The Doctor Is In

Anthony Fauci, MD, has been the director of the National Institute of Allergy and Infectious Diseases at the National Institutes of Health since 1984. Here he speaks with POZ editor-in-chief Regan Hofmann about finding a cure for AIDS.

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As the director of the National Institute of Allergy and Infectious Diseases (NIAID), Anthony Fauci, MD, oversees one of the biggest, and richest AIDS research portfolios in the world (NIAID's total 2010 budget is $4.98 billion). Under his watchful eye, basic and applied science is developed in order to prevent, diagnose and treat infectious diseases (like HIV/AIDS). A key advisor to the White House and Department of Health and Human Services, Fauci was one of the original architects for the President's Emergency Plan for AIDS Relief, and he has been instrumental in developing highly effective strategies for the therapy of people living with HIV, as well as being a champion of the search for an AIDS vaccine. Medically, his own work in labs has led to a greater understanding of how HIV destroys the immune system. The list of his awards (including the Presidential Medal of Freedom) and affiliations is too extensive for this small space. He's an author, a father, a runner and the guy who has long personified the intersection of Big Government, science and AIDS.

Years ago, when the HIV community demonstrated outside the National Institutes of Health (NIH), lobbying for early access to experimental treatment, Fauci suggested to security that several community members be brought into his office so he could understand their needs. While we may not always have liked what we've heard, Fauci's constant willingness to interact with the community is laudable.

One thing is for sure. When we need him, this doctor is always in.

Why is HIV such a difficult virus to control and cure?
It's unique among human viruses in that it has the capacity, because of its genetic makeup, to integrate itself into the genome of your cells without killing the cells. Unlike other [viral] infections, like influenza, that your immune system can suppress and finally get rid of, once HIV integrates itself into your cells it forms a reservoir that remains untouched by your immune system or the medications. HIV's ability to integrate itself into the genetic makeup of your cells is very unique—and very unfortunate.

Are we seeing a legitimate resurgence in interest, dedication and energy put toward finding

a cure?
Yes, I'm fairly certain—at least in my circles—that there is a new energy and a dedication to search for the cure. There are a couple of things that are converging right now. One is the excitement about the feasibility of the cure—the multiple ways you could approach it. The other is the necessity of having a cure given what we're facing with the number of new infections and the fact that we [currently] need to keep people on therapy for the rest of their lives.

Can you explain the difference between the types of cures and why some say there is a link between treatment and the cure?
[There are two types of cures:] an eradication cure and a functional cure. [A functional cure] is optimally for someone who has been on treatment and whose viral load has been brought to below detectable levels. It means a person can actually contain the viral replication without medication.

When you take the person off therapy, [the virus] stays below detectable levels so the chance of transmission [is reduced]. There are a lot of ways to do that. The drugs we have now to treat people can effectively suppress their virus to below detectable levels and have an amazing impact on their longevity. But when you stop therapy, [the virus] will rebound in the vast majority of people. If you are talking about an eradication cure [one that removes all HIV from the body] then you've really got to talk about the development of new modalities of therapy that we don't have in our [arsenal] right now.

The earlier you treat an individual, the smaller their viral (or latent) reservoir is. We have data that [show] if you start therapy very early in someone and get their viral load below detectable levels, the size of their reservoir is much smaller than if you take a comparable person and don't start therapy until years after [he or she contracted the] virus. You may still get their viral loads below detectable levels, but the size of their viral reservoir is considerably larger and is just sitting there ready to rebound.

Also, if you treat people earlier in the course of their infection, you will preserve some, if not a lot, of their HIV-specific immune function. A person who has a larger viral latent reservoir and a much-diminished immune capability [is not as promising a candidate for a functional cure]. And the chance of a "therapeutic vaccine" [a potential form of a functional cure] being successful in someone who started therapy very early is much greater than in someone who [started] treatment late. That's why the search for a cure goes hand in hand with aggressive testing, access to care and treating individuals early in the course of their disease. Preferably [we would treat people] within weeks [after they contracted the virus]. Most of the time this is not practical, but even if you can access the patient within three months, you can have a significant impact with therapy so the person has a very small reservoir after a few years of treatment. I would say start as soon as possible, but three months and perhaps six months [after infection] is still good.

Do you think people are afraid to talk about the cure? If so, why?
I think people are appropriately circumspect about talking about a cure. In 1996 and 1997 when protease inhibitors began to be used widely, there were mathematical formulas that said if you treat somebody over x number of years the virus should disappear. I think that was an interesting concept, but at the time many of us were skeptical because several things weren't taken into account. Namely that reservoirs might last longer than projected. And the idea that when you get the virus below a detectable level that doesn't necessarily mean there isn't some residual viral replication going on. Unless your immune system is capable of suppressing the virus from rebounding, you're not going to [control the virus] no matter how effective the drug is.

So there is an understandable reluctance to talk about a cure. That's the reason whenever I talk about the cure, I don't talk about it as something that's inevitable. I talk about it as a goal I believe is worth trying for. It is not going to be easy. But I believe it is feasible and it is one of our highest priorities.

Are there things we should be doing differently related to our approach to cure research?
There is always room for improvement. When you broach a problem like this, there are a lot of unknowns and you have to strike a delicate balance between the ideas of individual investigators as well as programs you push in order to get to a certain goal.

Individual research that people are doing may not necessarily flash up on the radar screen as research [that could prove useful in the development of an AIDS] cure, but it may be the fundamental basis of a discovery. That's the reason it's so difficult to tally all of the research [dollars] that are being spent on the AIDS cure.

How do you attract new scientists and young thinkers as well as researchers from other fields to get involved with HIV research?
One of the problems [with] trying to stimulate interest in a program, and trying to get people who are not in AIDS research involved, is that they tend to follow the money. We are in an unfortunate situation where we've had a flat budget for the past several years. You can try with a modest amount like we did with the Martin Delaney grant [which awards $8.5 million a year for five years to support the search for a functional cure], but you're not going to attract a lot of people from outside the field unless you start [seeing] things that look like they may be breakthroughs. Then people will jump in and say, "I'll show you what I can do with my own approach toward it."

To be honest, there really are not a lot of overwhelmingly creative and new great ideas out there. We are searching for them, but it is unclear if there's a linear relationship between how much money you pour into [a given field of research] and how good the [resulting] ideas are going to be.

So the Delaney grant is intended to motivate, flush out and inspire some new thinking.
Exactly. [In the request for proposals, we encouraged scientists] to do anything they want, [as long as they believed it would help show] how we're going to get a cure.

Where does the Berlin patient fall on that curve? (The Berlin patient is an HIV-positive man who, after receiving a bone marrow transplant with cells specifically designed to prevent HIV replication, seems to have cleared HIV from his body.)
I think the Berlin patient falls under the category of a proof of a concept. [He is living proof that something other than antiretroviral medications can control HIV.] But [replicating the procedure] could be very impractical for large numbers of people. You are not going to transplant stem cells into anybody but the very rare individual. The justification for the Berlin patient transplant is that he would have died [from leukemia] if he didn't get the transplant. You have a lot of people out there who are doing reasonably well on drugs and want to come off them, but it's just not feasible [for them to undergo this procedure] because the risk of killing them is so high.

The Berlin patient proved if a positive person had cells placed in his or her body that are not able to be infected with the virus, the virus is not going to infect those cells. But how do we safely transfer the CCR5 gene mutation to another person? We're wondering whether or not that will ever be done. With all due respect to the Berlin patient, it may turn out that the concept is never going to be translated into a practical therapy approach.

Is there anything being studied that excites you—anything you think is a little closer to having a practical application?
Everything is in the early stages, and I haven't seen everybody's work, but of what I have seen, no one has shown me anything that has made me say, "Wow."

If we had to put an emphasis on treatment, prevention or research—even temporarily—would it be fair to say that emphasis should be placed on AIDS research?
I think we have to be careful with that. The answer is theoretically yes, but you can say the same thing for vaccines, the same thing for microbicides. It's tough to say that we [need] to pull [funding away from one area] to fund something else.

The AIDS Policy Project in Philadelphia released a report claiming that only 3 percent of the NIH's overall budget is dedicated to AIDS cure research funding—is that true?
No. The NIH spent about $45–55 million [on AIDS cure research in 2009]. But that does not include a lot of the things that [contribute to] working toward the cure—like intensive testing, treating people early so you can keep their viral reservoir low. The total AIDS spending at NIAID was $1.63 billion in 2009; as I mentioned, the total NIAID AIDS cure spending was $45–55 million in 2009. We gave the Philadelphia group all the information they asked for. But the problem when you give out specific numbers is you don't capture all of the indirect things that feed into [the search for a cure].

What has it been like for you to work with the HIV community?
It's been an extraordinary experience working with the community. Right from the beginning it was very clear to me that there was a tremendous amount of frustration, anger, fear and pain that drove the [early] activists to be very confrontational, but I actually learned a lot from what they were saying. I [came from] a different perspective, which allowed me to sit down and talk to them and figure out how we could optimize their energy and their insight, in order to make things better—from the research agenda to the user-friendliness of the clinical trial process to the regulatory elements of what the FDA would allow or not allow. One of the things I learned early on was the line from The Godfather, "This is business, not personal." I was never put aback by the anger and the frustration—I just tried to empathize with how they felt, and I think that's the thing that got me through some of those very tense moments. The activists were—and are continuing to be—extremely helpful to us. My feeling is the activists should continue to keep their ears to the ground about the kinds of things that are [needed]. Sometimes you can't do anything about it, but I personally always keep an open ear to what people have to say.

The epidemic has evolved culturally, socially, scientifically, financially and politically. What three things would you like to see done?
We really need to emphasize the whole issue of aggressively testing and linking to care and treatment. The other thing is to pull out all the stops on prevention—be it microbicides, vaccines, testing or counseling. And finally, the thing that started our conversation: the cure. They're all linked—they're three separate things—but they're all linked.

You have an amazing legacy in the scientific world. Where do you go from here?
I'm going to stick it out until we have this thing really under control. We've got some major goals ahead of us that are challenging and daunting but exciting. One of which is a vaccine. Another goal is preventive modalities for women that work like microbicides. And the other goal is getting people who are on therapy to be able to stop their therapy. I have a lot more to do—that's what keeps me in the game.

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