Famed London Man “Probably” Cured of HIV

The man was treated for lymphoma with a stem cell transplant using immune cells that had an uncommon, naturally occurring resistance to HIV.

March 10, 2020 By Benjamin Ryan

One year following the initial report on the case, researchers now believe that an HIV-positive man living in London has “probably” become the second person in history to be cured of the virus.

Up until now, the man has been known only as “the London Patient.” But on March 8, The New York Times revealed that his name is Adam Castillejo. He is a 40-year-old living in the English capital who, according to the Times, “exudes good health and cheer.”

Castillejo was treated in 2016 for Hodgkin lymphoma with a stem cell transplant from a donor who had an uncommon, naturally occurring resistance to HIV. Now, 30 months after his antiretroviral (ARV) treatment was interrupted, researchers have been unable to detect within him virus capable of replicating, even through the use of ultra-sensitive tests conducted on samples drawn from numerous parts of his body.

Typically, after an individual living with HIV has interrupted ARV treatment, the virus rebounds within two to three weeks.

Ravindra K. Gupta, MD, PhD, of University College London presented findings from the London Patient case study in a poster presentation at the 2020 Conference on Retroviruses and Opportunistic Infections (CROI) in Boston this week. (Due to the coronavirus outbreak, the in-person conference was canceled, and all presentations were delivered virtually.) He and his colleagues also published their findings in The Lancet HIV on March 10.

Gupta presented initial findings from the case at the 2019 CROI in Seattle, at which point the Castillejo had gone 18 months without taking antiretroviral treatment and had not experienced a viral rebound. At that time, Gupta stated that the London Patient, as he was then solely known, was in a state of long-term remission, but he was not yet prepared to deem him cured of HIV.

Gupta subsequently published the 18-month follow-up findings in the journal Nature.

To date, one person has been officially cured of HIV: the American Timothy Ray Brown, known also

as “the Berlin Patient,” because of where he was living when in 2007 he received a pair of treatments very similar to those that Castillejo underwent. Brown had acute myeloid leukemia, which, like lymphoma, is a cancer of the blood.

Timothy Ray Brown, aka the Berlin Patient, watches as Ravindra K. Gupta presents findings about a new case of likely cure of HIV at CROI 2019.Benjamin Ryan

Researchers have been cautious about proclaiming Castillejo cured due to the fact that even when an HIV-positive person goes off ARV treatment for lengthy periods without any viable virus detected in their body, there remains a chance, however diminishingly small, that HIV will rebound. This fact is the product of the mysteries of the viral reservoir, in which HIV can hide in long-lived, resting immune cells, in some cases for many years, before the cells return to churning out new copies of the virus.

The HIV research community learned a particularly painful lesson about the hazards of jumping the gun on proclaiming individuals cured from the case of the so-called Mississippi Baby. In 2013, notwithstanding the cautiousness of the researcher who first presented the findings of the case in categorizing her as cured, word spun around the globe that the baby girl had indeed been "functionally cured" of the virus.

The baby had received atypically aggressive ARV treatment initiated very soon after birth. At the time of the initial report, the 28-month-old toddler had been off ARVs for 10 months with no viral rebound. But her virus wound up rebounding 27 months after she stopped receiving ARVs, and she was put back on treatment for the virus.

Brown and Castillejo alike were treated for—and cured of—their blood cancers with stem cell transplants from donors found through an international registry whose CD4 immune cells lacked the gene that expresses the CCR5 coreceptor on their surface. Because the virus predominantly attaches to that coreceptor to initiate the process of infecting CD4 cells—there is another, less commonly used coreceptor called CXCR4—an immune system made up largely of immune cells lacking CCR5 is likely one in which HIV cannot establish a chronic infection.

Like Castillejo's donor, people with two copies of this CCR5-based genetic abnormality, which includes about 10% of those with Northern European ancestry, are known as being homozygous for the CCR5-delta32 mutation.

Castillejo and his medical team decided to interrupt his ARVs in September 2017, 16 months after his stem cell transplant, and to keep him under close monitoring. Gupta's initial case report at CROI 2019 indicated that extremely sensitive tests could not detect HIV in his body.

At CROI 2020 and in The Lancet HIV, Gupta again reported on Castillejo's case, now that 30 months have passed since his ARV treatment interruption. Numerous extremely sensitive tests still could find no HIV in his body, including in his cerebrospinal fluid and semen and in samples taken from various points in his gastrointestinal tract.

Even in the face of fully suppressive ARV treatment of HIV, the virus can hide out and replicate in the central nervous system. The digestive tract is also a major HIV reservoir site. So the apparent absence of virus in these sites is key in determining whether Castillejo is in fact cured.

Highly sensitive tests did detect some evidence of “fossil” remains of the virus’s genetic code in Castillejo’s peripheral memory T cells and lymph nodes. These traces of HIV, which were not found intact inside the machinery of his cells, are believed to lack the capacity to produce viable new copies of the virus. A 2013 study of Brown’s case, published in PLOS Pathogens, found similar evidence of viral fossil remains.

Tests conducted 27 months after the ARV treatment interruption indicated that Castillejo’s CD4 and CD8 cell immune responses to HIV were absent.

As with Brown, the Castillejo’s HIV antibodies have declined over time.

More than 90% of Castillejo’s immune cells were a direct outgrowth of his stem cell transplant, meaning that he largely shared his immune system with his HIV-resistant donor. Gupta and his colleagues conducted mathematical modeling that suggested an almost certainty that the British man has been cured of HIV, considering he harbors such a high level of immune cells resistant to the virus.

To buttress their claims that this modeling is a solid basis on which to determine whether the British man is cured, the study authors drew a comparison to the herd immunity that communities experience when a high proportion of their members are vaccinated against a pathogen. Even if some people in this community do contract the pathogen, the infection cannot successfully spread from person to person and cause a major outbreak because so many people are already immune.

Similarly, even if Castillejo still had reservoir cells infected with HIV and such cells re-activated and began producing new virus, those viral copies, as well as any others produced by cells they managed to infect, would not encounter enough susceptive immune cells to send the viral load up exponentially and reestablish a chronic, lifelong infection.

Gupta told POZ that he considered Castillejo in a state of long-term remission from HIV and that it was highly likely that the man is indeed cured.

Ravindra K. Gupta of University College London presenting his findings from the London Patient case at CROI 2019Benjamin Ryan

In an accompanying editorial in The Lancet HIV, Jennifer M. Zerbato, PhD, and Sharon R. Lewin, MD, PhD, of the Peter Doherty Institute for Infection and Immunity at the University of Melbourne, argued that an apt definition of an HIV cure might be the lack of intact virus—meaning the virus's genetic material is fully woven inside a cell's machinery—rather than the lack of detectable virus.

Zerbato and Lewin were more circumspect in their assessment of Castillejo's case than Gupta and his coauthors. "In view of the many cells sampled in this case," the Australian scientists wrote in their editorial, "and the absence of any intact virus, is the London patient truly cured? The additional data provided in this follow-up case report is certainly exciting and encouraging but, in the end, only time will tell."

On that note, going forward, the research team monitoring Castillejo will conduct viral load testing every six months until 60 months have passed since the start of his ARV treatment interruption. After that, they will test his viral load yearly until the 120-month mark.

To read the study abstract, click here.

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