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treatment bulletine

AIDS 2022 reports and monkeypox crisis (3 August 2022)

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Introduction to ART: i-Base guide (June 2022)

The widely used i-Base guide to ART has been updated to include recommendations in the 2022 BHIVA guidelines.

Both online and print versions are now updated.

This guide covers information for people newly diagnosed, those about to start ART, and also those who have been living with HIV for many years and who want to learn more about treatment.

https://i-base.info/guides/starting



PrEP for women (June 2022)

A new leaflet about PrEP produced by and for women (with the Sophia Forum).

These small 16-page A7 leaflets were produced to raise awareness of access to PrEP.

Translations into key European and African languages are online and will be included on this page when available.

https://i-base.info/htb/43453



EDITORIAL

This issue of HTB leads reports from the 24th International AIDS Conference (AIDS 2022) held in Montreal from 29 July to 2 August 2022.

As always, the conference had an impressive scientific programme, and this should already be available online as open access.

Early reports in this issue include ART for children, new formulations, using doxycycline as PrEP for STIs and new cases of HIV cure and remission.

Throughout the next few weeks we will continue to post reports online, ahead of inclusion in the next edition of HTB.

We also include eight articles on the recent monkeypox outbreaks. i-Base called this a health crisis long before the WHO announced a global health emergency. And UK organisations collectively called on the urgency of emergency NHS funding.

This online Q&A was first posted in May, and is regularly updated.

https://i-base.info/monkeypox

Numbers have been increasing exponentially with more than 2600 cases now reported in the UK and more than 27,000 globally.

Vaccination programmes have started in the UK in people at high risk. It is important that people give the vaccine time to work, as immune responses might continue to get stronger over four weeks. There are data that people living with HIV might generate sightly lower responses, and more slowly. This makes the caution to wait four week more important.

Although not included in this issue, i-Base discuss vaccine efficacy in this online Q&A.

https://i-base.info/qa/20255

The MVA vaccine is approved based on receiving two shots, 28 days apart. But the global shortage will limit access in every country, using an initial single dose, perhaps with a second dose several months later. Although a longer delay to the second shot is unlikely to reduce final immune responses it will leave a longer time with lower levels of coverage. The vaccine is also primarily expected to reduce the risk or severe symptoms rather than blocking transmission, so some breakthrough infections are still expected.

Taken together, this suggest reducing high risk situations could be good for individual and community health. It would also give sexual health clinics a time to recover. Cutting back on anonymous sex, including in private parties, saunas, darkrooms and cruising grounds could help break the chain of infections.

Just for four weeks.





Supporting Ukraine

Simon Collins, HIV i-Base

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.

SPECIAL REPORT: MONKEYPOX IN THE UK

Time to take a break for August: four weeks out

An option for individual and community health and to help our sexual health clinics

Simon Collins, HIV i-Base

The body of latest research into monkeypox (MPX) has included new data suggesting greater concerns about transmission during asymptomatic infections and viral persistence of this particularly sticky virus on hard surfaces (washrooms, door handles, soap dispensers).

Language has also changed. There have been easier references to MPX already becoming endemic in some countries for the next months or now being endemic in gay, bisexual and other men who have sex with men.

This last suggestion is usually balanced by noting that viruses rarely follow social boundaries.

Public health information is still largely focused on what to do if you might have been at risk from MPX:

- Be aware of symptoms (from fatigue, to rash to ulcers).
- Self-isolate,
- Call a sexual health clinic or 111/





But more direct information about the easiest way to avoid MPX could also be developed.

- Talk to friends and partners about MPX.
- Exchange contact details with new partners not a bad idea at any time.
- The best way to avoid MPX is to take a break from settings where it is easy to have contact with multiple partners whether or not you have sex. MPX is very infectious.

This includes private parties, saunas, outdoor cruising areas, darkrooms and other sex-on-premises venues.

This information is to inform individual choice.

- It will be easier for some people and very difficult for others. Even doing this by enough people could also put a break in the outbreak.
- It would also support sexual health clinics who are first responders, so far with no additional funding.

Taking time for the vaccines to work

The MVA monkeypox vaccine is likely tto be very effective but also takes a little time to work.

Efficacy data are currently limited to immunogenicity results from several studies. Some of these suggest that waiting up to four weeks might be important for highest levels of protection. This is also included in advice from the UKHSA. [1, 2, 3, 4]

Two of these studies suggest that four weeks might be especially important for people living with HIV. These studies are important enough to be included in the EU SPC/EPAR and in the LIS evaluation that lead to vaccine an



i-Base leaflet. Table taken from the EU SPC/ EPAR, based on immunogenicity results from the MVA-011 study. Leaflet available online. [7]

SPC/EPAR and in the US evaluation that lead to vaccine approval by both agencies. [5, 6]

Currently, very limited information about efficacy and time to protection is being given to people getting the vaccine. If the caution to wait four weeks turns out to be important, assuming earlier protection could add to the current outbreak.

Many people are already reducing their risk especially if they are waiting for access to a vaccine. Awareness of MPX has steadily increased and it can range from mild but needing to self-isolate for three weeks, to painful and unpleasant, with possible scarring.

Severe infections have involved admission to intensive care units and a few cases have been fatal.

References

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https://www.nejm.org/doi/full/10.1056/NEJMoa1817307

- 3. Overton ET et al. Safety and immunogenicity of modified vaccinia ankara-Bavarian Nordic smallpox vaccine in vaccinia-naive and experienced HIV-positive individuals: an open-label, controlled clinical phase 2 trial. Open Forum Infect Dis. 2015 May 5;2(2):ofv040. doi: 10.1093/ofid/ofv040. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4567089
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- US Office of Vaccines Research and Review (OVRR). Review memorandum for Jynneos vaccine. (2018) https://www.fda.gov/media/131870/download (direct download)
- How good is the monkeypox vaccine? https://i-base.info/qa/20255

CONFERENCE REPORTS

24th International AIDS Conference (AIDS 2022)

29 July to 2 August 2022, Montreal, Canada

Simon Collins, HIV i-Base

Introduction

This year the IAS conference was held in Montreal and also as an impressive fully hybrid conference online.

As usual, the conference had a strong programme that covered all aspects of HIV treatment, prevention, activism and policy. Many specialist workshops were also held in the few days before the main conference.

The programme for the meeting is available online:

https://programme.aids2022.org

Several thousand abstracts and posters should also now be available online from the main programme. Many more e-posters are available than printed posters displayed at the meeting.

The programme also includes more than 100 satellite meetings, which are also available to watch online - another first for the meeting. If this is a model for future conferences, this could broaden access to many more people than could ever attend in person.

But attending in person is still vital. Unfortunately, hosting the conference in Canada was not a good choice for the meeting this year. Many delegates had visas denied before the meeting and others had their travel blocked by airlines and customs on the way to the conference.

This is especially disappointing as IAS conferences have previously been held in Montreal, Vancouver and Toronto.

This year, Canada's racist and arbitrary visa policies was such a significant problem that it was mentioned throughout the conference, including in a community protest at the opening session (where there was no official involvement of the Canadian government).

IAS now promises to change where they host future meetings. This is not a new problem, but Canada this year has been especially difficult.

The scientific programme however was strong, with important research on many subjects.

- New treatments and formulations.
- HIV prevention (including using the antibiotic doxycycline as PEP to reduce STIs).
- Research in key populations, including women and children.
- Studies on the global monkeypox crisis.
- Cure-related research (including new cases of cure and remission).

The following reports are included in this issue of HTB.

- Early data on injecting CAB/RPV-LA into thigh muscle
- Doxycycline PEP significantly reduces STIs in people at high risk of infections
- Another possible HIV cure case after stem cell transplantation for cancer; example of extended posttreatment control in Spain
- Other cure-related sessions at AIDS 2022



AIDS 2022: ANTIRETROVIRALS

Dolutegravir-based ART in children and adolescents: effective in six African countries

Polly Clayden, HIV i-Base

Dolutegravir (DTG)-based ART achieved and mostly maintained viral load suppression in children and adolescents in real-world settings in seven sites in six African countries. These findings from a retrospective chart review, conducted by Baylor International Pediatric AIDS Initiative, were presented at AIDS 2022.

The study covered the period from January 2016 to December 2021. It included children and adolescents ages 0 to 19 years old receiving DTG-based ART at clinics in Botswana, Eswatini, Lesotho, Malawi, Tanzania, and Uganda.



There were 11,799 children and adolescents who received DTG during the study period. Fifty six per cent were female. Most were over 10 years old: 10 to 14 years, 36.6% and 15 to 19 years, 40.2%. Only 2.6% were under 5 and the remaining 17.6% were 5 to 9 years old.

Only 20.6% of participants started DTG first-line, 44.2% had previously received NNRTI-based ART and 34.4% PI-based. Most (61.7%) received DTG with tenofovir disoproxil fumarate (TDF) and lamivudine (3TC); 32.2% with abacavir (ABC) and 3TC and 5.3% with zidovudine (AZT) and 3TC.

Mean follow up time from starting DTG was 22.4 months (SD +/-12.4) and there were 21,077 person-years of follow up.

Six months after starting DTG-based ART, 92.4% of participants with viral load results (n=8816) achieved viral suppression (<1000 copies/mL). At 24 months 91% of participants with viral load results (n=2074) were suppressed.

With 6 month suppression rates as the comparator for the analysis, up to 60 months, rates of viral suppression were largely similar across age groups and between female and male participants. In the later period the cohort was smaller with wider confidence intervals.

But among the 10 to 14 year age group, rates of suppression dropped by –3.9% and –5.1% at 24 and 30 months respectively and were statistically significant. This occurred during the peak of covid pandemic disruption to supply chain, access and transportation, which might at least partly explain the decline.

The study also looked at single drug substitutions among the cohort, which happened in 3738 participants. There was a modest but significant drop in viral suppression after 6 months (-1.8%) of switching to DTG, p<0.01. There was no difference by 18 months follow up.

Among the 210 participants with an unsuppressed viral load at time of switch to DTG, 80% achieved viral suppression at 6 months and this was maintained among participants with longer follow up.

COMMENT

These findings further support WHO recommendations and the widespread roll out of DTG among children and adolescents globally.

The study will continue with additional analyses including a closer look at DTG single drug substitution (while maintaining NRTI backbone).

It is important to emphasise that although some of the participants were followed up for as long as 60 months, very few had viral load results at the later timepoints. At 24 months, viral load data were available for 1888 participants but by 30 months this had dropped to 422.

Those under 10 years were also a smaller cohort with a lot of variability.

References

Bacha J et al. The fast and the continuous: dolutegravir-based antiretroviral therapy achieves impressive viral load suppression in CALHIV in the short- and long-term. AIDS 2022. 29 July – 2 August. Oral abstract 2849. https://programme.aids2022.org/Abstract/Abstract/?abstractid=2849 (abstract)

https://conference.aids2022.org/media-2078-outcomes-in-paediatric-and-adolescent-hiv-beyond-art (webcast)

Early data on injecting CAB/RPV-LA into thigh muscle

Kirk Taylor, HIV i-Base

AIDS 2022 included results from a phase 1 study looking at whether lateral thigh muscle could be an alternative injection site for long-acting cabotegravir/rilpivirine-LA (CAB/RPV-LA). [1]

Current formulations involve injections into gluteal muscle every two months by a health worker.

The study enrolled 15 HIV negative participants (9 men, 6 women). Median age was 33 years (range: 21 to 49) and 7/15 were Black and 5/15 Hispanic/Latinx. Median weight was 93 kg (range 67 to 107) and BMI was 31 kg/m² (range: 24 to 34).

The study protocol involved daily oral lead-in (CAB 30 mg plus RPV 25 mg) for 28 days, followed by a 14day washout and single 3 mL IM injections of CAB (600 mg) and RPV (900 mg) in the lateral thigh muscle. Pharmacokinetic (PK) parameters were observed for one year.

Median and geometric mean were > 4 x protein adjusted IC90 for both drugs at week 8. Although some individuals dropped below this target, all remained above the IC90 at this timepoint.

Median levels of both drugs dropped below the IC90 after approximately 18 weeks and became undetectable at 24 weeks for cabotegravir but remained detectable at 52 weeks for rilpivirine.

At week 8, CAB and RPV levels were 5.3-fold and 2.4-fold higher than their PA-IC90 threshold.

Low grade adverse events were reported by all 15/15 participants and included injection site reactions (ISRs), chills and headache. Grade 3 ISRs were due to pain at the injection site. Pain was reported up to 4 days post-injection and this was participants generally reported as acceptable.

These data indicate that giving LA formulations in thigh muscle achieves target plasma levels out to 8 weeks and that the injections were tolerable.

СОММЕNТ

These early data are encouraging but need to be confirmed in larger numbers and in people living with HIV (as HIV can affect PK).

If alternative injection sites are validated, this might allow self-administration of therapies.

Further studies are required to evaluate the potential of the thigh and other relevant muscles as potential injection sites.

References

 Hang K et al. Pharmacokinetics and tolerability of cabotegravir and rilpivirine long-acting intramuscular injections to the vastus lateralis (lateral thigh) muscles of healthy adult participants. AIDS 2022 (Montreal). 29th July to 2nd August. E-poster EPB176. https://programme.aids2022.org/Abstract/Abstract/?abstractid=9906 (abstract)

https://conference.aids2022.org/media-1455-pharmacokinetics-pk-and-tolerability-of-cabotegravir-cab-and-rilpivirine-rpv-long-acting-I (e-poster)

Simplifed lenacapavir dosing: PK results in HIV negative study

Kirk Taylor, HIV i-Base

AIDS 2022 included a pharmacokinetic (PK) study of a simplified dosing strategy for the long-acting capsid inhibitor lenacapavir, currently being studied for both treatment and prevention. [1]

If confirmed, the new strategy could help adherence and reduce the number of clinic visits.

This phase 1 open-label study of HIV negative participants explored PK profiles from standard and simplified dosing strategies.

Group 1 (n=31) received the current three oral lead-in doses (600 mg on days 1 and 2, and 300 mg on day 8) before a sub-cutaneous (SC) injection (927 mg) on day 15.

Group 2 (n=14) used a simplified strategy with oral (600 mg) plus SC (927 mg) lenacapavir on day 1, followed by a second oral dose (600 mg) on day 2.





PK parameters were monitored from pre-dose to day 197. The target plasma concentration was 15.5 ng/mL, equivalent to 4x the protein adjusted IC90.

Mean plasma levels for group 1 were consistently above the target from 2 hours post dose on day 2 until the final measurement on day 197. Tmax was reached 85 days post-SC injection.

Similar PK parameters were observed for the simplified regimen with concentrations consistently above the target from 2 hours post-dose on day 2 and an earlier Tmax at 70 days. However, the lower bound of the 95% CI dipped below the 4x pa IC90 threshold between days 168 and 182.

Participants were similar in each group, with median age about 32 years (range: 20 to 45) and median BMI was approximately 26 kg/m² (range: 22 to 30).

Adverse events were grade 1-2, mostly due to injection site reactions.

COMMENT

In HIV negative participants these PK profiles were comparable for simplified and standard dosing and remain above target levels for much of the study.

Median plasma concentrations remained above the 4x pa IC90 at all timepoints but results will need to be confirmed in people living with HIV as 90%Cl dropped below this level with the simplified strategy. The lower levels between days 168 to 182 may be explained by the relatively low sample size for group 2.

Lenacapavir has already been submitted to the EMA and US FDA for an indication in multidrug resistant HIV.

In July 2022, the EMA reported a positive recommendation for approval.

References

- Jogiraju V et al. Pharmacokinetics of a simplified subcutaneous lenacapavir regimen versus phase 2/3 regimen. AIDS 2022 (Montreal). 29th July to 2nd August. Abstract PESUB22. https://programme.aids2022.org/Abstract/Abstract/?abstractid=5490 (abstract) https://conference.aids2022.org/media-2508-pharmacokinetics-of-a-simplified-subcutaneous-lenacapavir-regimen-versus-phase-2-3-regimen
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AIDS 2022: PREVENTION

Doxycycline PEP significantly reduces STIs in people at high risk of infections

Simon Collins, HIV i-Base

One of the first presentations at AIDS 2022 included using the antibiotic doxycycline in people at high risk of sexually transmitted infections (STIs). [1]

This randomized, open-label study, planned to enroll 780 people attending sexual health clinics in Seattle or San Francisco in two cohorts; one was HIV positive, and the other HIV negative and on PrEP.

However, the study was unblinded early due to a recommendation from the Data and Safety Monitoring Board (DSMB) in May 2022 based on significantly reduced STIs in the active arm of both cohorts.

At the time of unblinding, the study had randomised 501 gay men (96%, n=482 and trans women (4%, n=19) who have sex with men 2:1 to either 200 mg doxycycline or standard of care. The primary endpoint was a diagnosis of gonorrhoea, chlamydia or syphilis within a three-month period.

Participants in the active arm were asked to take a single dose of doxycycline as soon as possible but within 72 hours of having sex (without a condom) and to not take more than one dose during 24 hours. Participants were given three months of doxycycline to keep at home, with standard advice to take with a glass of water and to stay upright for 30 minutes.



Results were stratified by HIV status (n=174) and use of PrEP (n=327).

Overall, baseline demographics were similar in the two cohorts. This included median age 38 (IQR: 32 to 47), with 67% white, 8% Black, 11% Asian, 15% other, and ethnicity included 30% Hispanic/Latinx.

There were a median of 9 male partners (IQR: 4 to 17) during the previous three months. At least one-third reported recent recreational drug use/chemsex during the same period. Rates of STIs during the previous 12 months were high: 69% gonorrhoea, 58% chlamydia and 20% syphilis.

Results in the intent-to-treat (ITT) analysis reported significant overall reduction in the risk of STIs in the active arm: RR 0.35 (95%CI: 0.27 to 0.46), p<0.0001), with similar results in each cohort.

The most common STIs were gonorrhoea and chlamydia, mainly in throat or rectum, with dual infections common. However, only 15% to 28% of infections were symptomatic, especially in the active arm.

Reductions in the active arm for each STI, and in both cohorts, were highly significant in each three-month period.

Safety results were also good with no grade 3 side effects associated with doxycycline and 88% of participants reporting the intervention to be acceptable or very acceptable.

Self-reported adherence was also high (taken for 87% of appropriate times). Each month, half the group took doxycycline <10 times, 30% took it 10 to 20 times and 16% took >20 doses (with some approaching daily dosing).

Although the majority of resistance tests are still ongoing, the US background rate of approximately 20% population tetracycline resistance to gonorrhoea was also seen in this study. Resistance was linked to reduced efficacy of doxycycline but not to development of new resistance.

$\mathsf{C} \ \mathsf{O} \ \mathsf{M} \ \mathsf{M} \ \mathsf{E} \ \mathsf{N} \ \mathsf{T}$

The reductions in STIs by more than 60% in people with very high background rates of STIs is impressive and significant. Background rates of tetracycline resistance and sensitivity are also likely to be important.

Background resistance to gonorrhea was significantly lower in this US study compared to roughly 50% reported in the French IPERGAY substudy. In IPERGAY, doxycycline PrEP significantly reduced rates of chlamydia and syphilis, but not gonorrhoea. [2]

Rates in London are comparable or higher to those in Paris.

The latest GRASP surveillance data published for 2020 showed tetracycline resistance in England and Wales at 65%, with the overall trend of increased resistance. [3]

This could be due to the change to using doxycycline for chlamydia in the UK. The CDC has also now changed its guidelines to use doxycycline so it is likely that resistance will also increase in the US.

It will be important to understand the effect of intermittent doxycycline use on the gut microbiome or other long-term outcomes. Also, whether other bacteria are affected by tetracycline resistance.

The results from this US study might need to be confirmed in a UK setting, but should at least be considered given the high rate of STIs experienced in some populations.

References

 Luetkemeyer A et al, Doxycycline post-exposure prophylaxis for STI prevention among MSM and transgender women on HIV PrEP or living with HIV: high efficacy to reduce incident STI's in a randomized trial https://programme.aids2022.org/Abstract/Abstract/?abstractid=13231

https://conference.aids2022.org/media-2109-co-chair-s-choice (webcast)

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- Antimicrobial resistance in Neisseria gonorrhoeae in England and Wales: Key findings from the Gonococcal Resistance to Antimicrobials Surveillance Programme (GRASP 2020). See graph on page 14. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1033882/GRASP_2020_Report.pdf (PDF)

Another possible HIV cure case after stem cell transplantation for cancer; example of extended post-treatment control in Spain

Richard Jefferys, TAG

The 24th International AIDS Conference (AIDS 2022) officially opened on Friday in Montreal, but a Zoom <u>press conference</u> two days earlier shared news of results from several studies, including two case reports relevant to HIV cure research. [1]

Jana Dickter from the City of Hope hospital in Los Angeles described another instance of "prolonged HIV-1 remission" after receipt of a stem cell transplant required to treat a life-threatening cancer, this time in a 66-year-old man. The stem cell donor was homozygous for the CCR5 delta-32 mutation, which causes immune cells to be resistant to most HIV variants. Dickter emphasised the unique aspects compared to previously reported cases:



- The person was older (63 at the time of the transplant procedure, 66 now).
- Has been living with HIV longer (over 31 years).
- Received a less immunosuppressive regimen during transplantation and a chemotherapy regimen that is better tolerated by older people.

As explained in a press release from the City of Hope, the stem cell transplant was administered in early 2019 after a diagnosis of acute myelogenous leukemia (AML). [2]

Antiretroviral therapy (ART) was stopped in March 2021 and the man has now been followed for over 17 months with no HIV viral load rebound or HIV DNA detected. Antibody responses against HIV have waned and virus-specific T-cell responses are no longer detectable. The AML is in remission. Regrettably, the details of these results were not available until Dickter presented at the conference on Monday August 1 (although the abstract text was available). [3]

Dickter noted that the particular protocol employed at City of Hope is likely better suited to older people with HIV who require stem cell transplants to treat cancers, and may offer additional opportunities to attempt cures if appropriate CCR5 delta-32 homozygote donors can be identified.

As with the New York City woman reported at CROI earlier this year, the researchers are being cautious and using the term remission to describe the case rather than cure, due to limited follow-up. [4]

It would be helpful for the HIV cure research field to come to consensus on how best to define cure in such cases, because news coverage tends not to adhere to these distinctions in terminology.

There's also an urgent need for consensus on how many cases of HIV cure/remission have been achieved by stem cell transplants from CCR5 delta-32 homozygote donors: both the International AIDS Society and City of Hope press releases erroneously state that this represents the "fourth" such case but in fact, there are five in total: [5]

- Timothy Ray Brown (aka the Berlin patient).
- Adam Castillejo (aka the London patient).
- The Düsseldorf patient.
- The New York patient.
- The City of Hope patient.

Details on each of the prior cases is included in TAG's latest Research Toward a Cure and Immune-Based Therapies Pipeline Report. [6]

Dr. Núria Climent delivered the second report, about a case of "exceptional post-treatment control" in a woman with HIV who'd participated in a clinical trial in Barcelona. The Hospital Clínic-IDIBAPS have issued a press release about the findings. If I'm understanding correctly, it also involves an older individual: the woman was 59 at the time of study enrollment and so is in her 70s now. [7]

The study was complicated, beginning by randomising people with recent HIV infection to receive either ART or ART plus the immunosuppressant drug cyclosporine. There was a total of 20 participants: 19 cisgender men and the one cisgender woman (who was assigned to receive ART plus cyclosporine). Results from this initial part of the study were published in 2016. [8]

The woman was then rolled over into another protocol that involved an analytical treatment interruption (ATI). [9]

A short course of GM-CSF and pegylated alpha interferon was given during the ATI, followed by another period of ART plus subcutaneous low-dose IL-2 before treatment was interrupted completely.

The crux of today's report is that the participant has now maintained an undetectable HIV viral load for more than 15 years off ART and has displayed a progressive decline in measures of the HIV reservoir during that time. HIV that's capable of replicating can still be detected at low levels, however, suggesting that control is being actively maintained by the immune system.

In laboratory tests, the researchers identified "memory-like" natural killer cells and gamma-delta CD8 T cells as contributors to suppressing HIV replication (these represent relatively small subsets of immune system cells whose potential role in suppressing HIV hasn't received much attention historically).

The woman does not have any genetic factors that have been associated with immunological control of HIV, and Climent explained that she experienced quite severe symptoms during primary infection (which was diagnosed at Feibig stage 5).

In response to questions, Climent noted that the woman was the only study participant who experienced post-treatment control, so the role (if any) of the immune-based interventions that were given is unclear. The researchers have also not tested for the presence of antiretrovirals in blood samples, which is necessary to confirm that the viral load control has occurred post-treatment. The formal presentation at the conference will occur on Sunday July 31. [10]

There's been at least one other report of extended post-treatment control in a person who received ART plus cyclosporine during early HIV infection. That case, described by researcher Guiseppe Pantaleo in 2009 as "the Lausanne Patient", was a man who had been off ART for over eight years at the time of the report. [11]

HIV cure research might potentially benefit from compiling all the historical reports of post-treatment control and assessing their current status (if the information is available). So far, the phenomenon appears rare, but it has the potential to offer clues to help develop curative interventions.

Several other sessions at AIDS 2022 that included HIV cure-related research have been compiled by Richard Jefferys. [12]

Source: TAG Basic Science Blog. (28 July 2022).

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Other cure-related sessions at AIDS 2022

Richard Jefferys, TAG

AIDS 2022 featured several sessions on HIV cure research, listed below.

Thursday 28 July

Pre-conference symposium: Pathways to an HIV cure: Research and advocacy priorities

https://www.iasociety.org/events/pathways-hiv-cure-research-and-advocacypriorities

Friday 29 July

Satellite: Africa HIV cure research: Strengthening industry-community engagement in clinical research

https://programme.aids2022.org/Programme/Session/57

Saturday 30 July

The view from the bench: Advances in HIV basic and translational research

https://programme.aids2022.org/Programme/Session/158

Late Breaker Track A

https://programme.aids2022.org/Programme/Session/830

Global Village: On the road to HIV cure gene therapy: Who can learn from whom?

https://programme.aids2022.org/Programme/Session/329

Novel insights into the nature of the HIV reservoir and mechanisms of persistence

https://programme.aids2022.org/Programme/Session/24

Sunday 31 July

Approaches for HIV cure and vaccine research

https://programme.aids2022.org/Programme/Session/80

Combining immunotherapeutic agents to achieve ARV-free remission of HIV

https://programme.aids2022.org/Programme/Session/17

Responding to the virus: Advances in HIV immunology

https://programme.aids2022.org/Programme/Session/157

Monday 1 August

Late Breaker Track B

https://programme.aids2022.org/Programme/Session/831

Finding the needle in the haystack: Progress in understanding the HIV reservoir

https://programme.aids2022.org/Programme/Session/155

Tuesday 2 August

Shake and bake: Promising strategies for HIV cure

https://programme.aids2022.org/Programme/Session/156



AIDS 2022: OTHER NEWS

Reports launched at AIDS 2022

Simon Collins, HIV i-Base

As with other large meetings, AIDS 2022 was used to launch numerous reports and special publications, a few of which are included below.

In Danger: UNAIDS Global AIDS Update 2022

UNAIDS

The report from UNAIDS was widely publicised as the conference opened and set the tone for most of the concerns about the importance of maintaining a global response to HIV.

The report shows that during the last two years of COVID-19 and other crises, the global HIV response has faltered, resources have shrunk, and millions of lives are at risk as a result.

Annual infections have increased in Eastern Europe and central Asia, Latin America, and the Middle East and North Africa, where rates were all previously falling.

The report is a call to action to tackle the inequalities driving AIDS. This is urgently required to prevent further new infections and to refocus our goals to end the AIDS pandemic by 2030.

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Advanced HIV Disease (AHD) Impact Report, 2022

CHAI

This concise 20-page report looks in detail at progress made since 2019 to avert preventable deaths among people with advanced HIV, best practices for implementation, and CHAI's perspective of what more will be needed to effectively end deaths from AHD-related opportunistic infections.

It reports that in 2020, there were still 680,000 AIDS-related deaths and that this was only 6% lower than the previous year.

Of these deaths, 210,000 were from TB and 85,000 from cryptococcal meningitis.

Advanced HIV disease contributes to these deaths, as AHD increases the risk of opportunistic infections and mortality.

The collaboration between CHAI and UNITAID works to influence and lever key stakeholders to strategically influence pricing, supply and demand to deliver better health. They also focus on areas that are otherwise overlooked.

This covers both diagnostics and treatments for HIV, TB and related complications.

References

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WHO guidelines on long-acting cabotegravir for HIV PrEP

World Health Organization (WHO)

This 15-page guideline outlines the rationale and evidence for a new recommendation to support the importance of long-acting cabotegravir injections (CAB-LA) as PrEP to prevent HIV.

This is a significant achievement driven by HIV advocates from the global south to demand access to the latest prevention options. CAB-LA was approved in the US and Europe based on results from international studies that were run in low-income countries that have some of the highest rates of HIV incidence.

Consistent with previous WHO guidelines, this guideline is based on a public health approach that considers effectiveness, acceptability, feasibility and resource needs across a variety of settings.

This guideline also highlights important considerations for effective implementation and the need for implementation science to address research gaps across a variety of geographies and populations.

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- 1. WHO press release. WHO recommends long-acting cabotegravir for HIV prevention. (28 July 2022). https://www.who.int/news/item/28-07-2022-who-recommends-long-acting-cabotegravir-for-hiv-prevention
- WHO. Guidelines on long-acting injectable cabotegravir for HIV prevention. (28 July 2022). https://www.who.int/publications/i/item/9789240054097

Chapters from the TAG Pipeline Report 2022

TAG

The following sections of the annual TAG pipeline report were published in July 2022 for AIDS 2022.

All chapters can be downloaded as PDF files.

- HIV antiretroviral therapy Richard Jefferys.
- HIV vaccines and passive immunisation Richard Jefferys.
- PrEP and microbicides Richard Jefferys.
- Research toward a cure and immune-based therapies Richard Jefferys.
- Long-Acting Technologies Trials Tracker for Hep C, Opioid Use and Overdose Prevention Therapy, and Malaria Joelle Dountio.

Reference

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https://www.treatmentactiongroup.org/resources/pipeline-report/2022-pipeline-report





An advocate's guide to research in pregnant and lactating populations

AVAC

A resource that provides background on the need for research in pregnant and lactating populations and how advocates can advance inclusion.

Reference

AVAC. An advocate's guide to research in pregnant and lactating populations. (July 2022).

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TREATMENT GUIDELINES

US guidelines on HIV-related OIs online for comment

Simon Collins, HIV i-Base

On 1 August 2022, the US guidelines on HIV-related opportunistic infections (OIs) were updated to include information about monkeypox. [1]

Rather than including detailed information, the guidelines defer to information from the US CDC about management of monkeypox in p3eople living with HIV. [2]

Earlier this year, the guidelines also updated sections on C. difficile and tuberculosis. [2]

The guidelines panel also ask for feedback by August 19, 2022.

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2. US CDC. Clinical Considerations for Treatment and Prophylaxis of Monkeypox Virus Infection in People with HIV. (Updated 21 July 2022). https://www.cdc.gov/poxvirus/monkeypox/clinicians/people-with-HIV.html

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COMPLICATIONS: MONKEYPOX

WHO declares the monkeypox pandemic a global health emergency

Simon Collins, HIV i-Base

On 23 July 2022, WHO declared monkeypox (MPX) a global health emergency. This increases the warning over the current monkeypox pandemic to the highest alert. [1, 2, 3]

Within the last two months, more than 15,000 cases have been reported in 70 new countries where MPX was previously not endemic. Many of these cases were in Europe, including more than 2000 in each of the UK, Germany and Spain, more than 1500 in France, and more than 2000 in the US. [4]



WHO also published detailed guidelines for countries to respond to the MPX pandemic. [5]

This includes estimating the basic reproduction number (R0) to be above 1.0 in gay, bisexual and other men who have sex with men and less than 1.0 in other settings. For example, the estimated R0 is 1.8 in Spain, in 1.6 in the UK and 1.4 in Portugal.

Vaccines as part of the public health response

WHO also notes the importance of offering a vaccine to people at highest risk.

Early in the outbreak, the UK was one of several countries to order supplies of the MPX vaccine (Imvanex). This initial order of 20,000 doses was expanded last week to add an additional 100,000 doses by September. Many people believe that this still underestimates the current need and demand. [6]

The vaccine is highly effective, with protection reaching more than 95%, two weeks after the second of two doses.

However, protection after a single dose might be significantly lower in people who are living with HIV and might take up to four weeks to develop. [7]

These important details are included in the full prescribing information but not in the information given to patients in the UK. [8.9]

More information about MPX is available in a regularly updated factsheet by i-Base and the UK-CAB. [10]

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https://i-base.info/htb/43458

- i-Base Q&A. How effective is the monkeypox vaccine? (22 July 2022) https://i-base.info/qa/20255
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UK organisations call for £51 million to urgently tackle monkeypox crisis

Simon Collins, HIV i-Base

On 12 July 2022, nine national organisations involved in sexual health and HIV, issued a statement calling for a more effective and coordinated response to the monkeypox crisis in the UK.

Over the last two months more than 1500 people have been diagnosed with monkeypox. Nearly all are gay, bisexual or other men who have sex with men. Nearly all either live in London or recently visited, though cases are now being reported in smaller numbers across the UK.



The rapid increase with cases roughly doubling every ten days was not predicted by the UK Health Security Agency (UKSHA).

Although MPX is not classed as a sexually transmitted infection, most cases are diagnosed and managed by sexual health clinics. No additional funding or support has been provided to clinics to cover the costs of the outbreak. People diagnosed with MPX are expected to self-isolate at home for up to three weeks (but without financial support similar to COVID). Details of a vaccine programme are still not available, although a very limited vaccine supply of 20,000 doses has been announced.

The statement, printed in full below, was sent to the Secretary of State for Health and Social Care, the chief executives of the NHS and the UKHSA, and the chair of the UK Joint Committee on Vaccination and Immunisation (JCVI). It calls for:

Rapid vaccine scale-up to cover hundreds of thousands of people at highest risk.

Financial support for those in isolation with monkeypox.

Emergency support for sexual health services that are currently overwhelmed.

Clear lines of accountability and responsibility for the response to MPX.

Professional health organisations involved in the statement included the British Association of Sexual Health and HIV (BASHH), the British HIV Association (BHIVA) and the Association of Directors of Public Health (ADPH). Community organisations include i-Base, LGBT Foundation, NAT, Prepster, THT and the UK-CAB.

СОММЕNТ

Other organisations join the statement as signatories on page 3 of this link:

https://www.surveymonkey.co.uk/r/9CNHTSR

Please include the organisation name and logo, plus the person signing and their role.

References

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- https://www.tht.org.uk/sites/default/files/2022-07/Consensus%20statement%20on%20monkeypox%2C%2012%20July.pdf (PDF)
- Press release. £51m urgently needed to stop monkeypox becoming endemic in the UK with sexual health clinics already overwhelmed by rising numbers, say experts. (12 July 2022).

https://www.tht.org.uk/news/ps51m-needed-stop-monkeypox-becoming-endemic-uk

EMA approves Imvanex vaccine against monkeypox in EU

Simon Collins, HIV i-Base

On 22 July 2022, the EU committee responsible for reviewing medicines (CHMP) recommended extending the indication for Imvanex to include monkeypox (MPX). [1]

Imvanex was approved in the EU as a smallpox vaccine in 2013. [2]

Imvanex was approved in the US both for smallpox and monkeypox in 2019 where it is marketed as JYYNEOS. [3]

This included additional information from some studies. [4]

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- 1. EMA News. EMA recommends approval of Imvanex for the prevention of monkeypox disease. (22 July 2022). https://www.ema.europa.eu/en/news/ema-recommends-approval-imvanex-prevention-monkeypox-disease
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Tecovirimat to treatment monkeypox: an urgent need for both RCT and expanded access

Simon Collins, HIV i-Base

A short perspective on the use of the antiviral tecovirimat for its potential to reduce symptoms of monkeypox is included in the current edition of the NEJM. [1]

Although tecovirimat is approved to treat smallpox, this was on the basis of efficacy data from animal studies against similar viruses, including monkeypox, supported by safety data in humans. Human studies against MPX were also being planned before the current global outbreak.

New RCTs will be critical to understanding any benefits and risk of tecovirimat for MPX, but these need to enroll rapidly, to get rapid results.

The pace of the current outbreak means that tecovirimat should also be widely available for expanded or named patient access, especially for people with the most difficult symptoms.

This has already been available for limited cases in the UK. The launch of an RCT should not limit wider access where joining a study is either not possible or appropriate.

Although initially difficult to access in the US, this was recently made much easier due to community demands.

Reference

https://www.nejm.org/doi/full/10.1056/NEJMp2210125





Sherwat A et al. Tecovirimat and the treatment of monkeypox — past, present, and future considerations. Perspective review. NEJM, doi: 10.1056/NEJMp2210125. (3 August 2022).

International study of 528 monkeypox (MPX) cases: results from the 2022 outbreak need to inform new management guidelines

Simon Collins, HIV i-Base

An international collaboration connecting researchers on four continents has published the most extensive and comprehensive review from the 2022 monkeypox (MPX) outbreak. [1]





The review includes 528 PCR-confirmed cases from April to June 2022, managed at 43 hospitals (26 in Europe, 10 in Canada) and is published in the NEJM.

Nearly all cases (98%) were in gay, bisexual or other men who have sex with men, with 95% reporting the potential for sexual transmission. One person was trans/non-binary and no cases were in women. Median age was 38 (range: 18 to 68), 75% were white.

HIV coinfection was reported in 41% of cases (n=241) and median CD4 was 680 cells/mm³ (IQR: 516 to 861). At least 96% of HIV positive cases were on ART, 95% with undetectable viral load. PrEP was used by 57% of the people who were HIV negative. Three people were newly diagnosed with HIV as part of MPX management.

Importantly, there are no obvious differences in baseline demographics, clinical symptoms or recovery times between people living with or without HIV. [2]

In the overall cohort, people were sexually active and were engaging with care to ensure they have good sexual health. PrEP use was high and HIV positive people were on effective ART. Most people had risk factors associated with previous MPX reports. This included, for example, having a median of five partners over the previous three months (IQR: 3 to 15) with 32% attending saunas or other sex-on-premises venues, 20% attending large events such as Pride and 20% reporting chemsex.

Nearly all cases (95%) presented with a rash, but only 58% of these matched the so-called typical form that progressed to being vesicular and pustular. Overall, 64% of people had less than 10 lesions, 11% had more than 20 lesions and 73% had at least one anal or genital lesion.

It is also notable that roughly 10% of cases (n=54) only had a single genital lesion, highlighting the potential for misdiagnoses as syphilis or another STI. There was also considerable variation in how lesions developed during infection, shown in the chronological photographs included in the online appendix. [2]

In a small subgroup of 30 cases with the most comprehensive medical records:

- Median time from first symptoms to positive PCR was 5 days (range, 2 to 20).
- Median time from the first skin lesion to additional lesions was 5 days (range: 2 to 11).
- The latest time point at which a lesion remained positive was 21 days.

Of the 23/30 cases with a clear exposure risk, the median incubation period was 7 days (range, 3 to 20).

When tested, MPX DNA was detected in nasopharyngeal tissue (26%), urine (3%), blood (7%) and semen (90%, 29/32). However, in addition to needing further research on whether the detected virus is replicant competent, close contact during sex is likely to explain most transmissions rather than contact with semen.

Even though 13% of people (n=70) were hospitalised, only 5% received antiviral treatment. This included tecovirimat (in 2%), IV or topical cidofovir (in 2%, and also no longer recommended) and vaccinia immune globulin (<1%).

Most hospitalisations were for pain management, including severe anorectal pain (n=21). Other difficult complications included tissue infections (n=18); pharyngitis (n=5); eye lesions (n=2); acute kidney injury (m=2); myocarditis (n=2); and to control wider infections (n=13).

Two other types of serious complications were reported. One case of epiglottitis in an HIV positive person with a CD4 count <200 cells/mm³; and two cases of myocarditis (one was HIV positive with a high CD4 count).

It is significant that no deaths were reported from this large cohort.

As a caution, the paper notes that because cases were identified by self-referral, this could underestimate asymptomatic infections.

The authors also discuss the importance of training for health workers and the active involvement of community organisations in the responses to MPX.

СОММЕNТ

This impressive observational study is the largest case series to report the 2022 MPX outbreak. It adds essential information that will impact on the management on MPX in all countries.

This data will also be submitted to expand the international case definitions to include genital and anal lesions.

The image library is just as essential for providing clear examples showing the diverse presentations of MPX.

With 2,137 cases in the UK and more than 15,500 cases in at least 58 previously non-endemic countries, MPX is now a crisis. [3]

The virus is now predicted to become endemic for many months, with outcomes largely dependent on rapid access to vaccines for populations at higher risk.

Activists and health professionals have urgently called for funding to manage infections and vaccination to minimise further spread. [4]

Vaccines are already becoming available in the UK and an announcement earlier this week that a further 100,000 doses are ordered and expected by September. [5, 6]

Many people believe this still underestimates both the numbers needed and the high interest from people wanting to access the vaccine. London clinics report that online appointments for vaccines become fully booked within ten minutes of being released. [7]

Similar overwhelming demand for vaccination has been reported from New York, also raising issues of equity of access. [8, 9]

The recommended vaccine (Imvanex, Jynneos) is currently produced by one supplier. Demand has been increasing over the last two months and this will continue. In addition to the early UK order for 20,000 doses, the EU just increased their 50,000 dose order for member states to 150,000 doses and the US had already stockpiled 1 million doses as a caution against bioterrorism.

The vaccine was approved based on strong efficacy and safety data, and vaccination will have a major role in the global response. This is based on receiving two doses, 28 days apart. [11]

Proposals to prioritise single-doses in vaccine progammes need to include estimates of likely efficacy in information given to people receiving the vaccine. This should include efficacy following single and double doses, the time needed for protection to develop, and whether responses are impacted by HIV status. [12]

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Monkeypox DNA detected at high levels in saliva and is common in semen and other samples

Simon Collins, HIV i-Base

Reports of the current monkeypox (MPX) outbreaks have emphasised skin-to-skin contact but underplayed the likely role of kissing and oral sex as a common factor in the crisis.

Although MPX is not classified as a sexually transmitted infection (STI) it is frequently linked to sexual contact.



A longitudinal study in 12 gay men in a Spanish cohort published in Eurosurveillance reports that MPX was commonly found in skin lesions, nasopharyngeal and rectal tissue, and in semen, urine and faecal samples. [1]

Median age was 38 years (range: 32 to 52). Three had an STI on diagnosis and most (9/12) had a previous history of STIs. All 4/12 that were HIV positive had undetectable viral load on ART with CD4 counts between 400 and 860 cells/mm3. PrEP was used by 7/8 HIV negative men.

All were sexually active with 8/12 having up to ten partners in the previous month. 'Sex-on-premises' venues or 'chemsex' parties were attended by 5/12 and 4/12 were linked to a confirmed MPX case.

MPX infection was not prevented in 4/12 who reported previous smallpox infection (not recorded in five others). Systemic symptoms (fever etc) were reported in 11/12.

MPX in other samples

At diagnosis, MPX DNA was detected in swabs of skin lesions in all 12 cases, usually with high viral load (Cq value range: 16–21) and some cases had additional oral, pharyngeal and rectal lesions.

MPX DNA was commonly detected in follow-up samples taken between 4 and 16 days later.

High viral loads were observed in some saliva, rectal swabs, semen, urine and faecal samples with intermittent shedding also observed.

MPX was detected in saliva from all 12 patients, and in some cases, at low Cq values indicative of very high viral loads.

Positive samples were reported for rectal (11/12) and nasopharyngeal swabs (10/12 cases), semen (7/9), urine (9/12) and faeces (8/12).

COMMENT

These results support a likely role of saliva in MPX transmission that would include risk from kissing and from oral sex.

Positive samples in semen suggest that MPX might be sexually transmitted without the need for other skin contact or kissing.

Continued follow-up in the cohort will be important to establish likely duration of MPX in samples, potentially after skin lesions have resolved and people are assumed cured and no longer required to self-isolate. It will also be important to look at recoverable levels of MPX.

It is useful that the UK recently extended the recommendation to use condoms for 12 weeks after MPX has resolved, in line with WHO guidelines. Previously, the recommendation was to use condoms for 8 weeks after skin lesions have completely resolved. [2]

By early August than 2600 people have been diagnosed with MPX in the UK. More than 27,000 cases have been reported globally, with over 4,500 in Spain and 7,000 in the US.

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Risk of monkeypox being infectious on hard surfaces and soft materials: guidelines for effective cleaning

Simon Collins, HIV i-Base

Data on the persistence of monkeypox (MPX) recovered from systematically swabbing surfaces in hospital rooms used for two cases in Germany was identified by PCR and isolated to assess continued infectivity. Results are published as a rapid communication in Eurosurveillance at the end of June. [1]



Numerous swabs were taken from flat surfaces, as well as on fabrics on day four of hospitalisation.

High levels of contamination were reported from a range of surfaces including door handles, soap dispensers, toilet seats, bedding, clothing and gloves used by investigators with up to 100,000 copies/cm2 as well as the successful recovery of monkeypox virus from samples with >1 million copies.

In patient samples, viral load was detected at levels up to 270 to 440 million copies in swabs from lesions and 1.3 to 21.0 million copies from throat swabs.

The paper notes that detection of viral DNA is not the same as infectious virus and that the current study does not prove that infection can occur from contact with these surfaces. The results do however show, even from just two cases, the importance of disinfecting shared skin-contact surfaces both by health workers and household contacts.

A literature review from June summarises the efficacy of biocidal agents and disinfectants against the monkeypox virus and other orthopoxviruses. [2]

Results include" "Vaccinia viruses could be inactivated by at least 4 logs in suspension tests and on artificially contaminated surfaces by 70% ethanol (in less 1 minute), 0.2% peracetic acid (less than 10 min) and 1% to 10% of a probiotic cleaner (60 minutes), mostly shown with different types of organic load. Hydrogen peroxide (14.4%) and iodine (0.04% to 1%) were effective in suspension tests, sodium hypochlorite (0.25% to 2.5%; 1 minute), 2% glutaraldehyde (10 minutes) and 0.55% orthophthalaldehyde (5 minutes) were effective on artificially contaminated surfaces.

Copper (99.9%) was equally effective against vaccinia virus and monkeypox virus in 3 minutes. Disinfectants with efficacy data obtained in suspension tests and under practical conditions with different types of organic load resembling compounds of the blood, the respiratory tract and skin lesions should be preferred for the inactivation of the monkeypox virus."

COMMENT

In early June, the US CDC published detailed information on the persistence of MPX on hard surfaces for several weeks and potentially longer for softer materials such as towels and bedding. [3]

MPX is a Tier 1 virus (large, enveloped, easier to disinfect), with approved disinfectants. Alcohol-based cleaners need to be >60%. The CDC link to a resource of almost 500 chemical compounds commonly approved as disinfectants. [4]

The short concise leaflet covers the importance of cleaning while isolating at home, even if you live alone. This is still the easiest information to read.

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Outcomes of 54 cases of monkeypox (MPX) in London: fewer early symptoms but higher rates of genital lesions – urgency of funding sexual health

Simon Collins, HIV i-Base

Results from a retrospective review of 54 early cases of PCR-confirmed monkeypox (MPX) seen at four sexual health clinics in central London from 14 – 25 May 2022 are published in the 1 July 2022 edition of Lancet Infectious Diseases. [1]



All cases were in gay/bisexual men (n=52/2) mainly seen at sexual health clinics, with two admitted through A&E. Median age was 41 (IQR: 34 to 45); 38/54 (70%) were

white, eight (15%) were Black or mixed race four (7%) were Asian and four (7%) were of other ethnicities. Although travel outside the UK was reported by half the cases, this was only to European countries.

Approximately 1 in 4 (13/54) were living with HIV (all on ART with CD4 >500 cells/mm3) and nearly everyone else was using PrEP.

Roughly two-thirds reported fatigue, one-third fever – generally lasting less than three days – but 10/54 (18%) reported no prodromal symptoms.

All cases included skin lesions: nearly all (89%) involving more that one body site and 94% including anogenital ulcers.

One in four patients were diagnosed with one or more STIs: 13 with gonococcal or chlamydial infections (6 with pharyngeal gonorrhoea, 2 for urethral gonorrhoea, 1 for rectal gonorrhoea, 4 for rectal chlamydia, and 2 for urethral chlamydia).

Although roughly half and one-third of cases reported having >5 or >10 partners in the previous three months, this is likely an underestimate in many cases.

Only 5/54 cases (9%) included hospital admission mainly for pain management or for antibiotic treatment for local skin complications including cellulitis.

This summary noted fewer initial symptoms and that genital lesions were more common that previously reported in Nigerian studies. Also that high rates of STIs suggest transmission due to skin to skin context in a sexual context, although it is unclear whether sexual fluids are an additional risk.

The study also describes procedures for developing a centralised clinic to safely diagnose and manage cases and the urgency of emergency funding to enable sexual health services to manage this new and extended outbreak.

C O M M E N T

So far, the rapid escalation to more than 1200 cases within six weeks doesn't appear to have been predicted though none of the early public health modelling for this outbreak has been publicly released.

Similar outbreaks have been reported in several other European countries, including Germany, Spain, France and Portugal. [2]

It is likely that updated modelling, also not released publicly, projects a significant increase in the weeks after Pride.

i-Base, together with some other community organisations has suggested the potential benefits from self-limiting use of situations where multiple partners in an anonymised setting for four weeks. This could reduce cases and protect health services until the current outbreaks is more clearly understood. [3, 4]

We also call for the urgency of emergency funding. [5]

Many countries, including the UK, have announced vaccine programmes for men at highest risk. [6]

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Ending the monkeypox outbreak through vaccination, contact tracing and early diagnosis

Kirk Taylor, HIV i-Base

By 25 July 2022, over 2,000 confirmed cases of monkeypox (MPX) have been identified in the UK. A commentary in the Lancet Infectious Disease discussed ways to reduce transmission and ultimately end the outbreak. [1]

The 'R' of previous MPX outbreaks in African countries was below 1, as each person passed the virus to fewer than one other contact. Cases tended to be single individuals or small localised groups. Transmissions were mainly within households and outbreaks were self-limiting.



However, MPX in endemic countries was never prioritised for international support. Many countries couldn't even test for MPX, so that many suspected cases were never confirmed. Limited access to healthcare, including no access to vaccines or treatment probably contributes to more serious outcomes and the higher death rates in these countries.

The rise in MPX cases in Nigeria and DRC were predominantly in children and adolescents with transmission from animals and looks directly related to ending the policy of smallpox vaccinations' These factors lead to experts estimating that R could be as high as 3.

The authors consider steps that to reduce R and end the MPX outbreak. Considering the long incubation period (up to 20 days), contact tracing, and vaccination for those at high risk, it may be possible to achieve an R below 1.

COMMENT

R numbers reported for the current MPX outbreaks are much more likely to be related to social dynamics than properties of the virus. WHO report that R is currently 1.6 in the UK, 1.8 in Spain and 1.4 in Portugal. [2]

The suggestion that contact tracing might contain MPX was based on a poor understanding of these social dynamics, especially with an incubation time that could be several weeks.

Contact tracing might help some individuals but numbers are now too high for this to limit PMX on a population level, especially without funding.

The health response is now rightly catching up with a vaccine programme.

The UKHSA did not originally include information about vaccine efficacy after single and double shots, the time needed for immune responses to develop and the possibility of lower responses to a single shot in people living with HIV. An updated version of patient information now covers some of these points, but not all. [3]

However, the agency has taken care to work with community organisations to minimise the risk of stigma against the networks where MPX was unlucky enough to first be affected.

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US doctors think it is already too late to contain monkeypox

Kirk Taylor, HIV i-Base

Since the first four cases were reported in the UK, more than 27,000 cases of monkeypox (MPX) have been reported globally.

Based on a poll of doctors, by STAT news, a majority think it will not be possible to contain the outbreak and the few that are more optimistic, think this will require considerable efforts. [1]



Self-isolation to limit further transmission is recommended until all lesions have healed which is usually about three weeks.

However, this is both complicated and challenging for many people unless they have similar social and financial support similar to that provided for COVID-19. Contact tracing has potential to be effective, as there is a long incubation period where people cannot transmit the virus.

Dr Rochelle Walensky of the CDC commented that containment within communities and networks of gay, bi and other men who have sex with men might be possible through direct community action, education and awareness of symptoms together with high vaccine uptake.

It is possible though that the turning point for containment has been missed. Mathematical modelling by the European CDC predicts a 75% chance of containing the outbreak if self-isolation, pre-exposure vaccination and contact tracing strategies are employed.

Vaccines are likely to be pivotal in any strategy to manage MPX but with increased production taking several months, it is likely that case numbers will continue to rise for now.

СОММЕNТ

Many health officials already accept that MPX will be endemic for many months. The ultimate aim of eradication is also unlikely without adequate emergency funding.

There is only a short window to limit the risk of MPX becoming established as a reservoir in rodents, pets or other species that would be a future source or transmission back to humans.

Funding is urgently needed for sexual health clinics where responding to MPX is already impacting on other services including PrEP and long-acting reversible contraception (LARC)

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COMPLICATIONS: COVID-19

Case report of COVID-19 transmission from sneezing cat

Kirk Taylor, HIV i-Base

Please, no laughing, this is not funny.

Researchers report the unfortunate case of a young vet in Taiwan who caught COVID-19 after being sneezed on by one of their less considerate feline clients.



The hypothesis is supported by genome analysis and the paper is available as an open access article online.



Such transmission events are rare, but this case report provides evidence that domestic pets can serve as an additional source of COVID-19.

COVID-19 has been detected in multiple animal species, including cats, dogs, tigers, lions and mink. Combined with evidence for reverse zoonoses (human-to-animal transmission), it is important to consider additional zoonotic transmission routes. These events are rare, and cats appear to have shorter infectious periods, shedding lower levels of virus overall.

Ref: Sila, T. *et al.* Suspected Cat-to-Human Transmission of SARS-CoV-2, Thailand, July-September 2021 Emerg Infect Dis . 2022 Jul;28(7):1485-1488. doi: 10.3201/eid2807.212605. Epub 2022 Jun 6.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9239874

Accumulating SARS-CoV-2 mutations in prolonged COVID-19 in advanced HIV off-ART

Kirk Taylor, HIV i-Base

This paper includes a case report that tracks the accumulation of more than 20 key mutations in an HIV positive person with prolonged COVID-19.



Once started, ART suppressed HIV and SARS-CoV-2 cleared within nine weeks.

The 22-year-old South African has been HIV positive since birth. At time of presentation her HIV was not well managed with viral load >100,000 copies/mL and CD4 count of 91 cells/mm³. Restarting ART reduced viral load but 8 months later, viremia remained high and COVID-19 illness persisted. Switching to a TLD regimen reduced viral load to ≥50 copies/mL and COVID-19 cleared within 6 to 9 weeks.

Ref: Maponga TG et al. Persistent SARS-CoV-2 infection with accumulation of mutations in a patient with poorly controlled HIV infection. Clinical Infectious Diseases, ciac548, doi: 10.1093/cid/ciac548 (06 July 2022).

https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciac548/6632801

No benefit from TDF/FTC against COVID-19

Simon Collins, HIV i-Base

Results from this open-label, double-randomised, phase 3 study in 355 participants (97% hospitalised at baseline), reported no benefits from TDF/FTC or from baricitinib on 28-day moprtality.



Reference

Montejano R et al. on behalf of the PANCOVID study Group, Tenofovir disoproxil fumarate/emtricitabine and baricitinib for patients at high risk of severe COVID-19: The PANCOVID Randomized Clinical Trial, Clinical Infectious Diseases, 2022; ciac628, doi:10.1093/cid/ciac628. (30 July 2022).

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HIV PREVENTION

PrEP for women (June 2022)

A new leaflet about PrEP produced by and for women (with the Sophia Forum).

These small 16-page A7 leaflets were produced to raise awareness of access to PrEP.

Translations into key European and African languages are online and will be included on this page when available.

https://i-base.info/htb/43453



Future meetings and webinars 2022

The following listing covers selected upcoming HIV-related meetings and workshops. Registration details, including for community and community press are included on the relevant websites.

Due to the new coronavirus health crisis, most meetings will now be virtual, including those that were rescheduled in the hope that COVID-19 restrictions would be relaxed.

Academic Medical Education (AME) meetings and workshops

Several AME workshops (previously Virology Education) are highlighted below but 35 meetings are planned each year. Many virtual meetings include free registrations for health workers, researchers and community.

https://academicmedicaleducation.com (meetings listings)

Webcasts from meetings (YouTube listing)

2022

HIV Paediatrics 2022

27 – 28 July 2022, Montreal, Canada, and virtual https://academicmedicaleducation.com

24th International AIDS Conference (AIDS 2022)

29 July – 2 August 2022, Montreal, Canada, and virtually https://www.aids2022.org

13th International Workshop on HIV & Aging

13 – 14 October 2022, USA (tbc) https://academicmedicaleducation.com

HIV Glasgow 2022

23 – 26 October 2022, Glasgow and hybrid https://www.hivglasgow.org

BHIVA Autumn Conference 2022

Friday 25 November 2022, London https://www.bhiva.org/HIVEventDiary

2023

19th European AIDS Conference (EACS 2023)

18-21 October 2023, Warsaw, Poland https://www.eacsociety.org

PUBLICATIONS & SERVICES FROM i-BASE

i-Base website

All i-Base publications are available online, including editions of the treatment guides.

http://www.i-Base.info

The site gives details about services including the UK Community Advisory Board (UK-CAB), our phone service and Q&A service, access to our archives and an extensive range of translated resources and links.

Publications and regular subscriptions can be ordered online.

The Q&A web pages enable people to ask questions about their own treatment:

http://www.i-base.info/qa

i-Base treatment guides

i-Base produces six booklets that comprehensively cover important aspects of treatment. Each guide is written in clear non-technical language. All guides are free to order individually or in bulk for use in clinics and are available online in web-page and PDF format.

http://www.i-base.info/guides

- 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)

Pocket guides

A series of pocket-size concertina folding leaflets that is designed to be a very simple and direct introduction to HIV treatment.

The five pocket leaflets are: Introduction to ART, HIV and pregnancy, ART and quality of life, UK guide to PrEP and HCV/HIV coinfection.

The leaflets use simple statements and quotes about ART, with short URL links to v U=U pages that have additional information in a similar easy format. 0.0 U=U resources for UK clinics: free posters, postcards and factsheets i-Base have produced a new series of posters, postcards and leaflets to help raise awareness about U=U in clincs. This project was developed with the Kobler Centre in London. UNDETECTABL UNTRANSMITTABLE As with all i-Base material, these resources are all free to UK clinics. V W N Until our online order form is updated to include the U=U resources, more copies can be orded by email or fax. email: subscriptions@i-base.org.uk IINDETECTA Customise U=U posters for your clinic UNTRANSMITTABLE i-Base can customise U=U posters to include pictures of doctors. nurses, pharmacists, peer advocates or any other staff that would like to help publicise U=U. 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



h-tb

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