



A Conversation with Dr. Glenn Treisman

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What do aging, HIV, and mental health have to do with one another? Quite a lot, according to Glenn Treisman, MD, director of the AIDS Psychiatry Service at Johns Hopkins Hospital and a professor at Johns Hopkins University School of Medicine.

Dr. Treisman recently answered BETA's questions about depression, cognitive impairment, and how people aging with HIV can protect their mental health and acuity.

BETA: To begin with, can you talk about your work at Johns Hopkins and what you specialize in?

Dr. Glenn Treisman: That's a complicated question! I have a PhD in pharmacology and I trained in psychiatry. I did a year of medicine, then I did geriatric psychiatry when I finished my residency....All of a sudden, the HIV clinic needed a psychiatrist because the last one quit. The one before that had quit, too, and so they sent me. That was in '88 or '89, and I've been there ever since.

I specialize in hepatitis C and HIV and psychiatric conditions that are associated with those two viruses. I also do chronic pain work and addictions work, but the core of my work is in HIV and hepatitis C. I've been doing HIV [work] for a long time; hepatitis C is more recent and less of a focus, but still a focus.

BETA: What do you focus on in your clinical work with HIV positive people?

Dr. Treisman: I focus on really four things: on depression; on people who are having difficult lives and need coaching; addictions; and people with difficult personalities or temperaments, and personality disorders and personality problems.

Those are the main things that make HIV treatment hard, and those are the same things that make people vulnerable to getting HIV. Those are the things I spend most of

my time on. I see a lot of people with cognitive impairment...I work with a lot of those patients, but there are way too many for any one of us to follow.

BETA: At San Francisco AIDS Foundation's satellite session, "HIV/AIDS and Aging: Emerging Issues in Research, Care, Treatment, and Prevention," at the 2010 International AIDS Conference, you mentioned that HIV and depression appear to perpetuate each other. That is, HIV causes inflammation in the brain, which in turn can lead to depression, which may then cause people to stop taking their meds, which then leads to more HIV in the body. Can you speak more about this idea?

Dr. Treisman: I'll start here: If you're depressed—if you have major depression of the disease kind—you are much more likely to have risk behaviors related to HIV. [It's likely] you are taking less care of yourself and you involve yourself in more risky sex. You are more likely to get addicted to drugs and alcohol. You are more likely to associate with partners who are dangerous or vulnerable. So, depression is a risk for getting infected.

For a summary of Dr. Treisman's satellite presentation—as well as perspectives on aging with HIV from other experts and advocates—see "Aging and HIV: Emerging Issues in Research, Treatment, and Care," in the Summer/Fall 2010 issue of *BETA*.

Once you get infected and HIV penetrates your brain, it causes inflammation, among other things, and all brain inflammation has been shown to be associated with the [clinical] sort of depression.

So, you look at people with almost any disorder with central nervous system inflammation—hepatitis C, multiple sclerosis [MS] (but interestingly, not Lou Gehrig’s Disease, [also known as amyotrophic lateral sclerosis, or ALS], which is a condition of the peripheral nervous system)—and there’s not a big increase in depression in those patients. But in MS, which is a central nervous system disease, there’s a huge increase in depression.

It’s not an issue of how sick you are, because ALS patients are often much sicker than MS patients. They say, “I’m depressed,” they say, “I’m sad.” But they don’t get the *disease* kind of depression.

There really are two kinds of depression: There’s the depression that’s an understandable psychological response to what’s going on in your life, and for the terms of our article, I’ll call that “demoralization.” And then there’s depression where the system that makes life fun and gives you reward isn’t working properly, and that’s what I’m talking about when I’m talking about depression or “major depression.” (I’ll use those terms interchangeably.) That is the condition that’s increased in people with MS and not increased in people with ALS.

People with HIV have very high rates of serious depression because they have a lot of CNS inflammation. So, you are more likely to get HIV if you’re depressed, the virus itself makes depression worse and causes depression, and then, as the activities of the virus cause depression, the depression causes people to be less willing to take medicine. Less taking care of themselves, less adherent to medical care, and more likely to take [recre-

ational] drugs. Therefore, it interferes with adherence, which makes the HIV worse, which makes the depression worse, which makes the HIV worse!

BETA: Do HIV drugs and drugs used to treat depression interact?

Dr. Treisman: They go really well together. There are two kinds of drug interactions. There are theoretical drug interactions where, based on metabolism, you would think two drugs might have an interaction, [and there are] demonstrated drug interactions.

There are relatively few demonstrated drug interactions. There are lots of theoretical ones, but in clinical practice you rarely have a problem. The reason for that is this: The drugs we use for depression that are SSRIs [selective serotonin reuptake inhibitors] and the SNRI serotonin-norepinephrine reuptake inhibitor drugs have a very large margin of safety. So, even if the HIV drugs push those way up—even if ritonavir [Norvir; a “booster” that raises blood levels of other drugs] interferes with the metabolism of those drugs and pushes those levels way up, it won’t really give you any trouble.

Drugs that have a narrow therapeutic index, like tricyclic antidepressants—we measure blood levels and other stuff... so we know if HIV medications are affecting those drugs. In clinical practice, we rarely have trouble.

What we do in clinical practice is, if we’re changing some of the HIV meds or putting them on an antidepressant when they’re on HIV meds, we monitor them carefully for clinical

signs of toxicity. If the drug is going up, we see it. The other thing you do is, if you’re changing some of the HIV medicine, you look for a recurrence of their depressive symptoms, because the drugs might interfere with each other.

BETA: You’ve been traveling around the world talking about HIV and aging. Since the Vienna forum, what has changed in this area of research?

Dr. Treisman: The hottest thing going on is the debate over what to do about cognitive impairment. That’s a very hot issue.

At the satellite in Vienna, I showed some very early data from Scott Letendre, MD, from the University of California, San Diego. What he showed is, if you increase CNS penetration [the ability of HIV medication to get into the CNS], you have lower CNS virology. You can show that if you lower CNS viral load, you have less cognitive impairment.

What they have not been able to show very well yet is, if you give drugs with better CNS penetration, do you get less cognitive impairment? Which is what you’d expect, but they have not been able to show that.

Now, there is one study that came out very recently that

does show an association between CPE [CNS penetration effectiveness] scores, which reflect CNS penetration, and cognitive impairment.

The other studies that have looked at it have not been able to see that association, so I don’t know what to make of the one study. But that study does show an association.

“There’s the depression that’s an understandable psychological response to what’s going on in your life, and then there’s depression where the system that makes life fun and gives you reward isn’t working properly.”

I know that Scott is trying to refine that work so that he can show it. What I showed at that symposium... is a recent piece of work by Scott showing that if you have better CNS penetration, you have less depression. And that goes along with CNS inflammation and (they predict) cognitive impairment down the road.

BETA: What are some early symptoms of neurocognitive change that people with HIV should be aware of?

Dr. Treisman: We used to know exactly what HIV dementia looked like when it came on, because it came on the same way in most people.

The problem we're having now is, the onset of HIV dementia is much more subtle and much more variable than it was ten years ago. What usually these people present with, though, is slowing of that part of the brain called the subcortical areas.

If you imagine a brain to be a telephone switchboard, the phones are the cortex of the brain—that's where information is stored and associations are made. That's where you go look for the information. The subcortical structure would be a switchboard. As

you get older, that switchboard slows down a little. It slows down partly because there's a lot more telephones, there's a lot more information. Each year, you store more information and, unfortunately, if you don't usually throw anything out, the brain starts to be cluttered up with all kinds of information! It's going to be a lot tougher to go through it all when you're older than when you're young.

So, at my age, I'll say, "You know the guy that played in that band—what was his name?" It took me a second to find that band, and to find the guy. It may take you five minutes, and as you get older it becomes more frustrating. Part of it is that your search function—your subcortical area—is slowed down, and part of it is that there's a lot of information in there to go through. You can't quite remember where you stored that bit.

That's a normal development in age. HIV accelerates that. HIV dementia makes that much worse. What people have is difficulty with storing information and retrieving it, difficulty with speed and processing, where you have to go back and forth.

One of the tests that I show at all conferences is a thing called the "Trail

B," which I think is a very subtle and selective test for HIV dementia. In the Trail A test, you connect the dots with numbers, 1-2-3-4-5, or letters, A-B-C-D-E-F-G [on the page]. You just draw the line from A to B to C. In the Trail B test, you go from 1 to A to 2 to B to 3 to C to 4 to D. You go back and forth [between numbers and letters]. And what your brain is doing is, it's going to the alphabet, getting a letter, then you go to another place for the number and get a number, then go back to the alphabet, and you have to remember what the last letter was in order to go to the next letter.

...That really slows down with people who have HIV dementia, and also with people with Parkinson's disease, and also people with Huntington's disease, and some people with multi-infarct dementia from high blood pressure and other brain ischemic-related changes where you're not getting enough oxygen.

It used to be we didn't care about the fact there was an overlap between Parkinson's disease and multi-infarct dementia, because we weren't seeing elderly patients [with HIV]. But now you have to be a little more wary, because we're getting to a group of patients who will have a little bit of multi-infarct change, and can have ischemic brain disease, and can have Parkinson's disease, and also have HIV. We are getting into an age group where we have to have more expert diagnosis than we used to.

...Another test we do for HIV dementia is called the grooved pegboard, which is a bunch of little pegs that you have to put into a pegboard. Those little pegs look pretty easy to put into the hole, but actually...it's hard to pick them out of the tray and get them oriented and turn them. So, if you do that with your left hand (if you're right-handed), it's more difficult than it looks. Patients with HIV dementia are very slowed down on that task,

FOR MORE INFORMATION ON AGING AND HIV

On October 13, 2010, San Francisco AIDS Foundation and several community partners held a public forum, titled "HIV & Aging: Now What?"

The forum brought together community members, advocates, health-care and service providers, and researchers for a dialog about the challenges of getting older with HIV and the latest research on HIV and aging.

This event was part of the foundation's HIVision forum series, which provides a safe venue for discussion of timely and potentially controversial topics in HIV prevention, treatment, and care.

To download the executive summary of the forum and learn more about past and upcoming HIVision events, visit www.sfaf.org/HIVision.

as well. Those two tasks are good for screening people.

But if you really want to figure out if you have HIV-induced dementia, then you're going to have to do a much more elaborate set of examinations.

We do things like digit-symbol substitution, and the Hoffmann Verbal Learning Task—they try to distinguish between cortical and subcortical function to try and see what's really

been damaged. This doesn't mean that HIV doesn't damage the cortex, by the way. It's just that it damages the subcortex much earlier.

HIV dementia is a devastating illness because it profoundly affects your ability to adhere to your medication....Having talked about all that, one of the burning questions is this—someone asked me this in Boston, and it's a very important question: When someone has HIV dementia, what do you do? You have a patient with HIV dementia. They also have a certain amount of cardiovascular risk, a certain amount of lipid risk, a certain tendency to be adherent or non-adherent, a certain need for a drug regimen that is easy to take. So there are all these elements that are being used to help you pick out your medicine. And, in fact, one of the things I try and emphasize in all my talks is, picking out HIV medicines isn't following a recipe. You have to know the patient and think about what the issues are for that patient.

For some patients, the only issue is how easy it is to take the drugs and how many side effects. For other patients, you have to think about things like cognitive impairment and central nervous system penetration, former

cardiac disease, their risk for dyslipidemia [abnormal levels of fats in the blood], their risk for changes in their body fat, their risk for neuropathy, and their risk for other things. It's complex.

If you're really being a doctor about it and not just following the guidebook, it's a complex issue to think about what medicines you're going to give somebody. And it's not as simple as, "This table shows which drugs to use."

"Picking out HIV medicines isn't following a recipe. You have to know the patient and think about what the issues are for that patient."

BETA: What can HIV positive people do to safeguard their cognitive function and protect their mental health as they age?

Dr. Treisman: My philosophy is, there's an interaction between all the other things that are healthy and "HIV remission." I tell people, you want to check your lipids and see where they are. You want to exercise and be physically fit. You want to make sure you don't have diabetes. You want to try to control your blood pressure and make sure you don't develop hypertension. Those are all things people can do.

There are things people argue about, such as whether you should be taking something like selenium and other "nutraceuticals" [nutrition-based interventions, like vitamin and mineral supplements]. There isn't any evidence-based data, but there are a lot of people who think that nutraceuticals are useful in helping dementia.

Mostly it's a matter of healthy lifestyle and not letting your brain get trashed. So if you drink less and don't fall on your head—I would give up sky diving and bungee jumping—there's a lot of things people can do to decrease their risk. There's clearly an association between head trauma,

for instance, and later development of cognitive impairment and other conditions. It hasn't been looked at as well for HIV dementia, but there is some evidence there for that. So we posit that keeping from being hit in the head is a good idea.

Then there's the question of whether or not we should be giving people CNS-penetrating regimens or not. I'm not prepared to say we should, but am prepared to say if somebody rolls in with early HIV-pattern cognitive impairment, you should try different regimens and you should think about other things that might reduce CNS inflammation.

BETA: How can people with HIV approach their health providers if they've begun experiencing symptoms of depression or cognitive decline? Can providers help facilitate those difficult conversations?

Dr. Treisman: You know, this is an odd question for me—most of the patients who come to talk to me are pretty forthcoming about what they're struggling with. If you're comfortable with it, the patient will be comfortable with it.

What I tell health-care providers is, ask the questions that you might want to be asked, and ask in a matter-of-fact way. Asking people about mental health is like this: "When you do stuff that should be fun, is it as fun as it usually would be? So tell me something you like to do. What do you like to do? You like to eat shrimp. You like to go bowling. Tell me something that is really fun for you. Fishing? So, how often do you go fishing now? And is it as fun as it should be?" Then you're not asking a question about mental health, you are asking a question about the *person*.

People don't want to do these checklists: "Are you sad? Do you cry? Do you do this? Do you do that?"

That's not as effective as examining the patient in the more traditional way. These are things that we examine in every patient—you listen to their heart and you ask them if they're having memory difficulties. And while you're examining them, you look to see how their memory is actually functioning during the exam.

So, you might ask them a question, and then ask them a different question related to it ten minutes later to see if they remember. You might let the patient go someplace and see if they repeat something that they already told you. You might ask patients if they remember your name. Do they remember the waiting room, who came with them that day, and all those kinds of things....These are the questions you need to ask everybody.

BETA: How do you feel about clinical trials for people who are experiencing HIV-related mental health problems or cognitive decline?

Dr. Treisman: I think they are a good idea, but they're not a very popular thing to approach for funding! It's hard to get funded to do clinical trials with vulnerable populations of patients.

Part of that is...that it is very hard to design a clinical trial with a group of older people and know what

it means, so the data we're seeing—[from people] who are my populations of patients, really—is the data that comes from “cohort” studies. There are very good cohort studies that look at typical populations of patients and can draw nice and useful conclusions about them.

People have this contempt for anything that isn't a randomized, double-blind, placebo-controlled trial. But the data are there, and sometimes the data from the cohort trials are more important.

BETA: Visits to a general provider's office are typically quick. How can HIV positive people best use that time to talk with their clinician about depression or symptoms of dementia?

Dr. Treisman: I think that doctors have to commit more time with their patients, and patients have to demand more time with their doctors. You have to say, “Listen, doctor, I have to talk to you about a couple of things today. Here is the list of things.”

Go in prepared about what you want to make sure you cover. If you're having stomach cramps at night keeping you awake, make sure you get to that. The doctor doesn't know you have that problem, and you want to make sure you get to it. If there are a couple of things, like you're having

stomach cramps at night, you can't find your teeth half the time, and you think the left side of your mouth is numb, you've got to get to all three of those things.

...If patients help doctors see how important this stuff is for them—they say, “Well, I need to know more about dementia”—it will help their providers be more interested in what's going on in dementia. Those of us doing a lot of work in a particular area try to keep people up to date. I run around trying to make sure everybody gets a chance to ask me their questions and discuss their issues.

There's a fairly famous quote from George Bernard Shaw, something like, “If I give you an apple and you give me an apple, we each have one apple. If I give you an idea and you give me an idea, we each have two ideas.”...Talking to people makes things grow. I try to do that.

I do think there's a much higher risk with CNS issues in an aging population. That risk goes up as you get older...I think that people are more aware of cognitive issues, more aware of affective disorders and the difficulties these people have, and more aware of central nervous system sequelae of HIV than they were before.

Jennifer Heflin is a writer, photographer, and activist living in San Francisco.

FOR MORE INFORMATION

You can read more about aging with HIV or managing cognitive and mental health issues in past editions of *BETA*:

- “Aging & HIV: A Conversation with Dr. Malcolm John” (Summer/Fall 2009)
- “HIV and the Brain” (Summer/Fall 2009)
- “Trauma: Frozen Moments, Frozen Lives” (Summer/Fall 2008)

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