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Toward an H.I.V. cure

Thirty years after the first cases were reported, AIDS is no longer a death sentence. But we still need to find a cure.

Françoise Barré-Sinoussi

Sunday marks 30 years since the first AIDS cases were reported. Since then, H.I.V. science has been translated into prevention and treatment breakthroughs, one of the greatest being the antiretroviral treatment that has ensured that millions of H.I.V.-positive people can lead healthy lives.

Furthermore, there is now robust evidence that early and highly active antiretroviral therapy can have a major impact on reducing H.I.V. transmission, demonstrating the "treatment as prevention" concept.

AIDS is no longer the death sentence it was, but there now remains extreme uncertainty concerning the long-term sustainability of treatment access, especially in resource-limited settings.

More than ever we need to find an H.I.V. cure. We need to invest in research that aims to find better and more cost-effective therapeutic strategies that may lead at least to a functional cure — the long-term remission of patients with a very efficient and persistent control of H.I.V. after discontinuation of treatment.

This begs the question: After 30 years of H.I.V. research, why have we still not found a cure?

The answer to that lies in the obstacles related to the complexity of the interaction between H.I.V. and its host, the persistence of H.I.V. in people on highly active antiretroviral therapy, and our limited knowledge on the very early stage of the infection. However, there are some promising signs that the pieces of the H.I.V. pathogenesis puzzle are beginning to fall in place.

What we have known for some time now is that latent H.I.V. reservoirs, where H.I.V. hides and persists, are one of the main barriers to finding a cure. It is precisely why treatment does not eradicate H.I.V. and why, when treatment is stopped, the virus rebounds.

What we haven't had until very recently are the scientific advances and new approaches to tackling those viral reservoirs. For instance, our basic understanding of the mechanisms of H.I.V. persistence in latent reservoirs is far superior than it was a decade ago. We are also witnessing promising developments from recent studies and small-scale testing reactivation agents that can reverse latency and "flush" the H.I.V. reservoirs.

We have also been aware that the so called "elite controllers" — those very few people who are infected with H.I.V. for at least a decade, do not take treatment and yet do not develop AIDS — were always going to be a vital part of future cure research.

Now we are gaining a better understanding of this unique group of patients. Some of the more recent science is showing that the elite controller status is related to the host genetics permitting robust cell-mediated immunity and/or restricting an infection in their CD4 lymphocytes and macrophages.

Understanding this group of people who efficiently control the virus replication and reservoirs, we believe, will be key in our search to attaining a "functional" cure that would allow long-term remission of infected individuals.

Last week's announcement that researchers had identified a new restriction factor that inhibits an early step of the H.I.V.-1 life cycle in immune cells is greatly encouraging as well. New findings on the innate control of H.I.V. have implications for treatments and can provide us with insight into therapeutic vaccine development.

In addition, there is now a "proof of concept," as scientists like to call it, for a cure. The case of the Berlin patient Timothy Brown, who received a stem-cell bone-marrow transplant in 2007 leading to the remission of his leukemia and now considered to be cured of AIDS, has now provided us with one.

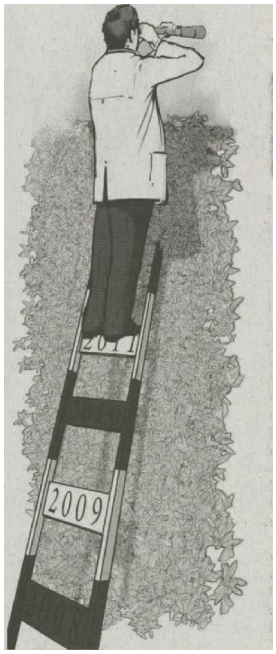
While it is clearly unrealistic to think that this medically heavy, extremely costly, barely reproducible therapeutic approach could be replicated and scaled-up, it has nevertheless got the scientific world talking about the possibility of a cure.

Developments in gene therapy are also encouraging. The recent work by Paul Cannon with the Sangamo group using gene editing to knock out the CCR5 receptor gene on which H.I.V. relies to enter into host cells indicates that gene therapy may well prove to be an effective intervention, more readily available than chemotherapy or stem cell transplants.

I believe that given our current knowledge and innovative tools and concepts, a functional cure is a more realistic goal for the near future.

A cure will require funding commitments, strong community engagement, rigorous and innovative scientific endeavor and, above all, further collaborative multidisciplinary science with a better connection between basic and clinical research — in short, all the same ingredients that got us where we are today with the global antiretroviral treatment.

Thirty years is a long time and yes, we still do not have a cure. But if we do not seriously start looking for one, now that the science is telling us that perhaps we should be, do we want to be here in another 30 years regretting that we did not try?



TIMOTHY MCFVENUE

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