PrEP breakthrough and drug resistance very rare

Another case of infection with HIV in a person consistently taking pre-exposure prophylaxis (PrEP) was reported last week at the 25th Conference on Retroviruses and Opportunistic Infections (CROI 2018) in Boston.

However, a lack of monitoring and a failure to test for HIV around the time he experienced what may have been HIV seroconversion symptoms means that it is difficult to be 100% certain that this is a case of PrEP failure.

Reports of HIV infection in people taking PrEP are extremely rare. Two cases were presented in
2016 of people who were infected with drug-resistant virus despite taking PrEP, one in Toronto and one in New York. A third case from Amsterdam in 2017 did not involve drug-resistant HIV.

In this case, because of lack of monitoring, it is impossible to say whether the patient caught HIV that was already resistant to the PrEP drugs tenofovir and emtricitabine, or whether resistance developed as a result of his staying on PrEP for a month after suspected symptoms of acute HIV infection were seen.

Another study presented at the conference set out to estimate how likely it is that people with detectable viral load might transmit HIV that is resistant to both the drugs used in PrEP. The researchers found that in King County, which contains Seattle, no more than 0.3% of the local HIV-positive population had viral loads over 10,000 copies/ml, and also high-level resistance to tenofovir and emtricitabine.

However, an even smaller proportion of newly diagnosed people – just three cases in ten years, or one in 606 of those diagnosed – had primary drug resistance, i.e. actually became infected with tenofovir/emtricitabine-resistant HIV. This is more likely to reflect the maximum frequency of people who could acquire drug-resistant HIV from someone else despite being on PrEP.

Related links

Read Another likely case of PrEP 'breakthrough' infection reported on aidsmap.com
Read How much 'PrEP-resistant' HIV is out there? on aidsmap.com
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Self-testing for HIV in South Africa and Burma

HIV self-testing is feasible and acceptable for men who have sex with men and transgender women in Burma and men who have sex with men in South Africa, two studies presented at last week’s CROI showed.

The confidentiality and privacy of self-testing, in relation to both HIV status and sexual behaviour, may have particular advantages for stigmatised groups. Self-testing has the potential to expand access to HIV testing and improve the frequency of HIV testing. However, some concerns have been raised about a lack of counselling for people who self-test and the possibility that people...
who test positive will not be linked to care.

The Burmese study randomised 577 men who have sex with men and transgender women to HIV self-testing using the Oraquick test or counselling and testing at a community-based organisation that serves men who have sex with men and transgender women. Both testing methods proved highly acceptable and the majority of participants in both study arms said they would prefer to self-test at home in future. Those in the self-testing arm were more likely to return for the second study visit (54% vs 46%). More new HIV diagnoses were reported in the self-testing arm (28 vs 16).

The South African study looked at the acceptability of oral or pinprick self-testing kits among men who have sex with men. It also examined how many people were reached when each participant was given five self-test kits to distribute to friends and family.

Most of the men (91%) used their test kit. Most tested on their own, but a third of participants sometimes tested with other people present, including taking a test at the same times as a friend, family member or partner. This suggests that self-testing can help open up discussion about HIV testing and HIV treatment – a number of participants told the researchers about improved dialogue with partners. The 127 men distributed kits to 376 friends, 217 family members and 135 sexual partners.

The researchers concluded that HIV self-testing is acceptable and feasible for South African men who have sex with men and can be disseminated through high-risk peer networks. It increases testing frequency and partner testing, potentially reducing late diagnosis and facilitating access to HIV treatment.

Related links

- Read this news story in full on aidsmap.com
- Download the presentation poster from the study in Burma from the conference website (PDF)
- Watch the webcast of the South African study presentation on the conference website

Lesotho making strong progress towards 90-90-90 targets

Lesotho, in spite of a high HIV prevalence of over 25%, is making substantial progress toward meeting the UNAIDS 90-90-90 targets, with a reported 77% of adults who tested positive in a household survey already knowing their HIV status.

To meet the 90-90-90 targets by 2020 – the goal set by UNAIDS – countries need to diagnose 90% of people with HIV, treat 90% of diagnosed people and achieve viral suppression in 90% of people on treatment. Hitting the targets means that 73% of people with HIV should have an undetectable viral load, greatly reducing HIV-related illness and death and new HIV infections.

Lesotho has the second highest HIV prevalence in the world. HIV is the leading cause of death and contributes to Lesotho having the lowest life expectancy among 195 countries. As part of a national response, Lesotho was the first country in sub-Saharan Africa to implement “Test and Treat” in 2016.

The LePHIA (Lesotho population-based HIV impact assessment) tested 11,682 adults in close to 11,000 households, chosen to be a representative national sample.
The total HIV prevalence was 25.6% (an estimated 306,000 people living with HIV). Women were disproportionately affected, with a prevalence of 30.4% compared to 20.8% among men.

90-90-90 target attainment was lower among men than women. Among men with HIV, 71% were already diagnosed, 89.4% of those diagnosed were on treatment and 88.4% of men on treatment were virally suppressed. This compared to 81.5%, 90.6% and 88.2% of women, respectively.

Men and women under 25 years of age were significantly less likely to know their HIV status. Similarly, men who had worked in the last week were significantly less likely to know their HIV status, suggesting that efforts to reach young men should focus on offering services near to workplaces and outside working hours, and also focus on migrant workers.

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Extended-release naltrexone improves viral suppression after release from jail


Good rates of viral suppression have been observed among prisoners treated with antiretroviral therapy (ART) while they are incarcerated. However, several studies have highlighted a rapid loss of virological control following release from prison. In one study, the proportion of people with an undetectable viral load fell from 59% to just 18% within three months of release. Such loss of virological control is often associated with pre-existing opioid or alcohol dependence.

Naltrexone is an opiate antagonist, which decreases the craving for alcohol and blocks the effects of opiates. Treatment with extended-release naltrexone has been shown to reduce relapse rates among people with a history of opioid or alcohol dependence.

Investigators wanted to see if therapy with this drug would have benefits for ART-treated HIV-positive people with opioid or alcohol dependence following their release from prison. They designed two randomised, placebo-controlled studies. The NEW HOPE study involved HIV-positive prisoners with opioid use disorders, whereas prisoners with alcohol abuse problems
were recruited to the INSPIRE study.

Participants in both studies were randomised to receive either monthly injections with extended-release naltrexone or a placebo. The primary study outcomes were maintenance or attainment of viral suppression (below 50 copies/ml).

The NEW HOPE study in previous opioid users found that treatment with extended-release naltrexone was associated with an almost threefold increase in the odds of viral suppression six months after release from prison. The INSPIRE study in previous alcohol users found that treatment with extended-release naltrexone was associated with a more than fourfold increase in viral suppression six months after release from prison.

There were no serious adverse events in either study.

“To reach the 90-90-90 goal for people with HIV released from prison or jail with opioid and/or alcohol disorders, high consideration should be given to including opioid and alcohol pharmacotherapies with antiretroviral therapy,” conclude the investigators. “Future research should involve assessment of extended-release naltrexone in other settings to achieve virological suppression in people with HIV as well as for HIV prevention.”

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Very early HIV treatment in children

Very early HIV treatment in infants is feasible and safe and leads to a small reservoir of infected cells, two studies from Botswana and Thailand show. The findings offer hope that infants diagnosed and treated soon after birth will have a better chance of controlling HIV if future research leads to interventions that can control HIV without prolonged treatment – a so-called functional cure.

Very early treatment in infants became a topic of scientific interest as a result of the case of the ‘Mississippi baby’. In 2013 US researchers reported that a child treated from 30 hours after birth was still controlling HIV after more than a year off treatment, perhaps because early treatment
had severely limited the number of cells in the child’s body that were infected with HIV – the HIV reservoir.

In most circumstances, the presence of HIV DNA in cells leads eventually to the production of new viruses and a rapid rebound in viral load if antiretroviral treatment is stopped. In the case of the Mississippi baby, viral load suddenly rebounded at the age of three years and nine months after more than two years off treatment.

Since that case was reported, several studies have investigated the feasibility of very early treatment initiation in infants, and its effects on the HIV reservoir. Part of the rationale for such studies is to determine how frequently and how successfully early treatment initiation limits the establishment of the reservoir of HIV-infected cells.

The Early Infant Treatment Study in Botswana found that infants who started treatment within days of birth had little or no HIV DNA integrated into cells and were not capable of producing new viruses from those cells after more than six months of treatment. Those children who had an undetectable viral load after 84 weeks of treatment were highly likely to have undetectable HIV DNA too.

The HIV-NAT research group in Thailand reported on the relationship between age at antiretroviral therapy initiation and the size of the HIV reservoir in two cohorts of infants that began treatment before six months of age. They found that the reservoir of infected cells shrank during the first year of treatment but remained stable after that time. However, they also found that in around half of children, it was impossible to make infected cells produce new viruses after a year or more of treatment, suggesting that detectable HIV DNA in these children was defective fragments.

Whether or not these children, and others like them, might be able to stop treatment and control HIV remains to be tested in carefully-designed studies. One concern is that interrupting treatment would lead to an increase in the viral reservoir that could not be reversed, undermining prospects that any subsequent breakthroughs in off-treatment control of HIV could benefit these individuals.

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Watch the webcast of the study presentation from Thailand on the conference website
Watch the webcast of the study presentation from Botswana on the conference website

Isoniazid preventive therapy in pregnant women with HIV: do the risks outweigh the benefits?

Isoniazid preventive therapy (IPT) during pregnancy and breastfeeding in women living with HIV on antiretroviral therapy (ART) resulted in a higher than expected rate of serious adverse events possibly attributable to isoniazid with no significant reduction in tuberculosis (TB) cases, participants heard last week at the conference.

The study also found that adverse pregnancy outcomes were significantly more frequent among women getting IPT during pregnancy compared to those who began IPT after delivery.

The World Health Organization, based on strong evidence, recommends IPT plus ART for people living with HIV. A six-month course of IPT – the minimum recommendation – reduces the risk of developing active TB. However, for pregnant and postpartum women the quality of evidence is weak. Additionally, retrospective data show that isoniazid is associated with increased liver
damage in pregnant and postpartum women.

The TB APPRISE randomised study carried out in TB-endemic areas in Africa, Asia and Haiti compared the safety and efficacy outcomes of starting IPT during pregnancy or delaying initiation until 12 weeks after delivery. The study found that serious adverse events occurred at a high frequency in both the immediate and the deferred IPT arms and that adverse birth outcomes such as stillbirth were more common in the immediate treatment arm. There was no significant reduction in the incidence of new maternal or infant TB cases in the immediate IPT arm compared to the deferred arm although the incidence was low in both arms.

These findings challenge current World Health Organization guidelines. Dr James McIntyre of Anova Health Institute, South Africa, chairing a press conference, supported the study team’s recommendation to re-evaluate the guidelines weighing the risks and benefits of starting isoniazid in pregnant women living with HIV.

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Third-line treatment successful in resource-limited settings


Third-line antiretroviral treatment will become a growing need in resource-limited settings but the best way to manage the virological failure of a second-line regimen is unclear. The ACTG A5288 study presented at CROI 2018 showed that use of drug resistance tests and new drugs can achieve viral suppression in a high proportion of people.

Study ACTG A5288 was an open-label trial comparing treatment strategies for people with viral loads of 1000 copies/ml or more after at least 24 weeks on a second-line antiretroviral therapy regimen containing a protease inhibitor. The aim of the study was to use newer antiretrovirals and contemporary management tools, including virus genotyping, to select appropriate third-line regimens and enable more people to achieve viral suppression. One group stayed on their existing second-line regimen because they had little or no drug resistance; current guidelines
recommend enhanced adherence support in these cases to achieve re-suppression. Others switched to a new regimen depending on their drug resistance profile.

The non-randomised study found that whereas participants who stayed on second-line treatment had a low rate of viral suppression at week 48 (44%) and developed new drug resistance, people who switched to regimens containing two or three new drugs (at least two of darunavir/ritonavir, etravirine or raltegravir) were much more likely to achieve viral suppression and less likely to develop further drug resistance. Almost 90% of those who received at least two new drugs achieved viral suppression.

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