

Transcript Details

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Examining HIV "Elite Controller" Patients

CONTROL OF VIREMIA IN HIV-INFECTED PATIENTS.

Chronic viral infections can manifest in 2 different ways: One group such as EBV are immunologically contained after the acute infection. The other group such as HIV can lead to persistent viremia and progressive clinical disease. There are patients who are able to escape the latter without antiviral medications.

Welcome to The Clinicians Roundtable. I am Dr. Leslie Lundt, your host, and with me today is the director of the Center for AIDS Research at Harvard University, Dr. Bruce Walker. Dr. Walker is also a Professor of Medicine at Harvard Medical School, Director of the Partners AIDS Research Center at Massachusetts General and Howard Hughes Medical Institute investigator. He splits his time between the lab where his research focusses on cellular immune responses to HIV and treating the patients with HIV.

DR. LESLIE LUNDT:

Welcome to ReachMD, Dr. Walker.

DR. BRUCE WALKER

Thank you, glad to be here.

DR. LESLIE LUNDT:

I appreciate you fitting us in, in the midst of all of your responsibilities. Dr. Walker more than 60 million people worldwide has been infected with HIV. Until a vaccine becomes a reality, you have been looking at ways to decrease the viral load to reduce the risk of transmission. What have you found so far?

DR. BRUCE WALKER

Well, what we have found is an extraordinary group of people that I think provide the evidence that actually we may be able to ultimately get the upper hand against this disease. What we have been studying are rare group of individuals who become HIV infected and actually never get sick. So, you might ask what's the longest anybody has been infected with HIV without taking medications and the answer to that question is now 30 years and counting.

DR. LESLIE LUNDT:

30 years?

DR. BRUCE WALKER

A lot of people that were infected in 1978 who are still alive and well have no CD4 decline and have never taken anti-HIV medications, look for all intention purposes entirely well and yet they are clearly infected.

DR. LESLIE LUNDT:

How many of these people are there?

DR. BRUCE WALKER

The frequency is higher than one might think. We estimated to be about 1 in 300, and right now, we are trying to identify and recruit as many of these patients as we possibly can all around the world to try and understand exactly how they achieve this extraordinary equilibrium with the virus.

DR. LESLIE LUNDT:

Now you mentioned that this has been a global effort. Tell us a bit about how you do that?

DR. BRUCE WALKER

Well, actually the reason that I am delighted to be on your radio show today is because I believe it's probably reaching exactly the audience that we need to reach. Most of the patients that we are looking for are actually not sick and if they are being followed by physicians they are often not followed in specialty practices, but are followed by general practitioner since they haven't been sick and has had no HIV-related complications, they are often just in regular medical care and the way that we have been able to recruit the 500 or so patients that we have thus far has been largely by directly contacting physicians. Some of these have been physicians that have large HIV practices. So if you had 300 patients in your practice, the likelihood is that one of those would be one of these so called elite controllers, a person who is infected, clearly has antibodies, has an undetectable viral load by RNA PCR, the standard assays that are done commercially, and is entirely well.

DR. LESLIE LUNDT:

Might there be many more of these people that do not even know have HIV?

DR. BRUCE WALKER

Well, I think that's probably the case. So, we figure in the United States probably around 900,000 HIV infected individuals. The best estimates are that two thirds of those individuals know that they are HIV infected. So that would be about 600,000 people would know their infection status. Given the way medicine is practiced in the US, most of those individuals would have had a viral load test done. So, if it's 1 in 300 patients, we expect that there are probably 2000 patients anyway in the United States that should know their status and might be recruitable, but there would be 3000 patients out there, 1000 of them not even knowing that they are HIV infected.

DR. LESLIE LUNDT:

Are there epidemiological factors that you have been able to associate so far with HIV control?

DR. BRUCE WALKER

Well, that's a really interesting question and the answer to that is no. There is not anything epidemiologically that we have been able to link to this. It really appears to be something that is not influenced by other infections or diseases that people may have when they get exposed to HIV, but rather it appears to be something that the immune system is doing to keep the virus in check much the way that one would normally keep EBV in check or other chronic viral infections in check. I think that's what makes this group so extraordinarily important for people to study. In a sense if everybody who became HIV infected were able to do what these elite controllers do, we would see the epidemic retreat and the reason for that is that at the very low viral loads that these individuals have, the likelihood that they will transmit to somebody else, although still possible, is much, much reduced and the likelihood at the levels of viremia that they experience that they themselves will progress is also very much reduced. So if you have somebody who gets infected and themselves does not get sick and is unlikely to transmit it to somebody else by doing the simple math that the epidemic is going to get smaller and so what we and a lot of other people are trying to do is to understand exactly how this happens. I must say when one sits down as I do in my office to talk to one of these patients, one gets the sense that the answer is right there in these people and we just have to fish it out.

If you are just joining us, you are listening to The Clinicians Roundtable on ReachMD, The Channel for Medical Professionals. I am Dr. Leslie Lundt, your host, and with me today is AIDS Researcher, Dr. Bruce Walker. We are discussing the control of viremia in HIV-infected patients.

DR. LESLIE LUNDT:

So we are on the cusp of what's potentially really exciting and global sort of discovery.

DR. BRUCE WALKER

Well, you know, I think the challenge to us as clinician scientist is to figure out exactly what's going on in these individuals and the hope is that we will find out something that leads us in the direction of an intervention that can recreate this kind of extraordinary equilibrium in other people that wouldn't normally have it. Now that's an optimistic view of this that in fact one can convert somebody who is not an elite controller into an elite controller, but I think there is got to be room for optimism as we are facing this global epidemic. I returned this morning from South Africa and I have to say that on the front line, things are getting no better, but really getting worst in terms of the numbers of people infected. There are treatments available now in the places that are hardest hit by the epidemic, but a solution to this global epidemic is going to require a vaccine that might be in the form of a prophylactic vaccine to prevent infection or what's called a therapeutic vaccine in a way to modulate the immune system to get people to lower viral load the same way that these elite controllers do.

DR. LESLIE LUNDT:

What are the potential antiviral mechanisms that play in these elite controllers?

DR. BRUCE WALKER

Well, that's also a really interesting question. So, the question is could it be just that these people are infected with the wimpy virus or could it be that their immune systems are somehow really jazzed up in doing a really effective job. Our data thus far indicate that these people are getting infected with normally virulent viruses, but that once those viruses get into their body, their immune systems particularly their cellular immune systems, CD4 and CD8 T cells that are directed against HIV infected cells are the mediators of control in this instance, but it is interesting that part of that control probably relates to mutations that are arising in the viruses once they get into somebody. Those mutations are being induced by the immune responses that are generated against the virus. This is a quite wily virus and it can mutate quite readily to try and escape from immune responses and we think what is partly happening is that the immune system is forcing the virus to make mutations that it does not want to make that impairs its fitness and that may be part of what's doing this. So, it is a combination both of immune response that helps to curtail the infection plus the induction of mutations that happens in the viruses that's trying to escape from detection by the immune system in an infected individual, and if those mutations turn the virus into something that is less able to replicate itself than that actually has an impact on the rapidity with which it can infect cells and cause

disease.

DR. LESLIE LUNDT:

This may be a naive question, but remember I am a psychiatrist. Okay, what is the difference between what we would call a long-term non-progressor that has HIV and these elite controllers or is there a difference?

DR. BRUCE WALKER

That's a really important question. Initially, when we started looking at people that had been infected for a long time and did not seem to be getting sick, the term long-term non-progressor was coined and the parameters that were used to define those individuals were mainly CD4 count and duration of infection. So by some criteria, it would be 8 years infected with a CD4 count of greater than 500. Other people define those long-term non-progressors as 10 years infected with a CD4 count of greater than 600. So, quite a number of different definitions used. We and others have coined the term elite controller based on viral load basically the level of viremia, and for an elite controller, we defined that if somebody that has had documented infection for at least a year and has a viral load of 50 copies or less on at least 3 determinations. We are really desperate to find additional people to enroll in these studies that we are doing right now and so any physicians that are out there or any patients that may be hearing this radio report, we would really encourage to get in touch with us and again these are people that are not on therapy, but have viral loads of less than 50 copies and I can give you details about how to reach us.

DR. LESLIE LUNDT:

Yeah, please.

DR. BRUCE WALKER

Or people can look at our website that we have created www.hivcontrollers.org.

DR. LESLIE LUNDT:

www.hivcontrollers.org. Great. Or again people can also look at our website reachmd.com and find information there as well. Well, thank you so much for taking time to speak with us today.

DR. BRUCE WALKER

Thank you very much. I appreciate it.

DR. LESLIE LUNDT:

We have been talking with Dr. Bruce Walker about these elite controllers, people that without medication being able to control their HIV infections for decades. I am Dr. Leslie Lundt. You are listening to ReachMD, The Channel for Medical Professionals. For a complete program guide and downloadable pod cast, visit our website at www.reachmd.com.