Progress and Controversies in Cure Research

December 12, 2012 By David Evans

I just returned from one of the most fascinating and promising conferences on HIV cure research that I've ever attended. Held November 28 to 30 in Washington, D.C., the Division of AIDS from the National Institutes of Health (NIH) sponsored a meeting that brought together many of the researchers funded by or collaborating with the Martin Delaney cure research collaboratories.

Martin Delaney, Marty to me, was a mentor and close friend and founded the advocacy group Project Inform in 1985. One of the giants of AIDS treatment advocacy, it is fitting that the research collaboratories--public private partnership to move cure research as rapidly as possible from the test tube to the bedside--bear his name and I am certain he would have been as thrilled as I was with the quality of the science presented and discussed at the meeting.

Progress

Though the meeting, as any government-funded meeting, was technically open to the public, some of the data presented has not yet been presented formally at conferences or published in journals. For this reason, we were asked not reveal all of what we learned over the course of the meeting just yet, at least not in detail, but I can say that evidence of progress was certainly evident and is likely to be reported in fuller detail soon.

I expect that much of what I learned will be presented in the coming months at the Conference on Retroviruses and Opportunistic Infections (CROI) taking place in March in Atlanta, or the International AIDS Society (IAS) meeting to be held in July in Malaysia, or at another upcoming meeting.

Roughly speaking, however, we learned of both adults and children who appear to have gained extraordinary control over the virus due to very early antiretroviral (ARV) therapy, we're talking about people who started within days or weeks and not months or years.

One of the cohorts described, from France, has been previously presented, but further details were fleshed out at the meeting. Though it is rare that people rush to get tested immediately following an initial exposure to HIV, some do. In France, about 200 people have been located in the French health care system who initiated treatment during acute infection, which is typically defined as the period between initial exposure and the development of antibodies against the virus, usually a

matter of weeks. After a number of years on treatment, some of these individuals treated during acute infection decided to try going without ARVs, and thus far about 11 of them have been able to remain off treatment for several years with only very low levels of detectable virus. In essence, they look just like people on effective ARV therapy except that they are no longer taking any of the drugs.

Are they cured? No, not in the traditional sense, nor do we know how long they will continue to control the virus on their own. Even elite controllers, people who nature blessed with the right genes to keep HIV under control naturally, sometimes do see virus creep back and CD4 cells fall. Nevertheless, French researchers estimate that perhaps as many as 10 percent of people who start treatment this early may later be able to go without it for long periods of time. This is a small step down the road toward a cure, at least a “functional” cure, but still important.

We also learned of progress in cure research in HIV-infected children. Unfortunately, I can’t report in more detail than that, but I encourage you to look in the coming months for an exciting announcement to come from pediatric HIV researchers.

Things are also looking promising for people with HIV who are also diagnosed with chemotherapy-resistant cancer. Though stem-cell replacement carries serious health risks, and though many people with HIV and malignancy eventually relapse and succumb to the cancer, there is tantalizing data suggesting that a variety of stem cell strategies could indeed result in a cure in these people in the not too distant future.

Hurdles

Thankfully we have now progressed from asking whether a cure will ever be found to just how long it will be until a cure might be realized in such a way that it will be available to a large number of people with HIV.

Unanswered questions and controversies remain. Among the most important is how to determine where the virus is and whether a given therapy causes latent forms of HIV to awaken or to be eliminated. One of the key challenges is the fact that in many people on ARV therapy, latent virus is present in only one in every million cells. This not only requires that people give up lots of blood to find the virus, but that extremely sensitive tests be used to detect it.

Right now the gold standard is incredibly expensive and laborious. First researchers find infected cells and then they prompt those cells to reproduce HIV. Only those cells that produce versions of the virus that is capable of reproducing and infecting other cells are counted as being productively infected. Unfortunately, very few labs are capable of running such a test and if we are to test cure strategies more widely they will require a test that is much less expensive and much easier to run with a lot less blood or tissue being taken. Researchers are working on this, but it will likely be at least two or three years before we are able to begin to validate these easier tests. In the meantime, we will do our best to determine which kinds of therapies are able to wake up silent sleeping HIV--something we need to do in order to exterminate the virus and the cells that carry it.

Another important controversy is where HIV lives in the bodies of HIV-positive people. Some think it is really only necessary to get therapies into CD4 cells of the lymph nodes and lymph-like tissue in order to eradicate HIV. Others believe that other cells types such as macrophages in lymph tissue and in the brain will need to be reached as well. As with cell-based tests, it's going to take a bit of time to figure this out.

Lastly, in order for "shock and kill" strategies to work--whereby treatments are used to flush out sleeping HIV and kill it--we will have to ensure that current ARV therapy is good enough to stop all virus from reproducing. Unfortunately, recent studies have indicated that current therapy, while amazingly effective, doesn't reach all cells equally. In fact, some of the most potent drugs may not make it into the lymph nodes (where most HIV lives) at all. Whether this is true or important will take further research, much of which is underway.

What's the bottom line?

In all, cure research is probably going to proceed much as most other research, including early ARV research and cancer chemotherapy. At first, we will probably be able to cure a small number of people for reasons we don't entirely understand. Those early experiments will be a vital step along the path to a wider cure strategy, but won't take us all the way. There's much still to learn, but it I believe it is incredibly encouraging that we have moved so quickly from disbelieving in a cure and having no dedicated money for it, to a wide scope of researchers determined to further cure research with millions of dollars dedicated to the effort.

Are we doing enough quickly enough? That is an arguable point and one that activists, including myself and others at Project Inform and elsewhere will have to content with. In the meantime, I can genuinely say that progress is being made and that the day when cure patient #2 or #3 is announced is likely going to be announced within years and not decades.

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