	Individual's subjective perceptions and feelings of difficulties or obstacles that may be encountered in mpox prevention.
Self-efficacy	2.00–10.00	8.00 (8.00, 10.00)	4.00 (4.00, 5.00)	Individuals confidence in developing good sexual behaviors.

* The normality test results of mpox attitude scores and scores in all dimensions showed that the data did not follow normal distribution (P<0.05) (Supplementary Table S2). Therefore, median and interquartile intervals were used to describe attitude scores.

Review

The Current State and Progress of Mpox Vaccine Research

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ABSTRACT

On July 23, 2022, the World Health Organization (WHO) declared the monkeypox (mpox) outbreak a "Public Health Emergency of International Concern." Since 2022, outbreaks of mpox in many countries around the world have primarily resulted in fatalities among immunocompromised individuals, such as untreated HIV/AIDS patients. Since the eradication of smallpox was declared by the WHO in 1980, the global vaccination against smallpox has been gradually discontinued. China also stopped routine smallpox vaccination in 1981. The protective effect of the smallpox vaccine has decreased over time due to aging and declining immunity in those who were vaccinated. For individuals, timely vaccination against smallpox is an effective means of protection against mpox. However, due to safety concerns with the smallpox vaccine and the limitations of current mpox vaccines, there is no vaccine that is safe, effective, and has low side effects applied in clinical settings. This article provides a comprehensive review of the development of mpox virus (MPXV) vaccines, their application in special populations, and the current state of vaccine research, considering the etiology, transmission, and prevention of the MPXV. Vaccination, as an effective method of epidemic prevention, can provide long-term immune protection and effectively reduce the severity of infection. However, as there is no licensed specific MPXV vaccine available globally, the vaccines currently used for mpox prevention are mostly smallpox vaccines. These smallpox vaccines can offer some degree of protection against mpox by activating cross-protection in the body.

INTRODUCTION

Overview of Mpox Virus (MPXV)

MPXV belongs to the Orthopoxvirus genus of the Poxviridae family, which includes other members like smallpox virus, vaccinia virus, cowpox virus, and rabbitpox virus, among its 14 members (*1*). MPXV is an enveloped double-stranded DNA virus with a size of about 200–250 nm, surrounded by a lipoprotein outer membrane, appearing oval or brick-shaped. Studies indicate that secondary transmission of MPXV among humans mainly occurs through prolonged contact with infected individuals, respiratory droplet transmission, direct or indirect contact with bodily fluids, and contaminated sources (*2*). Additionally, vertical transmission of the MPXV has been confirmed. In pregnant women infected with mpox, the virus's DNA can be detected in fetal tissue, the umbilical cord, and the placenta (*3*). Recent cases of mpox in multiple countries have shown that transmission through intimate contact, especially sexual transmission, is increasing. A report published in August 2022 identified MPXV in semen (*4*) and recent reports from various countries have linked mpox infections to close contact among males, primarily through sexual activity. The characteristic of close-contact transmission of the MPXV suggests that the infected population will continue to expand, with cases among women already reported internationally (*5*) and the first female case reported in the mainland of China on September 8, 2023.

The Development History of the Smallpox Vaccine

Due to the high genetic sequence similarity among Orthopoxviruses, they share many immunological epitopes and markers. The earliest evidence from animal studies in the 1960s showed that antibodies induced by the smallpox vaccine could bind and recognize various Orthopoxvirus proteins, providing cross-protection against mpox (*6*). Most people who were vaccinated with the Tian Tan strain (smallpox vaccine) before 1981 still maintain a certain level of MPXV-specific antibodies. Most of the Chinese population maintains vaccinia virus-specific IgG antibodies for 42 years or longer after vaccination, offering some degree of protection against mpox (*7*). This enduring immunity aligns with other studies indicating that smallpox vaccines, including more recent versions, offer effective cross-immunity against

mpox. This applies both as pre- and post-exposure prophylaxis (*8*). An England study demonstrated a 78% effectiveness of the Modified Vaccinia Ankara - Bavarian Nordic (MVA-BN) vaccine in preventing symptomatic Mpox 14 days after initial pre-exposure vaccination (*9*). Additionally, an observational study from the 2022 outbreak showed that post-exposure vaccination with a third-generation smallpox vaccine had an adjusted effectiveness of 88.8% [95% confidence interval (*CI*): 76.0–94.7] (*10*).

Historically, the smallpox vaccine has undergone several iterations and upgrades. Based on the vaccine's preparation methods and protective principles, the smallpox vaccines used in clinical settings and those currently approved are divided into three generations (Table 1).

First-Generation Live Virus Vaccines

The first-generation smallpox vaccines were prepared from live, non-attenuated vaccinia viruses (VACV). Strains commonly used for producing the first-generation smallpox vaccines include the NYCBH strain (used in West Africa and North America), Lister/Elstree strain (UK), Tian Tan strain (China), and EM-63 strain (Russia and India) (*11*). With the rapid development of "vaccine farms" in the United States and Europe (*12*), extracting the virus from animals and preparing smallpox vaccines became a widely adopted and relatively safe method at the time, contributing significantly to the eventual eradication of smallpox. However, due to the use of live, non-attenuated vaccinia viruses sourced from live animals, the first-generation vaccines had notable safety and reliability concerns. Tens of deaths per million vaccinations were reported with the NYCBH strain, and up to 200 deaths per million occurred during the vaccination process with the Lister strain (*13*). The Dryvax vaccine, prepared from the NYCBH strain, could lead to side effects such as acute vaccinia syndrome, vaccine-related myocarditis, or myopericarditis (*14*). Due to these safety concerns and side effects, the use of first-generation smallpox vaccines has been discontinued.

Second-Generation Live Virus Vaccines

To reduce microbial contamination seen in the production of first-generation vaccines and to improve the side effects associated with them, second-generation vaccines utilized tissue culture or cell line cultures of live vaccinia virus, replacing the original vaccine production method. Main products of the second generation include ACAM1000, ACAM2000, CJ-50300, and APSV.

ACAM1000 and ACAM2000, derived from monoclonal virus isolates of the first-generation Dryvax vaccine, have shown immunogenicity in tests that are comparable to the first-generation live virus vaccines (*15*). They exhibit a reduced level of severe side effects

TABLE 1. The development of smallpox vaccines.

Generation	Vaccine name	Strain name	Preparation method	Advantages	Disadvantages
First-generation live virus vaccine	Dryvax	NYCBH strain	Unattenuated live vaccinia virus	Made significant contributions to the global eradication of smallpox campaign.	Live virus safety and reliability are lower, can produce serious side effects.
	Lister	Lister strain			
	Tiantan	Tiantan strain			
Second-generation live virus vaccine	ACAM2000	NYCBH strain	Unattenuated live vaccinia virus	Improved and simplified the production process of the first-generation vaccine, enhancing safety.	There is a certain probability of exhibiting serious adverse reactions, performing poorly in patients with compromised immune function.
	Elstree-BN	Lister strain			
	CJ-50300	NYCBH strain			
Third-generation attenuated vaccine	MVA	Ankara strain	Attenuated live vaccinia virus	Significantly improved safety, the strain's replication capability is reduced, suitable for patients with compromised immune function.	Situations with relatively low levels of neutralizing antibodies in vaccinated individuals exist, clinical reliability needs to be verified.
	LC16m8	Lister strain		Compared to the first and second-generation smallpox vaccines, enhanced safety, reduced theovvurrence of adverse reactions.	Clinical reliability needs to be verified.
	NYVAC	Copenhagen strain		Enhanced safety.	
	dVV-L	NYCBH strain			

compared to the first-generation vaccines but can still cause serious side effects, including encephalitis, encephalomyelitis, encephalopathy, and erythema multiforme. These vaccines are contraindicated in individuals with compromised immune function [such as those with leukemia, lymphoma, human immunodeficiency virus (HIV), infections, and acquired immune deficiency syndrome (AIDS)], potential heart disease, and in pregnant women. ACAM2000 carries a risk of causing myocarditis and/or pericarditis, with an average of 5.7 cases per 1,000 primary vaccine doses (*16*). In 2007, ACAM2000 was licensed by the U.S. Food and Drug Administration, replacing Dryvax as the only available smallpox vaccine in the United States (*17*).

Third-Generation Attenuated Vaccines

Compared to the unattenuated live viruses used in the first two generations of vaccines, the third generation selected vaccinia viruses that had been passaged multiple times, resulting in reduced virulence and replication capabilities. There are mainly four strains used for the third-generation attenuated vaccines: Ankara strain, Lister strain, Copenhagen strain, and NYCBH strain. Among these, the Modified Vaccinia Ankara (MVA) vaccine and the LC16m8 vaccine are particularly representative (*18*).

The Ankara strain vaccine for the modified vaccinia virus. Replication of MVA is weakened in primary chicken embryo fibroblast (CEF) cells after more than 570 continuous passages, making it suitable for the preparation of third-generation attenuated smallpox vaccines. The reduced replication ability of MVA in mammals (*19*) makes it an ideal choice for immunocompromised patients (*20*). Clinical efficacy data show that volunteers who received two doses of MVA vaccine achieved similar overall peak neutralizing antibody titers to those observed after a single dose of ACAM2000 vaccine (*21*). Although no safety issues related to MVA vaccine have been reported so far (*22*), the administration of this vaccine can still cause certain side effects, including injection site reactions, headache, myalgia, fatigue, nausea, fever, and lymphadenopathy. There are also reports indicating that the levels of neutralizing antibodies against MPXV generated by the administration of two doses of JYNNEOS vaccine in healthy individuals are relatively low with poor neutralizing capacity (*21*).

The LC16m8 vaccine. In the 1970s, Japan developed a highly attenuated live vaccine, LC16m8, at the Chiba Serum Institute, aiming to replace first-generation vaccines such as Lister and Dryvax. The virus in LC16m8 is attenuated due to the lack of the B5R envelope protein gene, and its replication ability in vaccine recipients is limited (*23*). LC16m8 showed no severe adverse reactions in 100,000 infants and was proven to have the same immunogenicity as its parent strain. Although LC16m8 is the only smallpox vaccine approved for use in children, its effectiveness against MPXV in humans has not yet been reported. In response to mpox outbreaks, LC16m8 has been approved in Japan as a smallpox vaccine for children and other non-immunocompromised individuals (*24*). Side effects of the LC1618 vaccine include lymph node enlargement, fatigue, fever, rash, erythema, and swelling at the injection site, with side effects being more common in first-time vaccine recipients than in those receiving revaccination.

The development of smallpox vaccines has undergone significant advancements in three generations. The initial generation employed live, non-attenuated vaccinia viruses, specifically the NYCBH and Lister strains. Although effective, these vaccines raised safety concerns. The second generation, exemplified by ACAM2000, improved safety by utilizing tissue culture methods but still posed risks for certain populations. The third generation vaccines, such as MVA and LC16m8, offered enhanced safety with reduced virulence, making them suitable for a broader range of individuals, including those with compromised immune systems.

THE APPLICATION OF SMALLPOX VACCINE

The Application of Smallpox Vaccine in Susceptible Populations

To address the increasingly severe mpox outbreak, medical institutions worldwide have implemented widespread measures. Containment of mpox requires a comprehensive approach, which includes pre- and post-exposure vaccinations for at-risk groups, early detection and screening, isolation or minimizing close contact, and dissemination of accurate information to potentially exposed individuals. The development and application of vaccines are particularly important. The MVA-BN-based JYNNEOS vaccine was approved by the U.S. Food and Drug Administration (FDA) on September 24, 2019, for the prevention of smallpox and mpox diseases (*25*). On June 23, 2023, JYNNEOS (also known as Imvamune or Imvanex)

became the only FDA-approved non-replicative smallpox and mpox vaccine for both military and non-military purposes. Currently, there are three options for mpox vaccination: ACAM2000, MVA-BN, and LC-16. All three vaccines have been approved for use against mpox in various jurisdictions. However, it is important to note that their availability varies across different geographical regions (*26*). The similarities and differences among these three vaccines are summarized in Table 2.

Application of smallpox vaccine in immunocompromised populations. Individuals with impaired immune function include those with active cancer, organ transplant recipients, those with immunodeficiencies, people undergoing immunosuppressive therapy, and HIV-infected individuals. Considering the principles of vaccine preparation, contraindications, and clinical trial results of various vaccines, not all smallpox vaccines are suitable for immunocompromised populations. For instance, ACAM2000 is not recommended for individuals with severe immunodeficiency, as it may cause severe localized or systemic vaccinia skin ulcer infections in those with weakened immune systems; LC16 is also not suitable for individuals with severe immunodeficiency or those undergoing immunosuppressive treatment (*23*), among others.

In a study involving 24 hematopoietic stem cell transplant recipients, researchers randomly divided the subjects into two groups, with one group receiving the MVA-BN vaccine, and then compared neutralizing antibody titers between the groups. The results showed that no vaccine-related severe adverse reactions occurred in the MVA-BN group, and the antibody titers indicated good immunogenicity of MVA-BN in this population (*27*). Another Phase II trial involving HIV-infected individuals (previously with AIDS) assessed the safety, tolerability, and immunogenicity of three dosing regimens of MVA-BN, concluding that MVA-BN demonstrated good tolerability and immunogenicity in the study population (*28*). These findings suggest that for patients with immunosuppression, high risk of infection, or exposure to vaccinia skin ulcer cases, priority should be given to vaccination with the MVA-BN vaccine.

Application of smallpox vaccine to pregnant women and newborns. The MPXV has been proven to be transmissible vertically, making pregnant women a focus of concern during mpox outbreaks. There is an urgent need to explore effective means to protect pregnant women and newborns. A case of household transmission following smallpox vaccination was reported in 2004 (*29*), where a male member of the household was vaccinated with the second-generation live virus vaccine ACAM2000. A week later, his wife developed vesicles on her areola. Approximately two weeks later, their breastfed daughter developed papules, and the PCR test for the smallpox virus was positive. This was the first global case of mother-to-child transmission via breastfeeding following vaccination. The CDC explicitly prohibits the vaccination of pregnant women, breastfeeding women, and infants under one year of age with the ACAM 2000 vaccine (*30*).

Compared to the ACAM 2000 vaccine, the JYNNEOS vaccine is a non-replicating, attenuated live vaccinia virus vaccine. JYNNEOS was tested in developmental toxicity studies in rats and rabbits. None of these studies reported vaccine-related fetal malformations, developmental delays before weaning, or impacts on maternal fertility (*31*). Currently, there is no clear evidence indicating a definitive relationship

TABLE 2. Similarities and differences of ACAM2000, JYNNEOS, and LC16m8 vaccines.

Feature	ACAM2000	JYNNEOS	LC16m8
Vaccine Type	Live vaccine, based on Vaccinia virus	Live, non-replicating vaccine, based on Modified Vaccinia Ankara	Live, attenuated vaccine, based on Vaccinia virus
Composition	Vaccinia virus	Modified Vaccinia Ankara	Vaccinia virus from Lister strain
Effectiveness	High efficacy, similar to Dryvax	Verified in clinical studies, similar immune response to ACAM2000	Good safety and immunogenicity shown in Japanese clinical trials
Side Effects	Muscle pain, fever, myocarditis and/or pericarditis, etc.	Redness, pain, swelling, and itching at the injection site, fatigue, headache, and muscle pain	Limited detailed information, but generally considered to have fewer side effects
Applicable Population	Not suitable for people with immune deficiencies, HIV, and potential heart disease, and in pregnant women, etc.	Vaccination may be postponed for certain groups(e.g., pregnant, breastfeeding women)	Widely used in children and adults(non-immunocompromised individuals)
Method of Administration	Bifurcated needle	Needle and syringe(subcutaneous administration)	Bifurcated needle
Storage Conditions	Generally refrigerated	Generally refrigerated	Generally refrigerated

between the use of JYNNEOS vaccine in pregnant women and pregnancy outcomes.

International cross-sectional studies on the vaccination of newborns with live smallpox vaccines indicate that the risk of adverse reactions to the vaccine in infants under one year old is very high. However, there is still no global consensus on the most appropriate timing for vaccinating newborns against smallpox.

THE NEW GENERATION OF MPOX VACCINES

Preparation of The New Generation of Mpox Vaccines

Despite the important role of smallpox vaccines in combating the current MPXV outbreak, their efficacy is still questioned. Their side effects and limitations in application hinder their protective function in specific populations, and their effectiveness in controlling and preventing MPXV is not entirely satisfactory. Therefore, in response to the current mpox outbreak, there is an urgent need for a safer, more effective, and highly specific vaccine targeted specifically at the MPXV. However, the research progress on mpox vaccines faces several challenges, including slow progress in animal experiments, lack of clinical trial data, and issues related to the current variations and specificity of the MPXV.

Recent reports have identified several potential vaccine targets for the MPXV and highlighted effective immunogens (such as L1R, B5R, A27L, and A33R). These immunogens can be integrated into vaccines to enhance their protective effect against MPXV infection. At the same time, due to the mechanisms of MPXV transmission and infection, intracellular mature virions (IMV) and extracellular enveloped virions (EEV) are also expected to become important targets for the development of specific vaccines against mpox (*32*).

The 4pox DNA Vaccine

The 4pox DNA vaccine is developed targeting the immunogenic sites L1, A27, B5, and A33. Compared to mRNA vaccines, which have less stability and require drug delivery systems such as lipid nanoparticles (LNP) to deliver mRNA to target cells, the 4pox DNA vaccine does not require formulation and has sufficient immunogenicity as demonstrated by researchers (*33*). Additionally, it offers protection similar to traditional smallpox vaccines (ACAM2000, MVA) and demonstrates superior performance in preventing virus transmission, reducing the likelihood of viral shedding.

Studies have shown that the 4pox DNA vaccine, inducing an immune response with a small amount of viral antigen, can produce protective immunity against lethal orthopoxvirus attacks in mice and non-human primates. In the MPXV model of non-human primates, two doses of the 4pox DNA vaccine provided protection equivalent to MVA (*34*). Subsequent studies further proved the effectiveness of the 4pox DNA vaccine in preventing aerosolized poxvirus in highly susceptible animal models (*33*). However, this vaccine has not yet undergone clinical validation, and further investigation is needed to assess its safety and reliability for human use.

Multivalent MRNA Vaccines

The principle of DNA and mRNA vaccines involves injecting genetic material into the host to express target proteins, thereby eliciting cellular and humoral immunity. In recent years, numerous research institutions globally have focused on the development of mRNA vaccines and have made certain advancements.

Internationally, research institutions have designed a multivalent mRNA vaccine candidate, MPXVac-097, targeting five MPXV antigens: A29L, E8L, M1R, A35R, and B6R. This vaccine has demonstrated specific T-cell responses against MPXV and protection against vaccinia virus attacks in mouse models (*35*). Domestic research targeting the mature virion (MV) and enveloped virion (EV) particles involved in MPXV replication has produced four types of mRNA vaccines using combinations of antigens from EV (A35R and B6R), MV (A29L, E8L, H3L, and M1R), and surface proteins of EV and MV (*36*). These vaccines were evaluated in mice for their protective efficacy. Studies indicate that mRNA vaccines with various combinations of EV and MV surface antigens protect the mouse model from lethal doses of vaccinia virus, with the vaccine containing both EV and MV antigens providing the strongest protection, laying the groundwork for the further development of safe and effective mRNA vaccines.

Protein-Based Subunit Vaccines

Subunit vaccines, unlike attenuated or live virus vaccines, do not contain the complete pathogen but

typically only antigenic components, such as proteins or polysaccharides, theoretically eliminating the risk of causing the disease. However, subunit vaccines also have drawbacks: they often require adjuvants or booster shots to achieve the desired efficacy in recipients. Researchers have experimented with vaccines in mice using CpG-ODN and aluminum as adjuvants, containing envelope proteins from MV and EV. Mice vaccinated with these showed significantly lower viral titers compared to the unvaccinated control group (*37*). Currently, protein-based subunit vaccines are still at the laboratory stage and have not yet undergone related clinical trials.

THE CURRENT PROGRESS OF MPOX VACCINE IN CHINA

Recently, there has been a focus on the development of mRNA vaccines in Chinese research institutions. Studies have shown that multivalent mRNA vaccines, which combine various EV and MV antigens, offer better protection in mouse models compared to traditional vaccines (*36*). The China National Biotec Group (CNBG) research team has encoded the mpox proteins M1R and A35R, and their research has demonstrated promising immune responses against A35R and M1R. They have tested three poxvirus mRNA vaccines (VGPox 1-3), which have shown similar levels of A35R antibodies. The mRNA encoding a fusion form of A35R and M1R (VGPox 1 and VGPox 2) effectively induces high levels of A35R and M1R IgG and can neutralize live viruses at early stages (*38*). The research team at the Seventh Affiliated Hospital of Sun Yat-sen University has selected highly conserved targets, including A27, A33, B5, and L1 antigens, using a 2003 isolate from Clade II of the mpox evolutionary branch. Serum from all mice was collected 21 days after the first immunization to assess humoral immunity. The combination of the four types of mRNA-LNP resulted in average IgG titers of 3,000, 4,965, 22,518, and 14,388, targeting each of the four MPXV antigens respectively. This provides strong evidence for the efficacy and safety of the vaccine (*39*).

Currently, there is no available vaccine against mpox in the Chinese population. However, domestic development of mpox vaccines is progressing rapidly, with China's own Mpox mRNA vaccine soon to enter clinical trials. According to "mpox prevention guideline for the public (2023)" released by the National Institute for Infectious Diseases (Huashan Hospital, Fudan University) and the Chinese Preventive Medicine Association, mpox vaccination is currently not recommended for the general population (*40*). However, research shows that there is a low vaccine hesitancy rate among high-risk populations, particularly men who have sex with men (MSM) in China. It is essential to enhance health education and implement the mpox vaccine inoculation plan to address the current mpox situation (*41*).

CONCLUSION AND DISCUSSION

On May 12, 2023, WHO declared that the mpox outbreak no longer constituted a Public Health Emergency of International Concern. However, the number of confirmed mpox cases in China is still on the rise, with 491 cases reported in July, a significant increase from 106 cases in June. In response, the National Health Commission of China included mpox in the category B infectious diseases for management on September 20, 2023, adopting preventive and control measures for category B infectious diseases. These developments not only reflect the challenges in epidemic prevention and control and the continuous risk of imported cases in China but also provide a realistic basis for the application and development of mpox vaccines in the mainland of China.

In light of the current progress in vaccine research both domestically and internationally, protection against MPXV still relies on the application of smallpox vaccines. The first-generation smallpox vaccines have been largely replaced by second and third-generation vaccines. These newer generations of smallpox vaccines are produced through more advanced and modern cell culture methods and have shown good immune effects in treating mpox and other orthopoxvirus diseases. Clinical trials have confirmed that smallpox vaccines, represented by MVA-BN, have not caused severe adverse reactions in immunocompromised individuals, providing an important basis for expanding the eligible population for vaccination and reducing the mortality rate of mpox infections.

Currently, countries are intensifying efforts to develop next-generation (fourth-generation) vaccines. These efforts aim to address issues related to manufacturing processes and the ability to rapidly respond to new poxviruses, with the hope of further enhancing safety and protection, reducing the pathogenicity and transmissibility of the MPXV. The new generation of mpox-specific vaccines is expected to

be more suitable for vaccination in populations with immune deficiencies, skin diseases, or cardiovascular conditions. Although these vaccines are mostly in the experimental stage and have not yet entered clinical trials, requiring long-term testing and observation to verify their safety and reliability, the current results from related animal experiments strengthen our confidence in the new generation of vaccines for the prevention and treatment of mpox.

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Outbreak Reports

A Case of Acute HIV-1 and Monkeypox Coinfection After Condomless Insertive Anal Sex in the Previous 69 Days — Beijing Municipality, China, August–October, 2023

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Summary

What is already known about this topic?

The prevalence of monkeypox (mpox) infections is primarily observed among young men who engage in sexual activities with other men, and there is a possibility of sexual transmission. Co-occurring sexually transmitted infections have also been documented.

What is added by this report?

In this report, we present a case of a patient in China who was simultaneously diagnosed with mpox, and acute human immunodeficiency virus (HIV) infection. The patient exhibited symptoms of fever and widespread papules on the trunk, face, and genital area.

What are the implications for public health practice?

It is crucial for health agencies to prioritize HIV testing when mpox is suspected or diagnosed in individuals with recent engagement in high-risk sexual behavior.

Ongoing mpox infections reported in countries outside of Africa exhibit distinct characteristics. These infections are primarily observed in men who have sex with men (MSM) (*1*). Sexual intercourse is responsible for transmitting 95% of these infections, with a prevalence of 98% among MSM (*1*). The majority of cases present with well-defined, firm skin lesions that display a central indentation. These lesions are commonly found on the genitalia, anogenital area, oral mucosa, or rectal mucosa, which aligns with sites of skin contact during sexual activities. Published studies indicate that up to 50% of these infections involve co-infection with at least one other sexually transmitted infection (STI) (*2*). Previous research has shown that 28%–47% of the confirmed cases involve individuals living with human immunodeficiency virus (HIV) (*3*).

The high rates of sexually transmitted infections (STIs) among MSM with mpox emphasize the importance of STI testing. Inflammatory and ulcerative mucosal conditions, as well as STI pathogens, are closely linked to the acquisition and transmission of HIV. In this report, we present a case of acute HIV infection in a person who was being evaluated for mpox at our hospital, a referral center for monkeypox virus (MPXV) infection in Beijing Municipality, China.

INVESTIGATION AND RESULTS

A 29-year-old cisgender man presented with a fever (maximum temperature of 39 °C) that began within the past 7 days after a night of heavy drinking following his layoff from work. He subsequently developed a sore throat, non-productive cough, vomiting, painful inguinal lymph node swelling, and skin lesions on his genitalia and perineum, as well as more distant lesions on his trunk, face, and limbs. On August 17, 2023, he was admitted to Beijing Youan Hospital as a suspected mpox case. He denied any relevant medical history and had no history of recent travel to areas with known infections or direct contact with individuals suspected or confirmed mpox before symptom onset. Physical examination revealed pharyngeal congestion, swollen tonsils, redness and swelling of the penis, and painful inguinal lymph node swelling, as well as diffuse skin lesions on the genitalia (Figure 1), trunk, face, and limbs.

He engaged in insertive condomless anal intercourse on August 3, 2023, with a partner whose HIV status was unknown. This occurred 14 days before the first appearance of a genital lesion. The individual reported conducting monthly HIV self-tests using rapid tests, as a precautionary measure due to concerns about acquired immunodeficiency syndrome (AIDS). All previous showed negative including the most recent one performed on August 10, 2023. The individual did not receive preexposure prophylaxis or postexposure prophylaxis for HIV.

Samples of skin lesions and oropharyngeal swabs

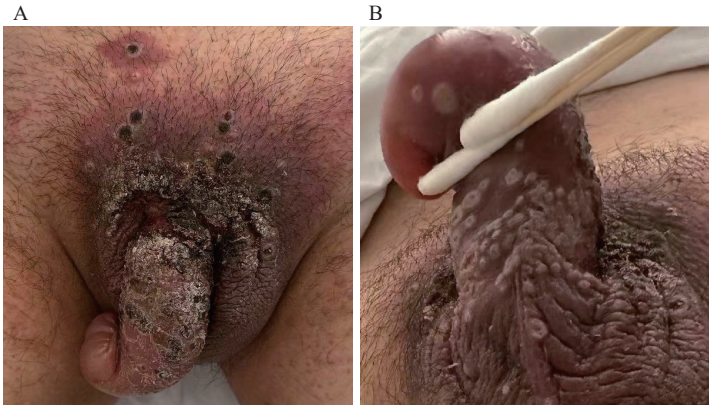

FIGURE 1. Skin lesions on the genitalia and perineum of the confirmed mpox case. (A) Several grouped umbilicated whitish papules on the perineum; (B) several grouped umbilicated whitish papules on the genitalia.

were collected from the patient for MPX-specific real-time polymerase chain reaction (rtPCR) assays conducted at China CDC. Confirmed cases are defined as individuals with positive PCR assay results [cycle threshold (Ct) value <40] for any type of sample. The patient's skin lesion (Ct 21.23) and oropharyngeal (Ct 31.97) samples tested positive for MPX PCR. The patient received care in an adult isolation unit where measures were taken to manage pain, prevent dehydration, and administer antibiotics for skin and soft tissue infection, according to National Guideline for Mpox Prevention and Control (*4*). As part of the routine initial laboratory assessment, we conducted an HIV rapid test using the HIV Ab test (Abogen Biosciences, China), which yielded a negative result. However, the patient's CD4 cell count was found to be only 34 cells/mm^3.

To further investigate, we performed a nonreactive 3rd generation serological test for HIV (Genscreen HIV 1/2, Bio-Rad). Subsequently, an HIV RNA test (m2000sp-m2000rt, Abbott Diagnostic, Chicago, IL) was conducted and showed a viral load of more than 1000,0000 copies/mL, indicating acute HIV infection. To verify these results, the HIV RNA test was repeated, yielding the same outcome.

On September 12, 2023, which was 39 days after the high-risk sexual behavior, an indeterminate result was obtained from the 4th-generation serological test for HIV (ARCHITECT HIV Ag/Ab Combo Abbott), along with the presence of p24 bands in the GEENIUS HIV 1/2 Bio-Rad immunoblot test (the Western Blot test, WB). Subsequently, on September 27, 2023, the 4th-generation serological test for HIV showed a reactive result, and on October 12, 2023, which was 69 days post the high-risk sexual behavior, the immunoblot test confirmed the presence of p17, p24,

TABLE 1. CD4 count, viral markers, and antibodies of HIV in the blood of the confirmed mpox case.

Test items	August 17, 2023	August 24, 2023	September 1, 2023	September 12, 2023	September 27, 2023	October 12, 2023	November 5, 2023
The viral shedding of MPXV (Ct value)							
Skin lesion	21.23	NA	NA	NA	Negative (scab)	NA	NA
Oropharyngeal	31.97	NA	NA	31	Negative	NA	Negative
CD4 count (cells/mm^3)	34	44	99	265	347	NA	410
HIV RNA (copies/mL)	NA	>10,000,000	>10,000,000	1,097	44	NA	TND
3rd generation serology for HIV	Negative	Negative	NA	Negative	Negative	Positive	Positive
4th generation serology for HIV	NA	NA	NA	Indeterminate	Positive	NA	Positive
Western blot	NA	NA	NA	Indeterminate (P24)	NA	Positive (p17, p24, gp41, gp120, gp160)	Positive (p17, p24, p31, gp41, gp120, gp160)

Note: The case reported a potential expose event of engaging in insertive condomless anal intercourse on August 3, 2023; and self-tested for HIV by a rapid HIV test with a negative result on August 10, 2023.
Abbreviation: NA=not available; TND=target not detected; MPXV=monkeypox virus; HIV=human immunodeficiency virus.

gp41, gp120, and gp160 bands. The results of the HIV tests conducted are summarized in Table 1. Following the diagnosis of acute HIV infection, the patient was initiated on antiretroviral treatment (ART) with bictegravir sodium, emtricitabine, and tenofovir alafenamide fumarate tablets on September 1, 2023.

The patient was found to be negative for hepatitis B, hepatitis C, and syphilis. Table 2 displays the laboratory test results at admission and during the follow-up after medical evaluation. The patient did not experience any complications related to the disease. The symptoms improved rapidly, and the skin lesions were completely scabbed or desquamated. He was discharged on September 11, 30 days after the first lesion was reported. During a follow-up visit on November 5, 2023, approximately two months after initiating ART, the patient tested negative for HIV RNA, and his CD4 cell count was measured at 410 cells/mm^3. The immunoblot test revealed the presence of p17, p24, p31, gp41, gp120, and gp160 bands, indicating a positive result. Additionally, a reactive 3rd-generation serological test confirmed the presence of HIV antibodies. The time from the history of HIV exposure within three months to the appearance of HIV antibodies was estimated.

DISCUSSION

The confirmed mpox case with acute HIV coinfection was confirmed by a nonreactive HIV rapid test enzyme immunoassay (EIA) that detects IgG to HIV, a 3rd-generation EIA test (IgM sensitive) for HIV, and a positive HIV RNA test. Additionally, the results of the 4th-generation antigen-antibody combination EIA, which detects p24 antigen, HIV IgM, and IgG antibodies, changed from indeterminate to positive. The immunoblot test for the presence of p24 also changed from indeterminate to positive, confirming the patient's acute HIV infection stage as Fiebig Ⅱ (*5*). The diagnosis of acute HIV is nearly always missed; however, most infected individuals remain ignorant of their HIV status until after the onset of AIDS. This is the first reported case of concurrent acute viral HIV and mpox coinfection in the Chinese mainland, highlighting the potential of mucosal surfaces as a route of concomitant acquisition of both infections. Similar cases of mpox with a concurrent acute HIV infection have been reported in Latin America, Portugal, and Brazil, where the HIV test results showed positive HIV RNA and positive HIV-1 antigen with a negative anti-HIV 1/2 antibody result (*6*–*8*). In an Italian case, mpox and recent HIV infection were diagnosed, and the patient had positive anti-HIV serology (*9*).

To our knowledge, the 3rd/4th generation HIV assays have shown higher sensitivity compared to the WB assay. In this case, both the 4th generation HIV serology assay and the WB assay yielded indeterminate results on September 12. However, the 3rd generation HIV assay using a gold-labeled reagent yielded a

TABLE 2. Laboratory tests at admission and follow-up of medical assessment.

Clinical index	August 17, 2023	August 21, 2023	August 24, 2023	August 29, 2023	September 11, 2023
Total leukocytes count (×10^9/L)	11.80	4.41	1.80	1.95	5.24
Neutrophil count (×10^9/L)	8.30	3.49	1.20	1.36	3.50
Lymphocyte count (×10^9/L)	1.50	0.70	0.55	0.44	1.00
Monocyte count (×10^9/L)	1.80	0.20	0.05	0.07	0.70
Hemoglobin (g/L)	135	132	131	123	127
Platelets (×10^9/L)	157	155	152	177	439
C-reactive protein (mg/L)	156.0	75.0	19.1	24.5	18.1
Procalcitonin (ng/dL)	0.22	0.20	0.13	0.10	0.07
ALT (U/L)	32	30	23	25	31
AST (U/L)	35	36	42	41	40
Total bilirubin (μmol/L)	6.1	6.0	5.1	5.5	6.5
Albumin (g/L)	33.5	34.0	36.2	38.0	41.2
Creatinine (μmol/L)	85	83	81	82	88

Abbreviation: ALT=alanine transaminase; AST=aspartate aminotransferase.

negative result. This discrepancy can be attributed to the different coated antigens used in the assays. The WB assay utilizes cleaved HIV-1 virus as the coated antigen, while the 3rd generation Abbott reagent uses genetically engineered gp41 and p24 antigens. The variations in the source and preparation of the coated antigens could explain why the window period for detecting single antibody reactions with the WB assay may be shorter than that of the 3rd generation gold-labeled reagent. Conversely, the window period for detecting multiple antibody reactions simultaneously with the WB assay may be longer than that of the 3rd generation gold-labeled reagent. This may account for the lack of an advantage of the 3rd generation HIV assay over the WB assay in this case.

On October 12th, both the 3rd generation HIV serology assay and the WB assay for multiple antibodies yielded positive results. This case presents an instance of early-stage acute HIV infection, characterized by the onset of viral latency and a significant increase in plasma levels of viral RNA levels. The rapid expansion of HIV and the subsequent rise in viral RNA levels have substantial clinical implications, as they coincide with the irreversible destruction of helper T cell reservoirs and the establishment of viral latency, which can lead to further adverse consequences. The timeframe from the last known HIV exposure within the past 14 days to the initial clinic visit and the infection date was estimated to be 7 days prior to the appearance of skin lesions. The interval between the detection of p24 antigen and the presence of HIV antibodies is approximately 54 days. The duration of Fiebig II, a specific stage of early HIV infection, is slightly longer than previously reported in other studies (*5*,*10*). Patients with acute early infection pose a higher risk of transmission compared to those with established infection partly due to their high viral load. Early initiation of ART can potentially limit the size of the latent pool of HIV-infected CD4 T cells. It is recommended to choose an ART regimen with a high barrier resistance, such as an integrase inhibitor or protease inhibitor, for optimal suppression of HIV viral load. Compared to previous studies on the concurrent infection of MPXV and acute HIV infection (*6*–*7*), our patient diagnosed with mpox and acute HIV showed a relatively mild clinical course. After initiating ART for less than a month, the patient demonstrated improved HIV control and immune reconstitution. These findings highlight the importance of recognizing HIV infection among MSM presenting with MPXV infections, and the potential link between sexual practices and HIV acquisition.

PUBLIC HEALTH RESPONSE

Patients with suspected mpox should be tested for HIV, unless they have already been diagnosed, particularly if they have engaged in recent high-risk sexual behavior.

Conflicts of interest: No conflicts of interest.

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