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hiv treatment bulletin (e)

Monkeypox outbreaks (1 June 2022)

CONTENTS

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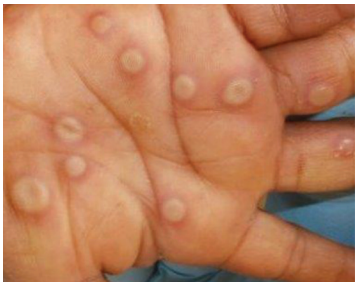
EDITORIAL



This issue of HTB includes several articles on different aspects of the current monkeypox outbreak.

This is important for HTB because the recent outbreak has included a high proportion of cases in people living with HIV.

During the last few weeks small numbers of early cases have led to more than 900 cases globally in more than 25 counties where MPX is non-endemic.

Of these, as of 1 June, more than 200 have been in the UK, 135 in Spain and 100 in Portugal, mostly either in or linked to capital cities.

Nearly all cases are so far in men, the majority being gay or bisexual men

The UK-SHA has published several resources on management and control of cases, including medical management and contact tracing, largely through sexual health clinics. BHIVA issued an early statement, already updated, EACS/ECDC hosted two open webinars and WHO, IAS and the US CDC have hosted similar events.

Good management includes providing clear and accurate information that informs people at highest risk on the importance of self-awareness of symptoms. These are most commonly fever and fatigue, followed by distinctive blisters, that ulcerate and then scab. Cases are infectious from first symptoms until the scab are all resolved. But condoms are currently recommended for eight weeks after the infection is cleared, in case sexual fluids prove to be a reservoir site which takes longer to clear.

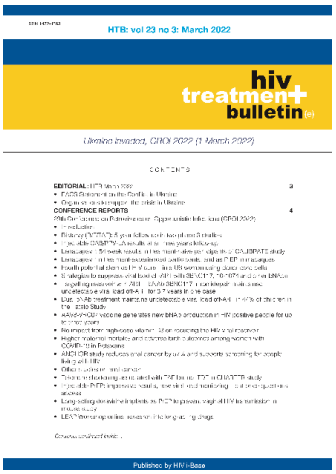
Most cases are mild and self-managed at home without treatment but in isolation, including from pets. Contact tracing is being used to limit further risk and spread.

This is complicated by the need to accurately informing gay and bisexual men without adding to discrimination and having to do this while still in the shadow of COVID-19.

We therefore include articles and linked resources to cover MPV in more detail.

Other contents include:

- Continued support for the war in Ukraine. This includes donating unused medicines and medical supplies and the chance to directly support HIV positive organisations in Ukraine. During the three months since Russia invaded Ukraine, the war has displaced more than 6.8 million people to neighbouring countries.
- Reports from CROI 2022 on the VESTED study and on an option to switch to dolutegravir for people currently stable on darunavir-based second-line ART.
- Optimistic news that generic access to cabotegravir-LA injections might help speed access to this option for PrEP in low income countries.
- Links to the draft BHIVS HIV guidelines, which have a limited time for comments.



Supporting Ukraine

It is more than three months since Russia invaded Ukraine, displacing more than a third of the population and causing more than 6.8 million people to flee to neighbouring countries.

The significant challenges to support people who remain in Ukraine and those who migrated involves both international and community-based organisations.

HTB includes the following two online resources: one to donate unused medicines and the other to highlight a range of organisations that can benefit from direct financial support.

Sending unused meds to Ukraine: emergency appeal

https://i-base.info/htb/42694

The call for HIV and other meds, and medical supplies is still important. This is even though International agencies and drug manufacturers are also organising to meet this demand.

This project is led by EACS and BHIVA and supported by the UK-CAB.

Medicines need to be in original packaging, ideally in unopened packs. All HIV and related meds are acceptable, ***even if they are past the use-by date.***

All donations will be screened beforehand to make sure they are suitable.

The link page includes further details, including postal addresses in the UK, Europe and the US.

Organisations to help support Ukraine

https://i-base.info/htb/42633

This page including 14 organisations that are helping people affected by the crisis in Ukraine.

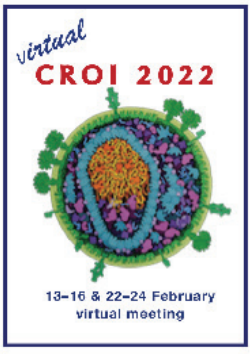
This includes organisations that are supporting people living with HIV that are still in Ukraine or who have migrated to other countries.

CONFERENCE REPORTS

29th Conference on Retroviruses and Opportunistic Infections (CROI 2022): further reports

13–16 and 22–24 February 2022

Introduction



The 29th Conference on Retroviruses and Opportunistic Infections (CROI), was held from 13–16 and 22–24 February 2022.

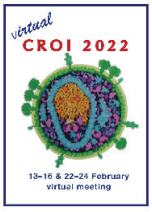
We continue to report from this meeting, with thiss issue including the following two reports.

- Updates from the VESTED study
- Switching to dolutegravir for adults on stable PI-based second-line ART

Updates from the VESTED study

Polly Clayden, HIV i-Base

Four sub-studies from the VESTED trial were presented at virtual CROI 2022. [1, 2, 3, 4]



VESTED (IMPAACT 2010) enrolled 643 women with HIV at 14–28 weeks gestational age in nine countries. [5] Participants were randomised to start ART with dolutegravir (DTG) plus emtricitabine (FTC)/tenofovir alafenamide (TAF); DTG/FTC/tenofovir disoproxil fumarate (TDF); or efavirenz (EFV)/FTC/TDF. Mothers and infants were followed until 50 weeks after delivery.

The trial found all three regimens to be safe and effective in pregnancy but DTG-containing regimens led to better viral suppression and DTG/FTC/TAF to lower adverse pregnancy outcomes. Infants were similar between arms but there was a higher proportion with low birth weight in the EFV arm.

Results shown at CROI 2022 were from substudies comparing the three regimens with respect to: infant growth, risk-benefit, subsequent pregnancies and glycated hemoglobin (HbA1c) and glucose in study participants.

Infant growth

The evaluation comparing the effect of the three maternal regimens on growth among exposed infants found those in the EFV/FTC/TDF arm were smaller than in both the DTG arms. Growth was similar in the infants exposed to TDF or TAF with DTG/FTC.

A high proportion of infants in all arms had severe stunting. This was highest (and occurred in one in five) among EFV/FTC/TDF-exposed 1-year olds.

The investigators evaluated infant growth at approximately 26 and 50 weeks of age by maternal regimen in a post hoc analysis. They calculated Z-scores for length-for-age (LAZ), weight-for-age (WAZ), and weight-for-length (WHZ) using WHO standards. They also estimated the proportion of infants in each arm with severe stunting (defined as LAZ below -2).

In this group of mostly breastfed infants (78%) exposed to maternal HIV and ART (4 infants aquired HIV; 0.6%) mean LAZ and WAZ were lower in the EFV/FTC/TDF arm than the DTG arms.

At week 26 and 50, mean LAZ differences between DTG/FTC/TDF and EFV/FTC/TDF arms were: 0.4 (95% CI 0.1 to 0.6), p=0.0056 and 0.3 (95% CI 0.1 to 0.6; p=0.01), respectively. For DTG/FTC/TAF vs EFV/FTC/TDF, these differences were: 0.4 (95% CI 0.1 to 0.7), p=0.0047 and 0.2 (95% CI -0.1 to 0.5; p=0.14).

All pairwise comparisons favoured DTG except for DTG/FTC/TAF at week 50. LAZ scores were similar in the TDF and TAF, DTG arms.

Notably mean LAZ scores for all arms tended to be below WHO norms with higher rates of stunting (LAZ below -2) in the EFV vs DTG arms at both timepoints: approx 15% vs 21%.

At the same time points, mean WAZ differences between DTG/FTC/TDF and EFV/FTC/TDF arms were: 0.3 (95% CI 0.0 to 0.5), p=0.035 and 0.3 (95% CI 0.1 and 0.6) p=0.0094, respectively. For DTG/FTC/TAF vs EFV/FTC/TDF these scores were: 0.2 (95% CI -0.0 to 0.5), p=0.077 and 0.3 (95% CI 0.1 and 0.6), p=0.019.

The EFV arm had the highest proportion of underweight infants (approximately 11%). There were also 3–4% obese infants across all arms with no evidence of a higher proportion in the TAF arm.

There were no mean differences between DTG/FTC/TAF and DTG/FTC/TDF arms in LAZ or WAZ at either week 26 or 50.

There were no differences between arms in WHZ.

The investigators recommended that infant growth should be factored into choice of optimal maternal ART regimen during pregnancy and breastfeeding.

Risk-benefit

In these analyses, DTG/FTC/TAF gave the best and clearest risk-benefit trade-off overall. DTG/FTC/TDF also had a better risk-benefit profile than EFV/FTC/TDF.

The investigators explained that understanding the risk-benefit trade-off for pregnancy and infant outcomes in clinical trials of pregnant women is complex due to multiple outcomes of interest. It can be misleading when risks and benefits are summarised in separate analyses.

For this evaluation they compared risk and benefit by arm using a desirability of outcome ranking (DOOR) with weights to account for severity of the outcome.

Mother-infant pair adverse outcomes were grouped according to the most severe outcome experienced: 1. infant death through one year of life, 2. spontaneous abortion or stillbirth, 3. infant HIV infection, 4. very preterm delivery (<32 weeks), 5. major congenital anomaly, 6. preterm delivery (<37 weeks), 7. small for gestational age (<10th percentile), 8. infant hospitalisation, 9. infant grade 3 or 4 adverse event.

The comparisons revealed: 79/216 (37%), 93/213 (44%), and 101/211 (48%) mother-infant pairs experienced at least one of the ranked outcomes in the DTG/FTC/TAF, DTG/FTC/TDF, and EFV/FTC/TDF arms, respectively.

Using ordinal logistic regression, there was a better risk-benefit trade-off for DTG/FTC/TAF compared with EFV/FTC/TDF: OR 0.60 (95% CI 0.42 to 0.88).

In the severity-weighted analysis, DTG/FTC/TAF also had a better risk-benefit trade-off compared with DTG/FTC/TDF and EFV/FTC/TDF, repectively: OR 0.64 (95% CI 0.49 to 0.84) and OR 0.28 (95% CI 0.21 to 0.36). DTG/FTC/TDF had a better risk-benefit trade-off relative to EFV/FTC/TDF: OR 0.41 (95% CI 0.32 to 0.53).

Subsequent pregnancies

Adverse pregnancy outcomes were very common among women who conceived on ART in VESTED – 35% of pregnancies ended in stillbirth or spontaneous abortion. Women with recent prior pregnancy loss were most at risk (but numbers were small).

This sub study looked at adverse pregnancy outcomes in women who became pregnant during postpartum follow-up (subsequent pregnancy).

These outcomes were: spontaneous abortion (<20 weeks), stillbirth (<20 weeks), preterm delivery (<37 weeks), small for gestational age (<10th percentile) and neonatal death (<28 days).

Due to a protocol amendment – based on concerns about neural tube defects among infants born to women who conceive on DTG – women who did not wish to use contraception after delivery were switched to (mostly) EFV.

Nineteen (3%) of 643 women had 20 subsequent pregnancies during follow up. They were taking the following regimens at conception: DTG/FTC/TAF (3), DTG/FTC/TDF (2), EFV/FTC/TDF (11, 1 woman with 2 pregnancies), non-study ART (2) and no ART (1).

Only 12/20 (60%) subsequent pregnancies resulted in live birth: 4/20 (20%) spontaneous abortions, 3/20 (15%) stillbirths, and 1/20 (5%) induced abortion. Three (25%) liveborn infants were preterm (24, 26 and 36 weeks' gestation).

At least one adverse pregnancy outcome occurred in 11/20 (58%) subsequent pregnancies, more frequently with EFV/FTC/TDF at conception (8 of 12 pregnancies; 67%) than with DTG-ART at conception (1/4 women).

Four of seven women who experienced spontaneous abortion or still birth in the subsequent pregnancy had a stillbirth in the index pregnancy and one a neonatal death.

The investigators rightly noted that the sample size was too small to formally test differences in outcomes of subsequent pregnancies by regimen.

They added that this finding should be considered in analyses of incident pregnancies occurring in trial participants.

HbA1c and glucose

This sub study did not find significant differences in maternal glycated hemoglobin (HbA1C) by ART regimen or clinically-important differences in maternal or infant random glucose. But only modest sample sizes of participants were assessed.

In VESTED, as observed elsewhere, DTG, particularly in combination with TAF, was associated with more weight gain than ART containing EFV or TDF (but better pregnancy outcomes were shown with DTG/FTC/TAF). The impact of this weight gain during pregnancy on gestational diabetes is unknown.

The investigators evaluated HbA1c and glucose in study participants. After a protocol amendment partway through the trial, maternal HbA1c and random glucose was sampled at study entry, 12 weeks after enrolment (antepartum) and delivery. Neonatal glucose was sampled within 48 hours of birth.

The evaluation compared the proportion of women with post-baseline HbA1c >5.7% (prediabetic) between arms and described the proportion with HbA1c >6.5% (diabetic).

HbA1c and/or glucose results were available for 348 mothers and 65 infants: 114 in the DTG/FTC/TAF; 116 in the DTG/FTC/TDF and 118 in the EFV/FTC/TDF arms.

Maternal medians at enrolment were: age 25.9 years, gestational age 21.5 weeks, BMI 24.1 kg/cm2, HIV-1 RNA 3.1 log10, and CD4 466 cells/mm3.

Maternal mean HbA1c levels and mean time-averaged HbA1c AUC did not differ significantly between arms.

Seven per cent of women in the DTG/FTC/TAF arm, 6.0% in the DTG/FTC/TDF arm, and 3.4% in the EFV/FTC/TDF arm had at least one post-baseline HbA1c >5.7%, p=0.21 for between-arm comparisons.

No woman had diabetes at baseline. One woman in the DTG/FTC/TAF arm developed HbA1c >6.5% post-baseline.

The DTG/FTC/TDF arm had slightly higher mean time-averaged AUC glucose (4.8 mmoL/L) vs the EFV/FTC/TDF arm (4.63 mmoL/L): mean difference 0.17 mmol/L (95% CI 0.00 to 0.34).

Mean infant glucose levels within approximately 48 hours birth were similar by arm.

COMMENT

Information about the impact of specific maternal ART regimens during pregnancy and breastfeeding on mothers and infants is limited.

Although modest sample size is almost always a limitation sub studies such as these, the value of large randomised trials to make many randomised comparisons looking at important issues such as these, over and above the primary outcomes cannot be underestimated. Along with other trials such as START and ADVANCE, VESTED has been a goldmine.

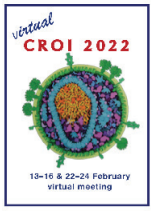
References

Unless stated otherwise, references are to the 29th Conference on Retroviruses and Opportunistic Infections, 12–16 and 22–24 February 2022, virtual meeting.

1. Stranix-Chibanda L et al. Growth of infants with perinatal exposure to maternal DTG vs EFV and TDF vs TAF. CROI 2022.12–16 February. Virtual. Oral abstract 30.
   https://www.croiconference.org/abstract/growth-of-infants-with-perinatal-exposure-to-maternal-dtg-vs-efv-and-tdf-vs-taf/ (abstract)
   http://www.croiwebcasts.org/console/player/50290 (webcast)
2. Brummel S et al. Risk-benefit trade-off for pregnancy and infant outcomes: DTG, EFV, TAF, AND TDF. CROI 2022. 12–16 February. Virtual. Poster abstract 679.
   https://www.croiconference.org/abstract/risk-benefit-trade-off-for-pregnancy-and-infant-outcomes-dtg-efv-taf-and-tdf/ (abstract)
   https://2jg4quetidw2blbbq2ixwziw-wpengine.netdna-ssl.com/wp-content/uploads/sites/2/posters/2022/CROI2022_Poster_679.pdf (poster)
3. Fairlie L et al. Adverse outcomes in subsequent pregnancies in the IMPAACT 2010 trial. CROI 2022. 12–16 February. Virtual. Poster abstract 680.
   https://www.croiconference.org/abstract/adverse-outcomes-in-subsequent-pregnancies-in-the-impaact-2010-trial/ (abstract)
   https://2jg4quetidw2blbbq2ixwziw-wpengine.netdna-ssl.com/wp-content/uploads/sites/2/posters/2022/CROI2022_Poster_680.pdf (poster)
4. Chinula L et al. Pregnancy hemoglobin A1c and glucose with DTG vs EFV, TDF vs TAF: IMPAACT 2010. CROI 2022. 12–16 February. Virtual. Poster abstract 687.
   https://www.croiconference.org/abstract/pregnancy-hemoglobin-a1c-and-glucose-with-dtg-vs-efv-tdf-vs-taf-impaact-2010/ (abstract)
   https://2jg4quetidw2blbbq2ixwziw-wpengine.netdna-ssl.com/wp-content/uploads/sites/2/posters/2022/CROI2022_Poster_687.pdf (poster)
5. Lockman S et al. Efficacy and safety of dolutegravir with emtricitabine and tenofovir alafenamide fumarate or tenofovir disoproxil fumarate, and efavirenz, emtricitabine, and tenofovir disoproxil fumarate HIV antiretroviral therapy regimens started in pregnancy (IMPAACT 2010/VESTED): a multicentre, open-label, randomised, controlled, phase 3 trial. The Lancet. Volume 397. Number 10281 p1237-1324. 3 April 2021.
   https://www.thelancet.com/journals/lancet/issue/vol397no10281/PIIS0140-6736(21)X0014-1

Switching to dolutegravir for adults on stable PI-based second-line ART

Polly Clayden, HIV i-Base



Switching from a boosted protease inhibitor to dolutegravir appears safe and effective for HIV treatment-experienced adults with undetectable viral load and no previous exposure to integrase inhibitors – according to findings from the Second-line Switch to DTG (2SD) study presented at CROI 2022.

This study is an open-label, randomised, controlled, non-inferiority trial, conducted at four sites in Kenya. Eligible participants were 18 years of age and above, virally suppressed for at least 12 weeks before enrolment and on a second-line regimen of a ritonavir-boosted protease inhibitor (PI/r) plus two nucleoside reverse transcriptase inhibitors (NRTIs) for at least 24 weeks, and with no previous integrase inhibitor exposure.

Participants were randomised (1:1) to switch to DTG or continue on their PI/r. Both arms remained on their NRTIs. The primary endpoint was proportion of participants with viral load above 50 copies/mL at week 48 (intention-to-treat-exposed [ITT-E] population; non-inferiority margin of 4%).

Between February and September 2020, 795 participants were randomised and 791 were treated and included in the analysis: 397 in the DTG arm and 394 in the PI/r arm. All were black African and a median of 46 years of age, 524 (66%) were women. They had been on a PI/r for about five and a half years – the majority (approximately 80%) received boosted atazanavir. Baseline characteristics were similar in both arms. Participants were not assessed for prior resistance.

At week 48, the proportion with viral load above 50 copies/mL was 5.0% (20/397) and 5.1% (20/394) in the DTG and PI/r arms, respectively: difference –0.04% (95% CI: –3.09 to +3.02). This met the study non-inferiority criteria.

No participants with virological failure had detectable genotypic resistance to either DTG or PI/r.

Treatment-related adverse events (AE) occurred in 92 (23.2%) participants on DTG and 78 (19.8%) participants on PI/r. Grade 3 or 4 AEs were similar (5.8% vs 6.9% for DTG vs PI/r), with no treatment-related serious AEs in either arm. One (0.3%) in the DTG and 3 (0.8%) in the PI/r arm discontinued study drug for any AE. There were no significant differences between arms in any AE comparisons.

There was greater weight gain the DTG vs PI/r arm: 2.1 vs 1.3% change from baseline (p=0.02).

C O M M E N T

Switching people who are virally suppressed from PI/r-based second-line to DTG has not previously been investigated.

The shortcomings of PI/r-containing regimens (particularly for low- and middle-income countries) have been well-documented: high pill-burden, tolerability, toxicity, drug interactions (including with TB treatment) and cost.

So these results are welcome and might offer a useful option – even without knowledge of prior resistance.

No data was presented comparing NRTI backbones and just over half of the participants received tenofovir and 3TC in this cohort.

Reference

Ombajo L et al. A randomized trial of switching treatment-experienced adults from PI/r to DTG. CROI 2022. 12–16 February. Virtual. Oral abstract 136.

https://www.croiconference.org/abstract/a-randomized-trial-of-switching-treatment-experienced-adults-from-pi-r-to-dtg/ (abstract)

http://www.croiwebcasts.org/p/2022croi/croi/136 (webcast)

ANTIRETROVIRALS

Draft BHIVA guidelines online for comment: deadline 9 June

Simon Collins, HIV i-Base

A major update to HIV treatment guidelines in currently online in draft format for comments.

Although several interim statements have been published, this is the first major update for five years. These updates have generally to provide guidance on newly approved drugs.

Two drafts are posted online: one with annotated comment and one that is easier to print.

The deadline for comments is 5 pm on Thursday 9 June 2022.

Reference

BHIVA guidelines on antiretroviral treatment for adults living with HIV-1 2022 - consultation open. (9 May 2022).

https://www.bhiva.org/treatment-guidelines-consultation

Lenacapavir in MDR HIV: phase 3 results of CAPELLA study published

Simon Collins, HIV i-Base

Full results from the phase 3 CAPELLA study of lenacapavir in people with multidrug resistant HIV are now published in the NEJM, together with editorial comment. [1, 2]

As the first capsid inhibitor, lenacapavir retains drug sensitivity to mutations associated with drug resistance to other drug classes, and has already been submitted to both the FDA and EMA for an MDR indication, in June and August 2021, respectively. [3]

The results were also presented at CROI 2022 and EACCS 2021 and in earlier issues of HTB. [4, 5]

Notably, lenacapavir is given by subcutaneous injection every six months, but it still needs to be used in combination with other active drugs. This is likely to include oral dosing, until other long-acting options become available.

Without this support, resistance to lenacapavir can develop easily if viral load remains unsuppressed or if adherence to other drugs in the combination is not high Viral failure was reported in 8/72 participants in CAPELLA, generally early, and with 4/8 linked to low adherence.

The CAPELLA study included a highly treatment-experienced population, with half having MDR to at least four classes and including resistance to fostemsavir and ibalizumab in roughly one-third of participants (to each drug).

Lenacapavir has so far been associated with few side effects, other than injection site reactions which are generally mild; only two participants reported grade 3 events, both of which resolved. None of the serious events reported in seven participants were judged related to lenacapavir.

The accompanying editorial positively notes that although numbers were small in CAPELLA, it included adolescents (older than 12), 25% woman, low CD4 count (median 150 cells/mm3, range: 3 to 1296). Viral load was also low however (<15,000 copies/mL), making it easier to achieve the secondary endpoints of suppression to undetectable (<50 copies/mL). Although the editorial refers to a relatively high baseline BMI, this doesn't seem to be included in online results.

The editorial also raises importance of safety issues in PrEP studies that are currently ongoing and on the challenge of generating safety data during pregnancy and access for people living in the global South.

References

1. Segal-Maurer S et al for CAPELLA Study Investigators. Capsid inhibition with lenacapavir in multidrug-resistant HIV-1 infection. N Engl J Med 2022; 386:1793-1803. DOI: 10.1056/NEJMoa2115542. (12 May 2022).
   https://www.nejm.org/doi/full/10.1056/NEJMoa2115542
2. Marrazzo J. Lenacapavir for HIV-1 — Potential Promise of a Long-Acting Antiretroviral Drug. N Engl J Med. Editorial comment. 2022; 386:1848-1849. DOI: 10.1056/NEJMe2204376. (12 May 2022).
   https://www.nejm.org/doi/full/10.1056/NEJMe2204376

3. Lenacapavir submitted to EMA for MDR HIV, HTB (21 September 2019).
https://i-base.info/htb/41294
4. CROI 2022: Lenacapavir in treatment-experienced participants, and as PrEP in macaques. HTB (1 March 2022).
https://i-base.info/htb/42123
5. EACS 2021: Lenacapavir: drug resistance after viral rebound in treatment experienced participants. HTB (30 November 2022).
https://i-base.info/htb/41606

ViiV licenses long-acting cabotegravir (CAB-LA) for generic access

Simon Collins, HIV i-Base

On 26 May 2022, ViiV Healthcare announced that it will now add long-acting cabotegravir injections (CAB-LA) to the Medicines Patent Pool (MPP) for use as PrEP. [1]

This will enable other manufacturers to make generic versions of this innovative and important new option to protect against HIV.

This is similar to the company's licensing of oral dolutegravir for generic use in HIV treatment (ART).

ViiV say they will be "working at pace with MPP to execute the licence, building on the experience of our valued and long-standing partnership. We are excited about this important step forward which reflects ViiV's commitment to voluntary licensing as an integral part of our access to medicines strategies."

The announcement follows recent high-profile demands from community activists for early and widespread access to long-acting PrEP in lower- and middle-income countries (LMICs). [2]

These demands were based on impressive results from clinical studies reporting higher rates of adherence and protection in international studies. They were also driven by concerns that access to CAB-LA in LMICs looked extremely limited unless it was available at a comparable price to oral PrEP.

It is also based on research from the Clinton Health Access Initiative (CHAI) showing that generic formulations of CAB-LA injections could be produced at around $15-23 for a year's course of six injections. [3]

This would be more cost effective (and more effective) than voluntary medical male circumcision which has been widely available for many years.

C O M M E N T

The announcement is welcomed and matches earlier commitments by ViiV Healthcare to license dolutegravir to MPP for global access to integrase inhibitor based ART.

This agreement also works well for ViiV Healthcare, who initially were unable to identify generic manufactures, although later said they were more open to this approach. [5]

It also ensures ViiV meets the commitment to make sure that medicines need to be available in countries where approval studies were run.

References

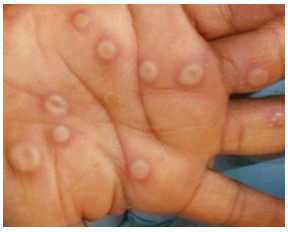
1. ViiV Healthcare. ViiV Healthcare commits to grant voluntary licence for patents relating to cabotegravir long-acting for PrEP to medicines patent pool. (27 May 2022).
https://viivhealthcare.com/hiv-news-and-media/news/press-releases/2022/may/viiv-healthcare-commits-to-grant-voluntary-licence-for-patents
2. AfroCAB. Communities demand ViiV/GSK accelerate access to CAB-LA in LMICs. (1 March 2022).
http://www.afrocab.info/2022/03/communities-demand-viiv-gsk-accelerate-access-to-cab-la-in-lmics (link page)
http://www.afrocab.info/wp-content/uploads/2022/03/CAB-LA-Community-Statement-Final_v2.pdf (PDF statement)
3. Ripin D. Approach for delivery of long-acting ARVs for treatment and prevention in LMICs: cabotegravir as a precedent-setting case study. LEAP conference, March 2022.
https://longactinghiv.org/files/inline-files/DavidRipin-LEAP2022.mp4 (MP3 recording)
4. ViiV Healthcare. ViiV Healthcare open to voluntary licensing as part of approach to enable greater access to cabotegravir la for prep in low- and middle-income countries
https://viivhealthcare.com/hiv-news-and-media/news/company-statements/viiv-healthcare-statement-on-voluntary-license/

COMPLICATIONS: MONKEYPOX

Monkeypox outbreak: Update and further information

Simon Collins, HIV i-Base

This issue of HTB includes several articles about the recent outbreak of monkeypox virus (MPV), with the UK reporting the highest numbers.



- Monkeypox cases in gay men in the UK: BHIVA and ECDC rapid statements
- Monkeypox DNA in semen supports advice to use condoms for eight weeks after infection has cleared
- Risk of monkeypox becoming endemic in Europe: ECDC assessment
- Seven cases of monkeypox virus in the UK from 2018 to 2021
- Monkeypox: Non-technical Q&A

C O M M E N T

The prompt health care responses in the UK and other countries are focused not only on tracing and managing cases linked to new network but also on preventing MPV from infecting other animals.

Over the next few weeks it will becomes more clear whether the rapid response has contained infections and prevented the infection from becoming endemic.

Please see references in these articles for further information.

OTHER LINKS

UK based general information

NHS. Monkeypox.

https://www.nhs.uk/conditions/monkeypox

Non-technical information about MPV in the UK. This includes who to contact if you are worried about symptoms.

UK Health Security Agency (UK-HSA). Monkeypox virus. (1 June 2022).

https://www.gov.uk/guidance/monkeypox

More detailed information from the UK government about all aspects of MPV including update on the current outbreak.

UK-HSA. Monkeypox cases confirmed in England – latest updates

https://www.gov.uk/government/news/monkeypox-cases-confirmed-in-england-latest-update

Updated information on UK cases.

Human Animal Infections and Risk Surveillance group (HAIRS).

Qualitative assessment of the risk to the UK human population of monkeypox infection in a canine, feline, mustelid, lagomorph or rodent UK pet. (27 May 2022).

https://www.gov.uk/government/publications/hairs-risk-assessment-monkeypox/qualitative-assessment-of-the-risk-to-the-uk-human-population-of-monkeypox-infection-in-a-canine-feline-mustelid-lagomorph-or-rodent-uk-pet

Includes guidance for isolation from pets.

UK Health Security Agency (UK-HSA). Principles for monkeypox control in the UK: 4 nations consensus statement. (30 May 2022).

https://www.gov.uk/government/publications/principles-for-monkeypox-control-in-the-uk-4-nations-consensus-statement/principles-for-monkeypox-control-in-the-uk-4-nations-consensus-statement

Includes updated guidelines for continued prevention in the UK.

Other health agencies

European Centre for Disease Prevention and Control (ECDC). Monkeypox multi-country outbreak: rapid assessment report. (23 May 2022).

https://www.ecdc.europa.eu/en/publications-data/risk-assessment-monkeypox-multi-country-outbreak (download page)

https://www.ecdc.europa.eu/sites/default/files/documents/Monkeypox-multi-country-outbreak.pdf (PDF)

US CDC. What clinicians need to know about monkeypox in the United States and other countries.

https://emergency.cdc.gov/coca/calls/2022/callinfo_052422.asp

This US talk on clinical management includes pictures of MPV compared to other common skin reactions.

US CDC. Monkeypox Outbreak — Nine States May 2022. Minhaj FS et al. MMWR Morb Mortal Wkly Rep. ePub.DOI: 10.15585/mmwr.mm7123e1. (3 June 2022).

https://www.cdc.gov/mmwr/volumes/71/wr/mm7123e1.htm

US CDC. Monitoring people who have been exposed.

https://www.cdc.gov/poxvirus/monkeypox/clinicians/monitoring.html

US CDC. Home page for information for doctors about MPV.

https://www.cdc.gov/poxvirus/monkeypox/clinicians/index.html

WHO. Multi-country monkeypox outbreak: situation update. (4 June 2022).

https://www.who.int/emergencies/disease-outbreak-news/item/2022-DON390

Detailed review of international cases and guidelines for appropriate monitoring and prevention.

HIV related sources

BHIVA rapid statement on monkeypox virus. (17 May 2022, updated 31 May 2022).

https://www.bhiva.org/BHIVA-rapid-statement-on-monkeypox-virus

EACS/ECDC. Informal webinars given on 24 and 31 May 2022.

https://i-base.info/wp-content/uploads/2022/05/Monkeypox_RRA_EACS_ECDCwebinar_2405022_for-sharing.pdf (PDF)

https://i-base.info/htb/wp-content/uploads/2022/05/Monkeypox_EACS-ECDC_webinar_310522.pdf (PDF)

Community and other information

i-Base and UK-CAB. Monkeypox: Q&A and resources.

https://i-base.info/monkeypox

Prepster and the UK Health Security Agency (HSA). UK Community webinar available online. Prepster Facebook page. (24 May 2022).

https://www.facebook.com/133703446979595/posts/1677130825970175

Excellent early online community discussion.

Monkeypox case tracker.

https://monkeypox.healthmap.org

Selected research papers

Eurosurveillance, 27(22), (2 June 2022).

https://www.eurosurveillance.org/content/eurosurveillance/browse

Open access publication including papers on risk of sexual transmission and on recent outbreaks in the UK, Portugal and Australia.

Clinical features and management of human monkeypox: a retrospective observational study in the UK. Adler H et al. The Lancet, DOI: 10.1016/S1473-3099(22)00228-6. (May 24 2022).

https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(22)00228-6/fulltext

Details of seven MPV cases reported in the UK between 2028 and 2021.

Epidemiological, clinical and virological characteristics of four cases of monkeypox support transmission through sexual contact, Italy, May 2022. Andrea A et al for the INMI Monkeypox Group.. Euro Surveill. 2022;27(22):pii=2200421. (2 Jun 2022).

https://doi.org/10.2807/1560-7917.ES.2022.27.22.2200421.

Clinical characteristics of human monkeypox, and risk factors for severe disease. Huhn GD et al. Clin Infect Dis. 2005 Dec 1541(12):1742-51.

https://pubmed.ncbi.nlm.nih.gov/16288398

Clinical Course and Outcome of Human Monkeypox in Nigeria. Ogoina D et al. Clin Infect Dis. 2020 Nov 571(8):e210-e214.3.

https://pubmed.ncbi.nlm.nih.gov/32052029

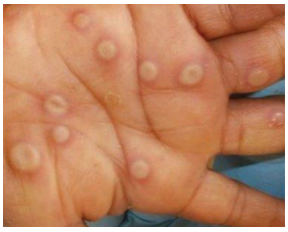
Includes reports of HIV positive cases.

Outbreak of human monkeypox in Nigeria in 2017-18: a clinical and epidemiological report. Yinka-Ogunleye A et al CDC Monkeypox Outbreak Team. Lancet Infect Dis. 2019 Aug19(8):872-879.2.

https://pubmed.ncbi.nlm.nih.gov/31285143

Monkeypox cases in gay men in the UK: BHIVA and EACS rapid statements

Simon Collins, HIV i-Base



On 7 May 2022, cases of monkeypox virus (MPV) were reported in the UK. Later updates confirmed 9 cases by 18 May, 20 cases by 20 May, 77 cases by 24 May and 220 cases by 1 June. [1]

Most cases were not linked to travel to countries where monkeypox is more common. They were, however, largely reported in gay or bisexual men, with the likelihood that transmission occurred in the UK.

This led to a rapid statements from BHIVA on the potential implications for people living with HIV, that has since been updated. [2]

This includes limited data on HIV and MPV coinfection, but does not include specific recommendations for people living with HIV. So far, HIV is not linked to any difference in symptoms and outcomes.

The statement will be updated as more information becomes available, including whether immune suppression is associated with any increased risk. It also includes information on treatment and vaccination, although cases are also too few for prophylaxis to be currently needed (unless there has been recent contact with a confirmed case).

One of the smallpox vaccines (Imvanex, non-replicating) protects against MPV and this can be used in people living with HIV. The vaccine is being offered to contacts of people with MPV to help stop further spread. However, BHIVA recommend that live vaccines are not recommended for people with reduced immunity (CD4 <200 cells/mm^3). [3]

Symptoms include fever, headache, muscle aches, backache, swollen lymph nodes, chills and exhaustion. A rash typically begins on the face and then spreads to other parts of the body including the genitals (especially in the recent cases). The rash can look like chickenpox, syphilis, herpes or varicella zoster (VZV), with distinct stages shown below.

The incubation period is usually 6 to 16 days but can be up to three weeks. Most people recover without complications. When the scab falls off a person is no longer infectious. [4, 5]

Recent UK cases reported rash that varied from 10 to 150 lesions. [6]

Sexual health clinics in central London report that MPV is affecting gay men in London. They advise people who are worried about similar symptoms to phone a clinic but not to drop-in services. This is also protect sexual health services as staff in contact with cases would also need to isolate. Also, to not share sheets and towels or to have sex until MPV has been ruled out. [7]

As this issue of HTB went to press, more than 550 cases have been reported globally in more than 20 non-endemic countries. [8, 9, 10]

C O M M E N T

As many of the cases reported so far have not been linked, the extent of current transmission networks is currently unclear, but is likely to be much larger.

Until more information becomes available over the next few weeks, this is a good reason to be cautious.

Luckily, most cases of monkeypox resolve within a few weeks without complications.

Treatments are available, including the use of vaccines. For details see BHIVA vaccine guidelines. Advice is for potential cases to self isolate for 21 days.

Unless this is taken seriously, numbers could easily increase considerably over the next two weeks.

More serious outcomes, including that monkeypox becomes endemic in Europe, is emphasised by the European Centre for Disease Prevention and Control (ECDC) who have published the most comprehensive review of cases so far. [11]

This is currently estimated to be a low risk, but will depend on how effectively further transmission is prevented.

Numbers of cases are being tracked and updated online, currently with more than 900 confirmed in 28 non-endemic countries. [12]

i-Base has published a non-technical factsheet on monkeypox that will be updated as needed.

https://i-base.info/monkeypox

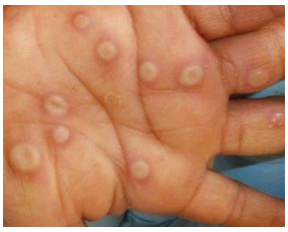
References

1. UK Health Security Agency (UK-HSA). Monkeypox cases confirmed in England – latest updates. (7 May 2022). https://www.gov.uk/government/news/monkeypox-cases-confirmed-in-england-latest-updates
2. BHIVA rapid statement on monkeypox virus. (17 May 2022, updated 31 May). https://www.bhiva.org/BHIVA-rapid-statement-on-monkeypox-virus
3. BHIVA. BHIVA guidelines on the use of vaccines in HIV-positive adults 2015. https://www.bhiva.org/vaccination-guidelines
4. European Centre for Disease Prevention and Control (ECDC) .Monkeypox cases reported in UK and Portugal/ (19 May 2022). https://www.ecdc.europa.eu/en/news-events/monkeypox-cases-reported-uk-and-portugal
5. UK Health Security Agency (UK-HSA). Monkeypox. (Updated 18 May 2022). https://www.gov.uk/guidance/monkeypox
6. Seven cases of monkeypox virus in the UK from 2018 to 2021. HTB (26 May 2022). https://i-base.info/htb/42959
7. 56 Dean Street. Monkeypox alert. https://www.dean.st/health-amp-wellbeing/monkeypox-alert-2022-ukhsa
8. STAT news. U.S. monkeypox case reported, as Spain, Portugal report infections in growing outbreak. (18 May 2022). https://www.statnews.com/2022/05/18/spain-portugal-report-monkeypox-cases-raising-specter-of-wider-outbreak
9. STAT news. 17 suspected monkeypox cases seen in Montreal, as European tally increases. (18 May 2022). https://www.statnews.com/2022/05/19/17-suspected-monkeypox-cases-seen-in-montreal-as-european-tally-increases
10. Australia's first monkeypox case spotted by GP. (19 May 2022). https://www1.racgp.org.au/newsgp/clinical/gp-identifies-first-probable-monkeypox-case-in-aus
11. European Centre for Disease Prevention and Control (ECDC). Monkeypox multi-country outbreak: rapid assessment report. (23 May 2022). https://www.ecdc.europa.eu/en/publications-data/risk-assessment-monkeypox-multi-country-outbreak (download page) https://www.ecdc.europa.eu/sites/default/files/documents/Monkeypox-multi-country-outbreak.pdf (PDF)
12. Monkeypox case tracker. https://monkeypox.healthmap.org
13. EACS/ECDC. Informal webinar given on 24 May 2022. https://i-base.info/wp-content/uploads/2022/05/Monkeypox_RRA_EACS_ECDCwebinar_2405022_for-sharing.pdf (PDF)
14. EASC/ECDC. Informal webinar given on 31 May 2022. https://i-base.info/htb/wp-content/uploads/2022/05/Monkeypox_EACS-ECDC_webinar_310522.pdf (PDF)

Monkeypox DNA in semen supports advice to use condoms for eight weeks after infection has cleared

Simon Collins, HIV i-Base

Although the recent outbreaks of monkeypox (MPX) were largely reported in sexual networks, it was not referred to as a sexually transmitted infection. This was largely due to lack of data about whether the virus (MPXV) was present in genital fluids.



However, a study published open-access in the 2 June issue of Eurosurveillance, reports that MPX DNA has been found in four men diagnosed in Italy between 17 and 22 May 2022.

All were in gay men in their 30s who had travelled in the first two weeks of May (including three to the event in Gran Canaria linked to other MPX cases. Two were HIV positive and on ART and two were HIV negative and on PrEP.

Only 3/4 had systemic symptoms (fever or fatigue). All had mostly genital and/or anal MPX ulcers, occurring 2-3 days after other symptoms, with 3/4 also having ulcers in other body areas (including thorax, arms, legs, hands and feet). Unlike the historical MPX pathogenesis that reports ulcers usually all developing at the same time, these were asynchronous in these four people.

Three different PCR tests were used to test semen samples. Initially for orthopoxviruses generically, then confirmed for MPXV DNA, and finally to determine MPXV clade.

MPXV DNA was positive in semen samples for all 3/4 men with results (5-7 days since first symptoms). However, although quantitative levels of viral load were not available, these are estimated as being very low, based on having a quantification cycle (Cq) range of 27 to 30.

Cq is a marker for viral load and for most PCR tests a Cq of 36 to 40 would be the equivalent to a negative result. This supports the researchers comment that at these levels it is unlikely that virus could be isolated.

Seminal fluid was only one of a panel of nine samples (also serum, plasma, MPX ulcers (skin and genital), throat swab, scab, faeces and saliva. Although many of these results were not yet available for all cases, especially at multiple timepoints, most of these other samples were also positive for MPXV DNA, but at a higher likely viral load.

C O M M E N T

The investigators are to be congratulated on producing this first early data, even with significant gaps where analyses are still ongoing, including PCR and viral culture in other compartments. It should therefore be a priority to promptly update this report as soon at the additional data become available.

It is also possible that the DNA detected might be spillover of virus (or fragments) into semen from urethritis/urethral or penile lesions, rather than being a true measure in semen.

The current study doesn't mean that MPX is a sexually transmitted infection. Or that it was sexually transmitted in these cases, even though all men had sex without condoms.

The results do support the caution to use condoms for eight weeks after MPX and its symptoms have resolved. The eight weeks is not evidence based, but a stop-gap measure while data are being collected at timepoints after recovery. Finding MPXV DNA during this eight-week period is likely to be more clinically important as genital fluids in very early stages are unlikely to contribute to further increasing the risk of transmission. [2]

This is in case genital fluids prove to be a reservoir site, as has been reported for other viral infections, including Zika and Ebola. [3]

This will require larger studies with longitudinal samples over three months.

The researchers also note the importance of further research as other viruses that can be detected in seminal fluid are not necessarily transmitted sexually. [3, 4]

The same issue of Eurosurveillance also includes case reports from the MPX outbreaks in Australia, Portugal and the UK. [5]

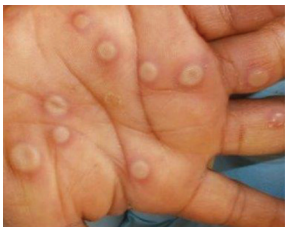
References

1. Andrea A et al for the INMI Monkeypox Group.. Epidemiological, clinical and virological characteristics of four cases of monkeypox support transmission through sexual contact, Italy, May 2022. Euro Surveill. 2022;27(22):pii=2200421. (2 Jun 2022).
https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2022.27.22.2200421
https://doi.org/10.2807/1560-7917.ES.2022.27.22.2200421.
2. UK Health Security Agency (UK-HSA). Principles for monkeypox control in the UK: 4 nations consensus statement. (30 May 2022).
https://www.gov.uk/government/publications/principles-for-monkeypox-control-in-the-uk-4-nations-consensus-statement/principles-for-monkeypox-control-in-the-uk-4-nations-consensus-statement
3. Le Tortorec A et al. From ancient to emerging infections: the odyssey of viruses in the male genital tract. Physiol Rev. 2020;100(3):1349-414. doi:10.1152/physrev.00021.2019. (20 May 2020).
https://journals.physiology.org/doi/full/10.1152/physrev.00021.2019
4. Matusali G et al. Infectious Toscana virus in seminal fluid of young man returning from Elba island, Italy. Emerg Infect Dis. 2022;28(4):865-9. (April 2022).
https://doi.org/10.3201/eid2804.211920.
5. Eurosurveillance, 27(22), (2 June 2022).
https://www.eurosurveillance.org/content/eurosurveillance/browse

Risk of monkeypox becoming endemic in Europe: ECDC assessment

Simon Collins, HIV i-Base

On 23 May 2022, the most comprehensive public report on the recent international cases of monkeypox virus (MPV) includes an important caution that MPV could become endemic in European countries. [1]



This assessment from the European Centre for Disease Control (ECDC) says that future risks depend on how effectively further transmission is prevented, and that this currently involves asking close contacts to isolate for three weeks until MPV can be ruled out.

Although MPV is reported as being difficult to transmit, there is only a short window period to establish control, given the extent of the current networks is unknown.

It also depends on MPV not being transmitted into other animal species.

ECDC in partnership with EACS also hosted two informal webinars on MPV on 24 and 31 May 2022. Slide sets from these are posted below. [4]

C O M M E N T

These implications are difficult coming at a time of reduced concern over COVID-19, but are essential to take seriously.

Unfortunately, further cases are likely to continue to rise given that transmission might be possible for several weeks. This might include a period before lesions occur. Effective prevention will also depend on contact tracing.

MPV is not currently classed as a sexually transmitted infection but because genital sores are a symptom, infections have been reported by sexual health clinics. STI clinics stress the importance of not using drop-in services (as staff would then need to isolate) but to phone first for advice or to call 111.

The ECDC document also reports a caution for people with reduced immunity, including older people living with HIV, and that any additional risk might be largely mitigated by effective ART.

BHIVA also produced a rapid statement, that will be updated as information changes. [2]

i-Base has published a non-technical factsheet on monkeypox that will be updated as needed. [3]

Slides from two EACS/ECDC webinars on 24 and 31 May 2022 are online. [4, 5]

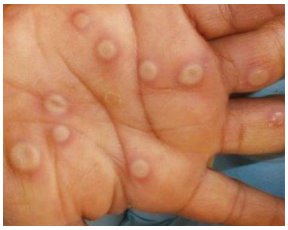
References

1. European Centre for Disease Prevention and Control (ECDC). Monkeypox multi-country outbreak: rapid assessment report. (23 May 2022).
https://www.ecdc.europa.eu/en/publications-data/risk-assessment-monkeypox-multi-country-outbreak (download page)
https://www.ecdc.europa.eu/sites/default/files/documents/Monkeypox-multi-country-outbreak.pdf (PDF)
2. Monkeypox cases in the UK: BHIVA statement. HTB (18 May 2022).
https://i-base.info/htb/42896
3. i-Base. Monkeypox: Q&A and update.(25 May2022).
https://i-base.info/monkeypox
4. EACS/ECDC. Informal webinar given on 24 May 2022.
https://i-base.info/wp-content/uploads/2022/05/Monkeypox_RRA_EACS_ECDCwebinar_2405022_for-sharing.pdf (PDF)
5. EASC/ECDC. Informal webinar given on 31 May 2022.
https://i-base.info/htb/wp-content/uploads/2022/05/Monkeypox_EACS-ECDC_webinar_310522.pdf (PDF)

Seven cases of monkeypox virus in the UK from 2018 to 2021

Simon Collins, HIV i-Base

A retrospective review of monkeypox virus reported in the UK from 2018 to 2021 published in Lancet Infectious Diseases will help inform management of cases linked to the current outbreak. [1]



This includes describing seven cases (four men and three women) who were managed in specialist infectious disease centres in Liverpool, London and Newcastle - highlighting the seriousness of this infection.

Three of the cases acquired MPV in the UK: one was a health worker who developed symptoms 18 days after contact with a patient, despite receiving the Imvanex smallpox vaccine at day 6, and two others were household contacts of an infection caught outside the UK (one adult and one child). The cases acquired outside the UK were from Nigeria. Adults were all aged 30 to 50 and the child was less than 2.

Notably, 5/7 of these cases spent more than 3 weeks in isolation (range 22 to 39 days) as PCR testing continued to be positive. One person also had a mild relapse six weeks after leaving hospital.

Otherwise, people staying in hospital until they were confirmed PCR negative in skin, blood and the respiratory tract with no further lesions.

Other details included swollen lymph nodes in 5/7 cases. The lesions were extensive, ranging from 10 to 150, with 3/7 having more than 100. All 7/7 included lesions on the face, trunk and arms, with 6/7 also on the hands and 5/7 on the genitals. Severe ulcers with delayed healing were reported in 3/7, including two deep tissue accesses.

Treatment included oral brincidofovir (200 mg once a week) in 3/7 cases started a week after the first rash which needed to be stopped early due to increase liver enzymes,

One was treated with oral tecovirimat (200 mg twice daily for 2 weeks), experienced no adverse effects, with no side effects. This case had the shortest duration of infection (10 days).

However, the small numbers mean that the authors caution that their report does not prove benefit from treatments or whether earlier use would have been better.

C O M M E N T

This paper highlights the importance of seeking prompt medical advice for anyone worried about the current outbreak.

It also shows the importance of phoning a clinic beforehand (or 111) and not using drop-in services without a specific appointment for MPV.

BHIVA and the ECDC have both posted rapid statements that will be updated as more information becomes available. [2, 3]

The ECDC have also published a detailed review and risk assessment for European cases. [4]

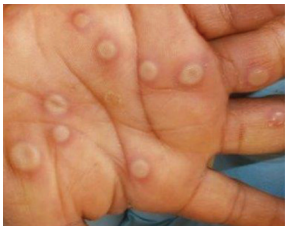
The US CDC have also posted webinar on case management that is now online with slides. [5]

Numbers of new confirmed and suspected international cases are being updated on a health web tracker. [6]

References
1. Adler H et al. Clinical features and management of human monkeypox: a retrospective observational study in the UK. The Lancet, DOI: 10.1016/S1473-3099(22)00228-6. (May 24 2022).
https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(22)00228-6/fulltext#.Yo1dNYaEDuw.twitter
2. Monkeypox cases in gay men in the UK: BHIVA and ECDC rapid statements. HTB (19 May 2022).
https://i-base.info/htb/42896
3. Risk of monkeypox becoming endemic in Europe: ECDC assessment. HTB (23 May 2022).
https://i-base.info/htb/42948
4. European Centre for Disease Prevention and Control (ECDC). Monkeypox multi-country outbreak: rapid assessment report. (23 May 2022).
https://www.ecdc.europa.eu/en/publications-data/risk-assessment-monkeypox-multi-country-outbreak (download page)
https://www.ecdc.europa.eu/sites/default/files/documents/Monkeypox-multi-country-outbreak.pdf (PDF)
5. US CDC. What Clinicians Need to Know about Monkeypox in the United States and Other Countries. (24 May 2022).
https://emergency.cdc.gov/coca/calls/2022/callinfo_052422.asp
6. Monkeypox case tracker.
https://monkeypox.healthmap.org

Monkeypox: Q&A and updates

Simon Collins, HIV i-Base and Alex Sparrowhawk, UK-CAB



This Q&A is about the recent cases of monkeypox (MPX) in the UK. At some point this name may be changed.

This page will be updated as new information becomes available. Last update 5 June 2022.

Monkeypox (MPX) is still very rare in the UK. But the recent outbreak is significant and needs to be taken seriously. For example, the WHO define one case in a country as an outbreak.

Information is organised into six sections.

1. MPX basics
2. Prevention and transmission
3. Testing and treatment
4. MPX and HIV
5. Other questions
6. References and more information

1. MPX: first questions

What is monkeypox?

Monkeypox is an infection caused by the monkeypox virus (MPV or MPxV).

MPX is usually rarely seen in the UK. However, during May 2022 MPX was reported in more than 220 people in the UK.

By early June, MPX has also been reported in over 900 people globally in countries where MPX is not usually seen. International travel links cases across Europe and in the UK to Canada, the US, Australia to 28 countries overall.

The risk of MPX needs to be taken seriously. This is both for your individual health and so that it doesn't become an established infection.

The name monkeypox may be changed. This is because the current name is linked to stigma. It is also not accurate as monkeys are rarely affected either.

Are there different strains of MPX?

Yes. Like most viruses there are different strains of the virus.

The two main strains are a mild form (linked to West Africa) and a more aggressive form (linked to Central Africa).

The current cases all involve the mild version.

There is also a call for the WHO to rename these strains. Just as in COVID, it is not helpful to stigmatise a region with an illness.

What are the main symptoms?

Many of the early general symptoms are similar to other infections like colds, flu and COVID.

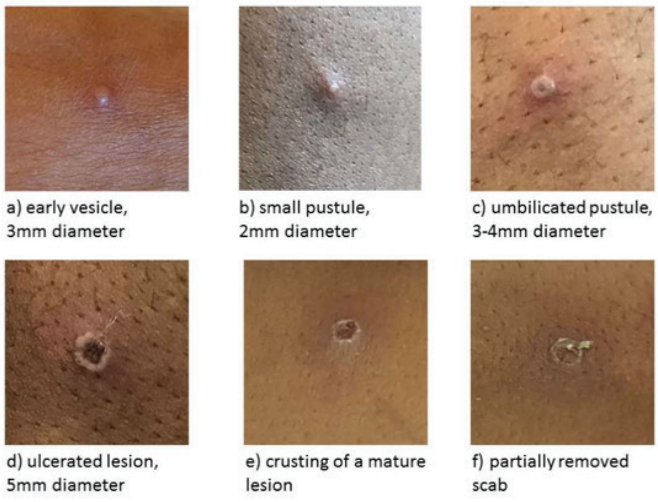
These include fever, headache, muscle aches, backache, swollen lymph nodes, chills and feeling very tired.

Sometimes they are mild. Some people do not get symptoms at all.

MPX spots, ulcers or blisters develop a few days after the symptoms above. This starts as red skin bumps, often in the genitals or face. It can evolve to fluid filled blisters that can break down into ulcers or sores. These develop into a scab that eventually falls off.

These can be in any part of the body. The sores can be painful, aggressive and unpleasant. They can also be itchy. Scratching can potentially spread the virus to other sites which could become very serious.

The examples below are the different stages of the ulcers. They can vary in size from a few millimetres to a centimetre in diameter.



a) early vesicle, 3mm diameter

b) small pustule, 2mm diameter

c) umbilicated pustule, 3-4mm diameter

d) ulcerated lesion, 5mm diameter

e) crusting of a mature lesion

f) partially removed scab

How are the MPX ulcers different to other infections?

Ulcers can be similar to several more common infections. These include chicken pox, syphilis, herpes, molluscum, cryptococcal infection, shingles (VZV) or even some heat rashes.

MPX ulcers are deeper and harder than seen with other infections

MPX ulcers can appear in crops every three to five days, and unlike chickenpox can take several days to evolve into blisters.

MPX ulcers often have a dip in the centre with a dot in the middle. This is called umbilicated.

There are other pictures at this link to the US CDC.
https://www.cdc.gov/poxvirus/monkeypox/clinicians/clinical-recognition.html

How serious is MPX?

Most cases are mild. With support, most people will be able to self-isolate at home.

However, 1 in 100 cases can include serious complications. This can involve inflammation of the lungs (pneumonitis), brain (encephalitis), eyes (keratitis) and bacterial infections.

The sores can become infected with bacteria, and if untreated appropriately, can lead to septicaemia (blood poisoning).

Serious infections need to be managed in hospital.

Is MPX an STI?

Original MPX was not called an STI. This was because the virus had not yet been found in sexual fluids.

Even though has now been detected in semen, this still doesn't make it an STI. Further research is needed to do this.

But saliva is likely to be infectious. This means that kissing and oral sex could be the risk that explains transmission in sexual networks.

MPX is transmitted via close contact whether or not this involves sex. This includes by close skin contact, or contact with infected clothes, towels and bed linen. Having sex involves close contact. Sexual contact is not necessary, but any spots or ulcers will be very infectious.

Even if later research finds MPX is infectious in sexual fluids, the larger risk is likely to come from close contact.

Condoms, for example, will not generally protect against MPX. However, one exception might be if MPX remains in sexual fluids after the infections is otherwise cleared. This has been seen with other infections, including Zika virus and Ebola.

Until there is more research, UK guidelines recommend that people with confirmed MPV use condoms for eight weeks after the infection has cleared.

Does MPX just affect gay men?

No, viruses do not care about sexuality.

Recent infections in gay men is because this is one of the networks of an early infection.

2. Transmission and prevention

What is the risk of catching MPX?

So far the risk of catching MPX is very low for everyone. This is because MPV is still rare in the UK.

But knowing about the risk is important in settings where MPX risks are already higher.

Casual social contact is generally very low risk in all settings.

But this can be higher with sexual partners and people you live with.

For both reasons, people diagnosed with MPX need to self-isolate until the infection is cleared.

How is MPX transmitted?

MPV can be spread in several ways.

- **Through droplets in the air.**

This usually involves spending extended time with someone in a room with poor ventilation. For example, spending more than 3 to 6 hours, where you are within two metres.

So casual contact in the same room is a very low risk, unless someone directly sneezes in your face.

But transmission by air is a much higher risk for people in the same household. This should involve taking special precautions to limit contact with people you live with.

- **By close contact with someone who has symptoms.**

This is especially after the ulcers have developed. This is because the fluid in MPX blisters will be highly infectious.

Skin contact with ulcers is a high risk of catching MPV.

- **By sharing sheets and towels.**

Sharing sheets and towels with someone with MPX can also be a route of transmission.

Washing sheets and towels can also be a risk. This is in case infectious material is shaken into the air.

A machine wash at a 60 degree cycle will be enough to sterilise sheets, clothes and towels.

Simple cleaning with household bleach will be enough to sterilise surfaces, toilets and bathrooms.

How long after an exposure risk does MPX take to develop?

Based on the limited data, it can take from 1 to 3 weeks until MPX produces symptoms.

For most people this is 10 to 12 days after contact.

When is someone infectious?

The risk of onward transmission starts as soon as there are symptoms.

The risk usually ends after the skin blisters and scabs have gone.

This is why it is important to call a doctor or clinic for advice. But please do not visit a doctor or clinic without calling first so this can be arranged properly.

Otherwise health workers might also need to isolate.

What if I have been exposed to MPX?

Recommendations on recent risk depend on whether the risk is high, medium or low risk.

High risk is defined as close contacts of people who develop MPX. This includes being withing 6 feet for more than three hours, sexual contact or direct contact with body fluids. It can also include contact with shared sheets and towels.

Please self-monitor for symptoms for the next three weeks. This can include taking your temperature twice a day which should stay below 38°C (100.4° F)

Seek medical advice if you develop any of the symptoms above, especially fever, rash, skin bumps, chills or swollen lymph nodes. In the UK this should be by calling a sexual health clinic or by calling 111.

It is important to self-isolate if you develop symptoms and follow health care advice.

People at higher risk might be offered PEP with vaccination. This will usually be from spending prolonged time with someone with diagnosed MPV or direct contact to ulcers or body fluids.

Vaccination is usually only offered to people at high risk.

How can I reduce my risk and stay safe?

The current advice for how to reduce your risks is likely to change every week.

This will depend on how successfully MPX is contained or on whether cases continue to rise. This might mean this advice changes, depending on where you live and on different social situations.

This also involves a personal approach to healthcare both for yourself and for the community. For example, to get medical advice if you feel unwell or develop unexpected skin bumps or ulcers. This will also help you access the best care to recover quickly.

One of the higher risks comes from contact with sexual partners, So reducing the numbers of partners, especially in a group setting will help. This is especially important at gay and bisexual venues in London.

Social events that involve being with many people for hours in a poorly ventilated space will be a higher risk than outdoor events with fewer people. This is whether or not anyone is having sex.

This will hopefully only for a short time, perhaps only for the next few weeks.

Will having MPX once protect me against catching it again?

Although this might be possible, there is currently not enough information to answers this question.

Even if it is possible, this would not be something to rely on before there is data.

Also, cases have been reported when cases have returned after the infection was thought to be cured. In these cases special tests are need to find out whether or not this is a new infection.

3. Diagnosis and treatment?

What if I have symptoms?

If you are worried about symptoms, please telephone a sexual health clinic (or 111 in the UK).

Contact by phone is important. The clinic will ask you about symptoms, including to describe any spots or skin blisters.

Please do NOT visit the clinic using a drop-in service. This could cause health workers to need to isolate and staffing is already under pressure.

Anyone in the UK can access free testing and treatment at a sexual health clinic.

How is MPX diagnosed?

A distinctive spots/blisters appearing a few days after other general symptoms is enough for MPX to be very likely, even before it is confirmed by a test.

This will involve a doctor checking that the skin bumps and blisters are not another infection.

However, testing is still important to rule out other pox viruses.

PCR testing is used to confirm MPX. This involves sending samples to a UK-HSA laboratory. The doctor will need to have your contact details so they can let you know the test result. The UK-HSA is responsible for all MPX cases.

If the sample tests positive, you will be asked about close contacts over the previous three weeks. This includes people you live with and any sexual partners. Sexual partners will not be told about you.

All information is handled privately but please talk to your doctor if you have questions about this.

How important is contact tracing?

Anyone diagnosed with MPX will be asked for details about people they have been in close contact with.

This will help to identify people who might be at risk, and may benefit from PEP.

Effective contact tracing could limit how serious MPX becomes in the UK. It will be done very carefully and sensitively. This is a specialist part of sexual health care.

People who are thought to be at high risk will then be asked to self-monitor for symptoms over the next three weeks. They will be monitored with a daily phone call, and they may be offered vaccination as PEP.

Can MPX be treated?

Yes. Although most people are likely to be monitored without direct treatment.

If needed, several oral drugs are being used to treat MPX, especially if symptoms are more than mild.

These include tecovirimat (twice daily for 2 weeks) or brincidofovir (once a week).

Both these drugs were approved to treat other infections similar to MPX. This means there is little direct evidence about whether they work for MPX.

As most infections are mild, treatment is only offered to more severe cases, or to people at higher risk of severe infection.

This can include people with reduced immune functions, children younger than 8, pregnancy, and selected other infections.

Vaccines are also being used to manage and reduce the risk from infection.

Which vaccines are used against MPX?

Two vaccines against smallpox are currently being used against MPX.

The main vaccine is called Imvanex (also called Imvamune, Jynneos and MVA). It is a live but non-replicating vaccine that is also approved against MPX in the US in 2019. This vaccine is safe to use by people living with HIV. It is given in two doses, 28 days apart.

Although the vaccine is safe, anyone with a CD4 count below 100 might be unlikely to generate an effective response.

An earlier vaccine called ACAM2000 was approved in 2007 but is a live replication-competent vaccine. Although it is given as a single dose it is not recommended in people living with HIV. It is also no longer available in the UK.

Are the vaccines effective?

The smallpox vaccine is likely to help even if given after contact. It should limit the risk of infection or limit the severity of illness if the infection develops. This may be up to 85% effective.

Vaccination for close contacts is most effective when given within four days of contact. However, it might still be effective for up to 14 days after.

Will smallpox vaccinations from childhood still be active?

Many adults older than 50 will have had the smallpox vaccine as a child.

It is possible that this may offer some protection against MPV.

Smallpox vaccinations were stopped in the UK in 1971 and immune responses become much lower after 10 years.

4. HIV and MPX

How does HIV affect MPX?

The British HIV Association (BHIVA) published a recent statement on MPX, that has also been updated.

This says that HIV should not increase your risk of catching MPX. It also should not make MPV a more serious infection.

So far, HIV is not linked to any difference in symptoms and outcomes.

This is based on you having an undetectable viral load and a CD4 count that is well above 200 cells/mm^3. This is a cautious approach because there is too little direct evidence about this.

The BHIVA statement also references a Nigerian study with worse outcomes for people living with HIV. Most of these cases were not on effective ART though, some with very low CD4 counts and most with detectable viral load.

Please see this link to BHIVA and ECDC statements about MPX.

https://i-base.info/htb/42896

5. Other questions

What are the differences between MPX and COVID?

Although everyone will worry about the similarities to COVID-19.

There are important differences that will stop MPX from becoming a pandemic.

MPX only becomes infectious after there are symptoms. COVID was devastating because it was infectious several days before anyone had symptoms.

MPX is heavier than the COVID virus, MPV is heavier. This makes it more likely to fall to the ground rather than stay in the air.

COVID infection was through the nose, throat and lungs. Although MPX can be caught from droplets in air in a confined space, but is more commonly caught by physical contact.

MPX is much less likely to mutate into different strains than COVID.

COVID was a more severe infection. Many people needed time in intensive care and in the most serious outcomes, people of all ages died.

What about transmission to animals?

This is an important concern with MPV.

Despite the name, MPX is more linked to infections in other animals. This includes in mice, rats and squirrels.

An outbreak in the US in 2003 was linked to prairie-dogs (which are not dogs).

The concern about other animals being carriers for MPX is that this might make it difficult to control the virus in the long-term.

It is also important for people who self-isolate at home to know whether this also needs to be from their pets. Advice was not initially given on this question, However, on 27 May the UK included the need for people diagnosed with MPX to also isolate from their pets. Similar guidance is made by the ECDC.

This is to reduce the risk that animals could become a long-term reservoir for MPV.

Gerbils, hamsters and other rodents have a very high risk of catching MPX. Other pets including cats and dogs should be kept isolated at home. However, it is difficult to set how “regular vet checks to ensure no clinical signs are observed” is expected to work.

While this advice is laudable in the case of pets, the guidance doesn’t extend to unwelcome rodents that are present despite complaining to your landlord. This might however be a fast-track way to prompt a response.

How worried should we be about MPX?

The WHO responded quickly to the recent news about MPX with two early reports on 21 and 30 May.

These recognised that what happens over the next few weeks will be very important. Currently the organisation says the MPX is a moderate risk to global health.

More than 500 cases have been reported in new countries. There is only a short time to try to prevent further spread. This means each country has to take MPX seriously.

Luckily MPX is very different to COVID-19 and no deaths have been reported from these cases.

6. References and further information

The following sources were used for the information on this page and/or are useful links for further information.

1. NHS. Monkeypox.
https://www.nhs.uk/conditions/monkeypox
Non-technical information about MPV in the UK. This includes who to contact if you are worried about symptoms.
2. UK Health Security Agency (UK-HSA). Monkeypox virus. (23 May 2022).
https://www.gov.uk/guidance/monkeypox
More detailed information from the UK government about all aspects of MPV including update on the current outbreak.
3. BHIVA rapid statement on monkeypox virus. (17 May 2022, updated 31 May 2022).
https://www.bhiva.org/BHIVA-rapid-statement-on-monkeypox-virus
4. European Centre for Disease Prevention and Control (ECDC). Monkeypox multi-country outbreak: rapid assessment report. (23 May 2022).
https://www.ecdc.europa.eu/en/publications-data/risk-assessment-monkeypox-multi-country-outbreak (download page)
https://www.ecdc.europa.eu/sites/default/files/documents/Monkeypox-multi-country-outbreak.pdf (PDF)
See also this slide set from an informal webinar given on 24 May 2022.
Monkeypox ECDC webinar (PDF)
5. Adler H et al. Clinical features and management of human monkeypox: a retrospective observational study in the UK. The Lancet, DOI: 10.1016/S1473-3099(22)00228-6. (May 24 2022).
https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(22)00228-6/fulltext
Details of seven MPV cases reported in the UK between 2028 and 2021.
6. US CDC. What clinicians need to know about monkeypox in the United States and other countries.
https://emergency.cdc.gov/coca/calls/2022/callinfo_052422.asp
This US talk on clinical management includes pictures of MPV compared to other common skin reactions.
7. US CDC. Monitoring people who have been exposed.
https://www.cdc.gov/poxvirus/monkeypox/clinicians/monitoring.html
8. US CDC. Home page for information for doctors about MPV.
https://www.cdc.gov/poxvirus/monkeypox/clinicians/index.html
9. International Monkeypox case tracker.
https://monkeypox.healthmap.org
10. Human Animal Infections and Risk Surveillance group (HAIRS). Qualitative assessment of the risk to the UK human population of monkeypox infection in a canine, feline, mustelid, lagomorph or rodent UK pet. (27 May 2022).
https://www.gov.uk/government/publications/hairs-risk-assessment-monkeypox/qualitative-assessment-of-the-risk-to-the-uk-human-population-of-monkeypox-infection-in-a-canine-feline-mustelid-lagomorph-or-rodent-uk-pet
11. Prepster and the UK Health Security Agency (HSA). UK Community webinar available online. Prepster Facebook page. (24 May 2022).
https://www.facebook.com/133703446979595/posts/1677130825970175
Excellent early community discussion.
12. UK Health Security Agency (UK-HSA). Principles for monkeypox control in the UK: 4 nations consensus statement. (30 May 2022).
https://www.gov.uk/government/publications/principles-for-monkeypox-control-in-the-uk-4-nations-consensus-statement/principles-for-monkeypox-control-in-the-uk-4-nations-consensus-statement
Includes updated guidelines for continued prevention in the UK.
13. WHO. Multi-country monkeypox outbreak in non-endemic countries: Update. (29 May 2022).
https://www.who.int/emergencies/disease-outbreak-news/item/2022-DON388
Detailed review of international cases and guidelines for appropriate monitoring and prevention.
14. EACS/ECDC. Informal webinar given on 24 May 2022.
Monkeypox EACS/ECDC webinar 1 (PDF)
15. EACS/ECDC. Informal webinar given on 31 May 2022.
Monkeypox_EACS/ECDC_webinar 2 (PDF)
16. Andrea A et al for the INMI Monkeypox Group.. Epidemiological, clinical and virological characteristics of four cases of monkeypox support transmission through sexual contact, Italy, May 2022. Euro Surveill. 2022;27(22):pii=2200421. (2 Jun 2022).
https://doi.org/10.2807/1560-7917.ES.2022.27.22.2200421.

COMPLICATIONS: COVID-19

Implications of SARS-CoV-2 in gut tissue for transmission of COVID-19 and long COVID

Simon Collins, HIV i-Base

Many questions related to the implications of SARS-CoV-2 involvement in gut tissue and the GI track are still unclear.

These are discussed in a recent article and editorial in JAMA, including the potential role in long COVID when this is not cleared early. Also whether this might continue to be a risk for further transmission. [1, 2]

Summary points from the main article include:

- Roughly 50% of people shed SARS-CoV-2 RNA in the week after COVID-19 diagnosis.
- RS-CoV-2 RNA can also be found in 4% people after seven months.
- Presence of fecal SARS-CoV-2 RNA is associated with GI symptoms.
- Active infection of GI tissue is likely.

References

1. Natarajan A et al. Gastrointestinal symptoms and fecal shedding of SARS-CoV-2 RNA suggest prolonged gastrointestinal infection. Med (2022). DOI: 10.1016/j.medj.2022.04.001. (12 April 2022).
https://www.cell.com/med/fulltext/S2666-6340(22)00167-2
2. Rubin R. SARS-CoV-2 RNA can persist in stool months after respiratory tract clears virus. doi:10.1001/jama.2022.7892. (18 May 2022).
https://jamanetwork.com/journals/jama/fullarticle/2792688

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http://www.i-Base.info

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- Introduction to ART (May 2022)
- HIV & quality of life: side effects & long-term health (Sept 2016)
- Guide to PrEP in the UK (February 2022)
- HIV testing and risks of sexual transmission (June 2021)
- Guide to changing treatment and drug resistance (August 2021)
- Guide to HIV, pregnancy & women's health (April 2019)

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The leaflets use simple statements and quotes about ART, with short URL links to v
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Personalising these for your clinic is cheap and easy and might be an especially nice way to highlight the good news.

For further information please contact Roy Trevelion at i-Base:

roy.trevelion@i-Base.org.uk

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