

[PrEP](#)

# Amsterdam PrEP failure patient had unusual course of HIV infection

## Researchers speculate that continued PrEP might stop local infections becoming systemic

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At last February's Conference on Retroviruses and Opportunistic Infections (CROI), [Dutch clinicians presented a so-far unique case](#) of a man who had apparently become infected with non-drug-resistant HIV while taking pre-exposure prophylaxis (PrEP) consistently. Two previous cases of PrEP failure had been reported, but in both cases, the men concerned had been infected with multidrug-resistant HIV. This case, therefore, raised concerns that PrEP may not be 100% effective.

The case has now been published as a paper in *The Lancet HIV* journal. The report confirms the details presented at CROI but adds interesting data on an unusual course of seroconversion. Although there is no direct evidence for this, the researchers hypothesise that the PrEP might have stopped a localised HIV infection in rectal tissue spreading through the body, and the infection only became a typical, systemic infection when PrEP was stopped.

Dr Elske Hoornenborg and colleagues report on the timeline of the case. The man concerned was a 50 year old who started PrEP in September 2015, soon after the start of the AmPrEP demonstration study.

He reported high levels of condomless anal sex, generally as the receptive partner; 50 partners in the three months before enrolment, with condomless sex reported with 37 of them.

He continued to have high numbers of condomless sex partners while on PrEP. AmPrEP required participants to keep a mobile-app sex diary, and between October 2015 and April 2016 he reported an average of 56 anal sex partners a month (with and without condoms), an average of 16 days per month on which he reported condomless sex, and an average of 3.6 condomless sex partners on the days when he did report it.

He was diagnosed with anal chlamydia and gonorrhoea in the first weeks of December 2015 and March 2016, and the day he was diagnosed with HIV he was also found to have rectal [Lymphogranuloma venereum \(LGV\)](#). *E.coli* bacteria were also detected in his urine.

HIV tests were negative when he entered the study and at months one, three and six. He was tested for HIV halfway through May 2016, almost eight months into the study, by a clinic elsewhere in the Netherlands because he had a fever and dysuria (difficulty urinating).

This result, which was a yes/no simple antibody test, was positive. Six days later he received confirmatory testing with a Western Blot assay and also an HIV viral load test. The Western Blot assay confirmed HIV infection, though with atypical results, so it was decided to take the man off PrEP in case he developed drug-resistant HIV. He started antiretroviral therapy (ART) with tenofovir, emtricitabine, darunavir and dolutegravir a month after his diagnosis.

Although AmPrEP offers participants a choice between daily and "on demand" PrEP (with the same protocol as used in the Ipergay trial), this participant chose daily PrEP. His PrEP adherence appeared to be consistent. The Dried Blood Spot sampling used in the study measures intracellular levels of drug

and thus can show average adherence over a period of time.

Dried blood spot tests conducted in March 2016 and again in May 2016, on the day he stopped PrEP, indicated a tenofovir diphosphate level of over 2230 femtomols per sample of the drug; the average level associated with daily dosing is 1560 femtomols. There seems little likelihood, therefore, that the man was not consistently adherent.

HIV infection typically becomes visible in laboratory tests as a sequence of events. First HIV RNA becomes detectable on viral load tests. Subsequently, the p24 HIV core protein and the p31 integrase enzyme usually appear, then the p17 matrix protein, and then finally antibodies to the HIV envelope gp120 protein.

In the case of this patient, HIV RNA was not detected (fewer than 40 copies/ml) during May and only became detectable (13,000 copies/ml) a month after diagnosis, with over 100,000 copies/ml a week after that, when he started ART. It was also only at this point that he started to show weak positivity for p24, and p17 a month after that. HIV DNA tests taken at this period also showed no evidence of intracellular, integrated HIV in blood or rectal tissue cells.

Nonetheless, his Western Blot result on 24 May was positive for antibodies to the gp120 protein – a reversal of the normal sequence.

What was going on? There is no direct evidence of this, but Hoornenborg and colleagues suggest that these results are consistent with the patient initially having a localised infection within cells in the rectal tissues – probably facilitated by the inflammation brought on by LGV as well as simply having high ‘doses’ of HIV rectally. At this point the man was still on PrEP, which would be acting as post-exposure prophylaxis and preventing the infection spreading further.

Either that or the patient actually was *not* infected at this point and what was observed was an immune reaction to HIV in the presence of PrEP.

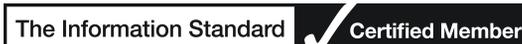
The PrEP was withdrawn on 24 May but might have continued to have some preventative effect for a week or two after this, which could explain the lack of detectable HIV viral load until three weeks after PrEP was withdrawn and a month after diagnosis. [Some animal studies during the development of PrEP](#) found that the viral loads in monkeys who seroconverted despite PrEP were unusually low, and in some cases remained so.

This raises an interesting clinical possibility – or dilemma, depending on how you look at it.

The authors say: “One might argue that if we had continued PrEP or had started combination therapy immediately, the infection could have been aborted, and with the knowledge gained from this case, one might consider this in future comparable cases.”

## Reference

Hoornenborg E et al. *Acquisition of wild-type HIV-1 infection in a patient on pre-exposure prophylaxis with high intracellular concentrations of tenofovir diphosphate: a case report*. The Lancet HIV, early online publication. [http://dx.doi.org/10.1016/52352-3018\(17\)30132-7](http://dx.doi.org/10.1016/52352-3018(17)30132-7). [See abstract here](#). 2017.



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